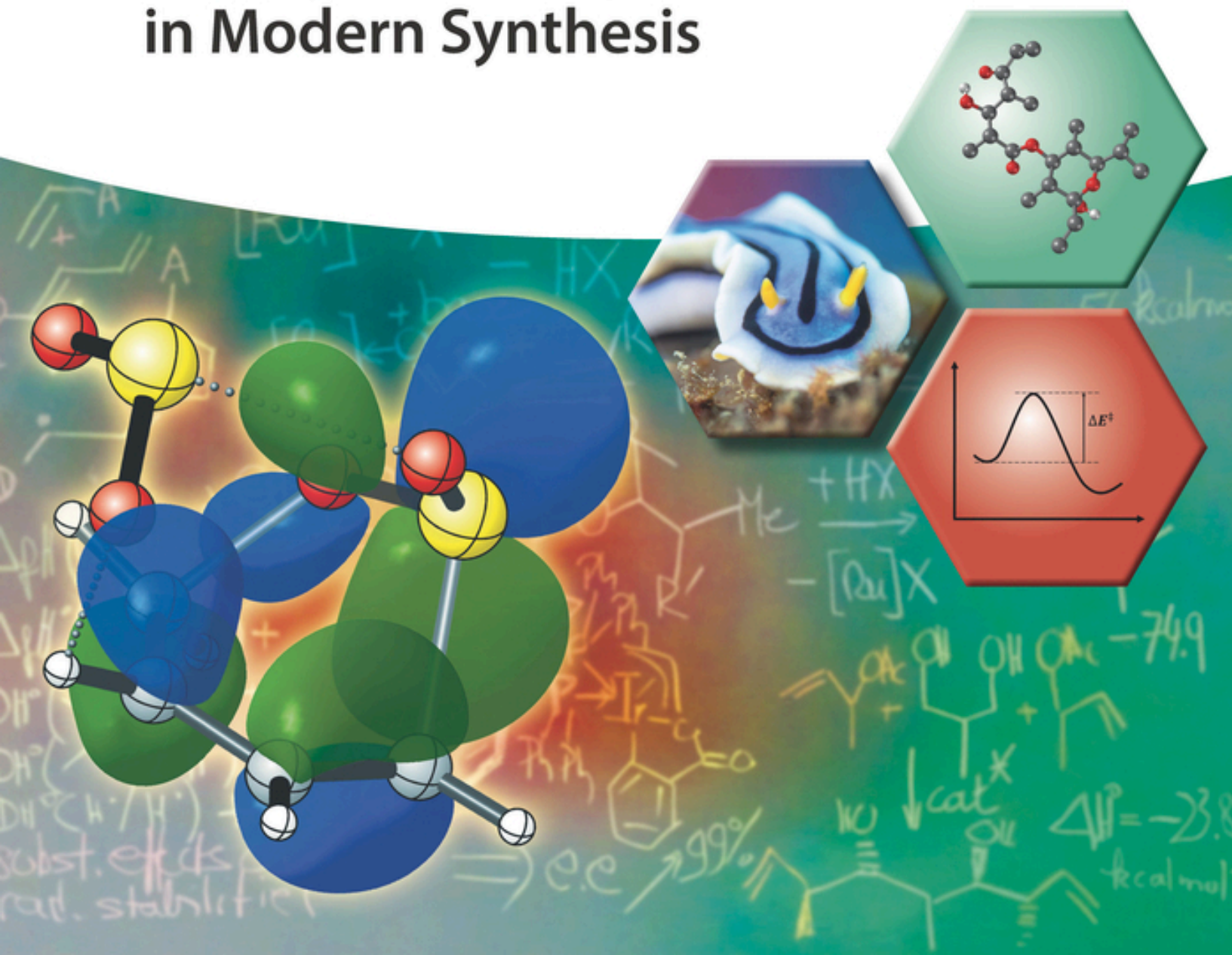


Pierre Vogel and Kendall N. Houk

Workbook Organic Chemistry

Theory, Reactivity and Mechanisms in Modern Synthesis



Organic Chemistry

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Workbook

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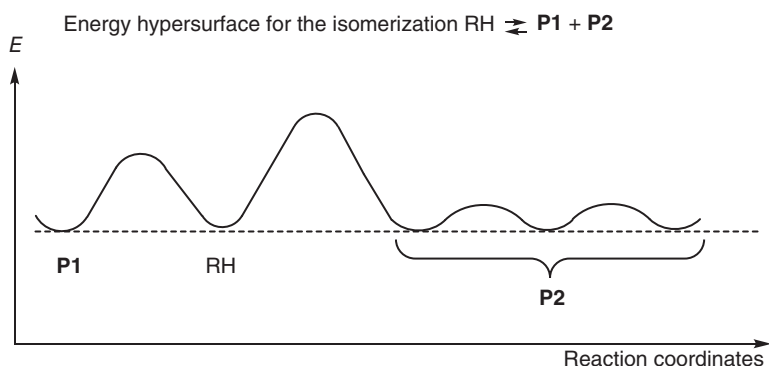
Equilibria and Thermochemistry

Answers to Problems

Problem 1.1 A hydrocarbon, RH, can be isomerized in reversible reactions into two isomeric compounds **P1** and **P2** with the same heat of reaction. Both have C_1 symmetry. **P1** is a rigid molecule, and **P2** is a flexible one adopting several conformations of similar stability. Which product will be preferred at equilibrium?

Answer

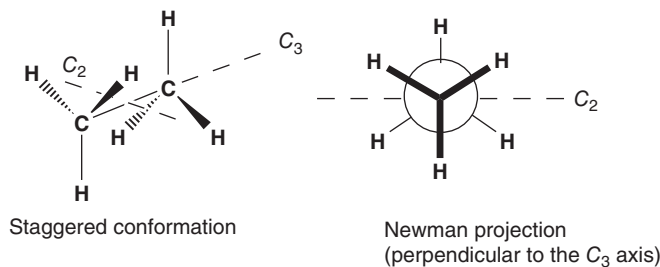
Products **P1** and **P2** equilibrate with RH in reversible reactions at temperature T . The preferred product will be that for which the free energy of reaction $\Delta_r G^T(\text{reactants} \rightleftharpoons \text{product } \mathbf{P1} \text{ or } \mathbf{P2}) = \Delta_r H^T - T\Delta_r S^T$ is the smallest. If $\Delta_r H^T(\text{RH} \rightleftharpoons \mathbf{P1}) = \Delta_r H^T(\text{RH} \rightleftharpoons \mathbf{P2})$, the product with the largest entropy ($S^T(\mathbf{P1})$, $S^T(\mathbf{P2})$), will be favored at equilibrium at temperature T . Entropy expresses the degree of freedom available to an ensemble of molecules of a given compound. It depends upon the number of different microscopic states available to these molecules, and this depends on the size of the molecules themselves (**P1** and **P2** have the same molecular weight as they are isomers of the starting material RH), and the energy separation between the microscopic states available to them. The microscopic states that contribute most to the entropy are translational and rotational states for which the energy separation between quantum levels are the smallest. A rigid molecule is a molecule that does not equilibrate with several conformers of similar stabilities. It has only one energy minimum along all the coordinates that describe its geometrical deformations, including torsion about its σ - and π -bonds and bond elongation. A flexible molecule evolves at temperature T among several energy minima. In other words, several energy minima are populated significantly at the given temperature T . This is the case for **P2**, not for **P1**. If those energy minima correspond to different geometries (no rotation symmetry axis, $\sigma = 1$) the flexible molecule has a larger entropy than the rigid molecule; thus $S^T(\mathbf{P2}) > S^T(\mathbf{P1})$, and $\Delta_r G^T(\text{RH} \rightleftharpoons \mathbf{P2}) < \Delta_r G^T(\text{RH} \rightleftharpoons \mathbf{P1})$. Product **P2** that is composed of flexible molecules will be formed to a larger extent than product **P1** composed of rigid molecules at temperature T .



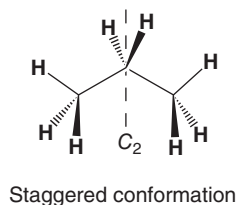
Problem 1.2 Define the symmetry numbers, σ , of ethane, propane, cyclopropane, cyclobutane, cyclohexanone, ferrocene, bicyclo[2.2.1]hepta-2,5-diene (norbornadiene), 1,4-difluorobenzene, *meso*-tartaric acid, and (*R,R*)-tartaric acid (see Figure 1.24 for the structure of the two latter compounds).

Answer

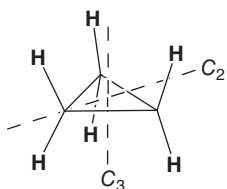
Ethane is a flexible molecule that adopts a preferred staggered conformation (c. 3 kcal mol^{-1} more stable than the eclipsed conformation (Section 2.5.1), transition state of the rotation about its $\sigma(\text{C}-\text{C})$ bond). Ethane has a C_3 - and three C_2 -axes that are interconverted by rotation about the C_3 -axis. Thus, the symmetry number $\sigma = 3 \times 2 = 6$.



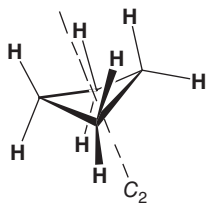
Propane is a flexible molecule for which the doubly staggered conformation is the most stable one (C_{2v} symmetry: one mirror plane of symmetry containing a C_2 -axis of rotation) has one C_2 -axis of rotation. Thus, the symmetry number $\sigma = 2$.



Cyclopropane is a rigid molecule (D_{3h} symmetry) with a C_3 - and three C_2 -axes of rotation. Rotation about the C_3 axis interconverts the C_2 -axis. Thus, the symmetry number $\sigma = 3 \times 2 = 6$.



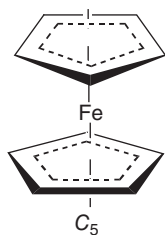
Cyclobutane adopts a puckered conformation (envelope, C_{2v} symmetry) with one C_2 -axis of rotation. Thus, its symmetry number $\sigma = 2$. The planar conformation (D_{4h} symmetry) is much less stable (Section 2.6.1).



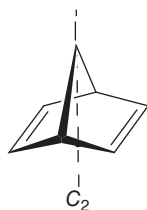
Cyclohexane adopts a chair conformation (Section 2.6.4) of C_s symmetry (one mirror plane of symmetry), no rotation axis. Thus, the symmetry number $\sigma = 1$.



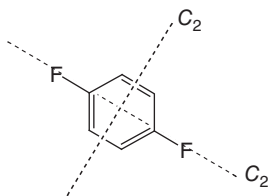
Ferrocene has a C_5 - and five C_2 -axes of rotation. The C_2 -axes are interconverted by rotation about the C_5 -axis. Thus, the symmetry number $\sigma = 5 \times 2 = 10$.



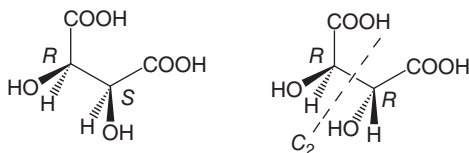
Bicyclo[2.2.1]hepta-2,5-diene (norbornadiene) is C_{2v} symmetrical (one mirror plane containing a C_2 -axis of rotation). Thus, the symmetry number $\sigma = 2$.



1,4-Difluorobenzene has two non-interconvertible C_2 -axis of rotation. Thus, the symmetry number $\sigma = 2 \times 2 = 4$.



Meso-tartaric acid is (*R,S*)-tartaric acid with a mirror plane of symmetry. It does not have any axis of rotation, and thus $\sigma = 1.0$. (*R,R*)-Tartaric acid has a C_2 -axis, and thus $\sigma = 2$.



Problem 1.3 Enantiomerically pure α -amino acids such as alanine (with one stereogenic center) are isomerized into their racemic mixtures. What is the Gibbs energy of this reaction at 25 °C?

Answer

Enantiomers are stereoisomers that have the same stability and the same properties except for their optical rotation (opposite $[\alpha]$ values at any wavelength) and chiroptical properties (opposite Cotton effect in their circular dichroism spectra). Enantiomers cannot have a mirror plane of symmetry. They might have C_1 -symmetry (no element of symmetry) like alanine, or have a rotation axis of symmetry like (*R,R*)-tartaric acid. The two enantiomers have the same enthalpy of formation and the same entropy. Thus,

$\Delta_r G^\ddagger((R)\text{-enantiomer}) \rightleftharpoons (S)\text{-enantiomer} = \Delta_r H^\ddagger((S)\text{-enantiomer}) - \Delta_r H^\ddagger((R)\text{-enantiomer}) - T\Delta_r S^\ddagger((S)\text{-enantiomer}) + T\Delta_r S^\ddagger((R)\text{-enantiomer}) = 0$. Thus, $RT \ln K = 0$. At equilibrium, $K = [(S)\text{-enantiomer}]/[(R)\text{-enantiomer}] = 1$.

Problem 1.4 What products do you expect to be formed combining HO· with organic compounds? What happens to NO in the air, to SO₂ in the air?

Answer

- Water is the most stable oxide of hydrogen. Hydrogen peroxide (H₂O₂) and the radicals hydroxyl (HO·) and hydroperoxyl (HOO·) are expected to be reactive compounds that tend to form water on combining them with organic and inorganic compounds containing hydrogen atoms.
- The most stable oxidized form of nitrogen is NO₂, and this is the brown gas of air pollution. Nitric oxide (NO) is an important diatomic molecule that regulates many biological functions, such as blood pressure and erection. It is produced from arginine by NO synthase in mammals. The drug Viagra inhibits an enzyme that normally reverses the action produced by NO. Within seconds of its formation in air, colorless NO undergoes oxidation to brown NO₂, and then to nitrite and nitrate (2NO₂ + H₂O ⇌ HNO₂ + HNO₃).
- Sulfur trioxide (SO₃) is the most stable oxidized form of sulfur. Burning sulfur does not produce SO₃ but SO₂, a major air pollutant. The oxidation of SO₂ by air into SO₃ requires special catalysts used in industrial sulfuric acid production. Sulfate from hydrolysis of SO₃ (SO₃ + H₂O ⇌ H₂SO₄) is involved in air pollution and acid rain, as sulfuric acid.

Problem 1.5 Propose a reaction for diimide (HN=NH) + cyclohexene and calculate its heat of reaction.

Answer

(*Z*)- and (*E*)-Diimide (HN=NH) are metastable combinations of nitrogen and hydrogen. They are sources of dihydrogen (Garbisch alkene hydrogenation, dyotropic transfer of dihydrogen, Section 5.6.2) liberating N₂.
 $\Delta_r H^\circ = \Delta_f H^\circ(\text{N}_2) + \Delta_f H^\circ(\text{cyclohexane}) - \Delta_f H^\circ(\text{(*Z*)-diimide}) - \Delta_f H^\circ(\text{cyclohexene}) = 0 - 29.5 - 50.9 + 1.03 = -79.4 \text{ kcal mol}^{-1}$.

Problem 1.6 Among the amino acids serine and cysteine, which of these gives stable adducts with cyclohex-2-enone at 37 °C when they are part of a protein?

Answer

Serine (HOCH₂CH(NH₂)COOH) incorporated in a protein has a primary alcohol function. Its addition to an alkene is not exothermic enough to lead to a stable adduct with cyclohexenone at 37 °C as indicated with the model equilibrium:

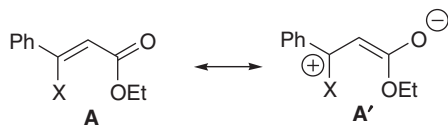
$\Delta_r H^\circ(\text{EtOH} + \text{CH}_2=\text{CH}_2 \rightleftharpoons \text{EtOEt}) = -51.7 - (-56.0) - 12.5 = -8.2 \text{ kcal mol}^{-1}$. The heat of reaction cannot compensate for the entropy of condensation $-T\Delta_r S^{310\text{K}} > 10 \text{ kcal mol}^{-1}$.

Cysteine is like serine but with a thiol function instead of a primary alcohol function for which a much higher heat of reaction is estimated for its addition to an alkene as shown with $\Delta_r H^\circ(\text{EtSH} + \text{CH}_2=\text{CH}_2 \rightleftharpoons \text{EtSEt}) = -19.9 - (-11.0) - 12.5 = -21.4 \text{ kcal mol}^{-1}$. Thus cysteine, not serine, incorporated in a protein will equilibrate with an adduct resulting from the conjugate addition of its thiol unit to cyclohex-2-enone.

Problem 1.7 Explain the difference in C=O bond stretching frequencies ($\nu_{\text{C=O}}$) between ethyl (*Z*)-3-fluorocinnamate (1736 cm⁻¹) and ethyl cinnamate ((*E*)-PhCH=CHCOOEt: 1715 cm⁻¹) [1].

Answer

The stretching frequency $\nu_{\text{C=O}}$ is proportional to the C=O bond strength. The latter depends on conjugation. Compared with saturated esters ($\nu_{\text{C=O}}$: 1750–1735 cm⁻¹), α,β -unsaturated esters have smaller $\nu_{\text{C=O}}$ (1730–1715 cm⁻¹) due to C=O bond elongation and weakening resulting from the π -conjugation.



On substituting a α,β -unsaturated ester by a β -fluoro group, one destabilizes the zwitterionic limiting structure A' because of the strong dipole realized by the C—F bond. Retrodonation $n(\text{F})/\pi^*(\text{C}=\text{C})$ is inexistent since

the amount of positive charge appearing at the β -center remains relatively weak (see electrostatic model of substituent effects on the stability of charged species). Thus the C=O bond in ethyl (*Z*)-3-fluorocinnamate (**A**, X = F, $\nu_{\text{C=O}}$: 1726 cm^{-1}) is stronger than the C=O bond in (*E*)-cinnamate (**A**, X = H, $\nu_{\text{C=O}}$: 1715 cm^{-1}) [1].

Problem 1.8 Estimate the standard heat of the esterification of ethanol with acetic acid. Estimate the variation of entropy of this reaction at 298.15 K and calculate the equilibrium constant at the same temperature and under one atmosphere, in tetrahydrofuran (THF) solution. Is the equilibrium constant the same under the same conditions for the esterification of anthracene-2-carboxylic acid with 2-hydroxyanthracene?

Answer

$$\Delta_r H^\circ(\text{EtOH} + \text{MeCOOH} \rightleftharpoons \text{MeCOOEt} + \text{H}_2\text{O}) = -106.5(\pm 0.2) - 57.8(\pm 0.01) - (-56.0)(\pm 0.5) - (-103.5)(\pm 0.6) = -4.8 \pm 1.3 \text{ kcal mol}^{-1} \text{ (Table 1.A.4).}$$

$$\Delta_r S^\circ(\text{EtOH} + \text{MeCOOH} \rightleftharpoons \text{MeCOOEt} + \text{H}_2\text{O}) = 86.7 + 45.1 - 67.6 - 66.7 = -2.5 \text{ eu. One thus obtains}$$

$$\Delta_r G^\circ(\text{EtOH} + \text{MeCOOH} \rightleftharpoons \text{MeCOOEt} + \text{H}_2\text{O}) = -4.8 - 298(0.0025) \approx -4.0 \text{ kcal mol}^{-1}, \text{ giving } K = \exp(-\Delta_r G^\circ/RT) = \exp.(4000/1.987 \times 298) = 858 \text{ at } 25^\circ\text{C for an ideal solution.}$$

If one considers only the entropy of translation and Eq. (1.31) for the calculation of the entropy of monoatomic molecules,

$$S_{\text{trans}} = 6.86 \log M_r(\text{g}) + 11.44 \log T - 2.31 \text{ eu}$$

$\Delta_r S_{\text{trans}}^\circ(\text{EtOH} + \text{MeCOOH} \rightleftharpoons \text{MeCOOEt} + \text{H}_2\text{O}) = 6.86 \log[M_r(\text{MeCOOEt}) \cdot M_r(\text{H}_2\text{O})/M_r(\text{EtOH}) \cdot M_r(\text{AcOH})] = 6.86 \log[88.1 \times 18/46.07 \times 60.05] = 6.86 \log(0.5732145) = -1.65 \text{ eu}$ is not nil because two molecules of similar size are equilibrated with a larger molecule and a smaller one (H_2O). Water molecule has a C_2 -axis of symmetry, its symmetry number $\sigma = 2$. The other molecules intervening in this equilibrium have $\sigma = 1$. The same molecular groups and freely rotating bonds are present in reactants and products. If one consider the loss of rotational entropy by forming H_2O , a correction of $-R \ln 2 = -1.987(0.693) = -1.37 \text{ eu}$ has to be considered. On this basis, the calculated $\Delta_r S_{\text{trans+rot}}^\circ(\text{EtOH} + \text{MeCOOH} \rightleftharpoons \text{MeCOOEt} + \text{H}_2\text{O}) = -1.65 - 1.37 \approx -3 \text{ eu}$, a value very close to the value of -2.5 eu estimated from the experimental entropies given for these compounds.

Experimental standard heats of formation and entropies of anthracene-2-yl anthracene-2-carboxylate ($M_r = 398.463$), of anthracene-2 carboxylic acid ($M_r = 222.245$), and of 2-hydroxyanthracene ($M_r = 194.234$) are not available. If one considers the model reaction $\text{PhCOOH} + \text{MeOH} \rightleftharpoons \text{PhCOOMe} + \text{H}_2\text{O}$ for which $\Delta_r H^\circ(\text{PhCOOH} + \text{MeOH} \rightleftharpoons \text{PhCOOMe} + \text{H}_2\text{O}) = -64.4 - 57.8 - (-70.3) - (-49) = -2.9 \text{ kcal mol}^{-1}$ is estimated (Table 1.A.4), one can predict that the exothermicity of the esterification of the anthracene derivatives should be less than of the formation of ethyl acetate because of steric effect. For the contribution of the entropy of translation to the equilibrium that converts anthracene-2 carboxylic acid and 2-hydroxyanthracene into the corresponding ester + water one estimates it to be more negative than in the case of the formation of ethyl acetate as given by

$$\Delta_r S_{\text{trans}}^\circ(2\text{-anthracenol} + 2\text{-anthracenecarboxylic acid} \rightleftharpoons \text{anthracen-2-yl anthracene-2-carboxylate} + \text{H}_2\text{O}) = 6.86 \log[M_r(\text{C}_{14}\text{H}_9\text{COOC}_{14}\text{H}_9) \cdot M_r(\text{H}_2\text{O})/M_r(\text{C}_{14}\text{H}_9\text{OH}) \cdot M_r(\text{C}_{14}\text{H}_9\text{COOH})] = 6.86 \log[398.5 \times 18.02/194.2 \times 222.2] = 6.86 \log(0.166414) = -5.34 \text{ eu. If one now considers the loss of rotational entropy due to the formation of water, one estimates}$$

$$\Delta_r S_{\text{trans+rot}}^\circ(2\text{-anthracenol} + 2\text{-anthracenecarboxylic acid} \rightleftharpoons \text{anthracen-2-yl anthracene-2-carboxylate} + \text{H}_2\text{O}) = -5.34 - 1.37 = -6.7 \text{ eu.}$$

The free enthalpy for this equilibrium at 25°C is estimated to be $\Delta_r G^\circ(2\text{-anthracenol} + 2\text{-anthracenecarboxylic acid} \rightleftharpoons \text{anthracen-2-yl anthracene-2-carboxylate} + \text{H}_2\text{O}) = -2.9 - 298(-0.0067) = -2.9 + 1.99 \approx -0.9 \text{ kcal mol}^{-1}$

From what precedes we can predict that $K(2\text{-anthracenol} + 2\text{-anthracenecarboxylic acid} \rightleftharpoons \text{anthracen-2-yl anthracene-2-carboxylate} + \text{H}_2\text{O}) < K(\text{EtOH} + \text{AcOH} \rightleftharpoons \text{AcOEt} + \text{H}_2\text{O})$.

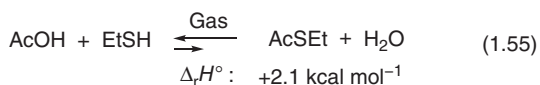
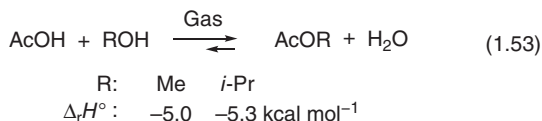
At 298 K and under one atmosphere for ideal solution in THF $K(2\text{-anthracenol} + 2\text{-anthracenecarboxylic acid} \rightleftharpoons \text{anthracen-2-yl anthracene-2-carboxylate} + \text{H}_2\text{O}) = \exp.(900/1.987 \times 298) = 4.6$.

Problem 1.9 The Newman–Kwart rearrangement is a valuable synthetic technique for converting phenols to thiophenols via their *O*- and *S*-thiocarbamates [2–4].

Explain why the *S*-thiocarbamates are more stable than their isomeric *O*-thionocarbamates.

Answer

In the equilibrium $\text{Ar}-\text{O}-(\text{C}=\text{S})-\text{X} \rightleftharpoons \text{Ar}-\text{S}-(\text{C}=\text{O})-\text{X}$, one exchanges a thioester moiety into a thioester function. Since carbon and sulfur have similar electronegativities (Table 1.A.5) the $\text{C}=\text{S}$ double bond is not as polar as the $\text{C}=\text{O}$ double bond. According to the Pauling theory, the $\text{C}=\text{S}$ bond is weaker than the $\text{C}=\text{O}$ bond. The $\text{C}=\text{S}$ bond is longer than the $\text{C}=\text{O}$ bond, which contributes also to make it weaker. For that reason $\text{Ar}-\text{S}-(\text{C}=\text{O})-\text{X}$ must be more stable than $\text{Ar}-\text{O}-(\text{C}=\text{S})-\text{X}$. Furthermore, part of the stability of an ester arises from the $n(\text{O})/\pi(\text{C}=\text{O})$ conjugation ($\text{ArO}-\text{C}=\text{O} \leftrightarrow \text{ArO}^{(+)}=\text{C}-\text{O}^{(-)}$) and $n(\text{C}=\text{O})/\sigma(\text{O})$ hyperconjugation ($\text{Ar}-\text{O}-\text{C}=\text{O} \leftrightarrow \text{Ar}-\text{O}^{(-)} + \text{C}^{(+)}=\text{O} \leftrightarrow \text{Ar}-\text{O}^{(-)} + \text{C}\equiv\text{O}^{(+)}$). In thioester the $n(\text{S})/\pi(\text{C}=\text{O})$ conjugation and $n(\text{C}=\text{O})/\sigma(\text{S})$ hyperconjugation intervene also but to a smaller extent than in ester as shown by the heat of the following reactions:



Problem 1.10 A mixture of 1 mmol cyclohex-2-enone, 1 mmol of thiophenol, and 5 mg of Et_3N is kept at 25 °C in 1 ml of CH_2Cl_2 . After 30 minutes at 25 °C, the ¹H-NMR spectra of the reaction mixture shows that the corresponding 1,4-adduct is formed almost completely. Attempted purification of the adduct by column chromatography on silica gel gives, however, only a low yield of adduct (10–20%) and recovered cyclohex-2-enone (80%) and thiophenol (80%). Why?

Answer

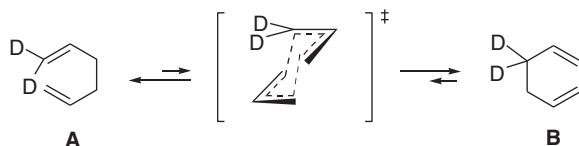
Thiol conjugate additions to conjugated enones are reversible in the presence of a base catalyst such as Et_3N at 25 °C. For a reaction using molar concentrations of thiophenol and cyclohex-2-enone the corresponding adduct (2-phenylthiocyclohexanone) forms to a large extent since the reaction has an exothermicity (c. -20 kcal mol⁻¹, see Problem 1.6) able to compensate for the cost of the entropy (c. 10 kcal mol⁻¹) of condensation at 25 °C. During the column chromatography on silica gel (SiO_2), the thiol, enone, 1,4-adduct, and catalyst interact with the solid support, more or less strongly. The most polar compound makes the strongest bonding with silicagel and thus is retained the longest on the column. The least polar compound is the least retained on the column and elutes the fastest. If the rate of elimination from the adduct giving thiophenol + cyclohex-2-enone is as fast as or faster than the rate of elution, the enone, thiol, and adduct will elute separately. Silica gel is acidic and catalyzes also the conjugate addition and elimination. The basic catalyst (Et_3N) remains on the column.

In order to avoid this type of problem due to the reversibility of the conjugate addition, one should extract the basic catalyst (Et_3N) from the final reaction mixture, for instance, by adding to it and at low temperature (<0 °C) a minimum amount of acidic alumina or silica gel to absorb it and then run a quick filtration at low temperature. Purification by chromatography should then be carried out on a cooled (circulating cooled [<-40 °C] ethanol in a double-walled column) column of silica gel. The extraction of Et_3N could also be done by extraction with a cooled (0 °C) diluted aqueous solution of HCl, and then washing with an aqueous solution of NaHCO_3 (to remove traces of HCl from the CH_2Cl_2 solution). HCl would catalyze the elimination from the adduct once the mixture is poured onto the chromatography column.

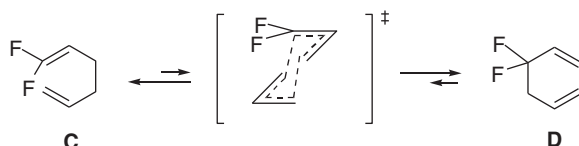
Problem 1.11 On heating 1,1-dideuteriohexa-1,5-diene equilibrates with 3,3-dideuteriohexa-1,5-diene (reversible Cope rearrangement: Section 5.5.9.1). Similarly 1,1-difluorohexa-1,5-diene equilibrates with 3,3-difluorohexa-1,5-diene. Which of these two last isomeric compounds is most stable? [5]

Answer

At equilibrium, there is a slight preference for D at the sp^3 center $K = [B]/[A] \approx 1.1$:

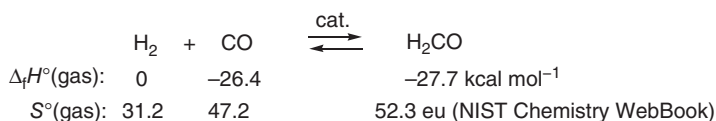


At equilibrium $K = [D]/[C] \gg 1/1$:

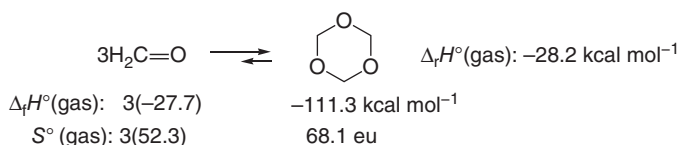


Compound **D** is more stable than **C** since geminal difluoro substitution prefers sp^3 -hybridized carbon centers rather than sp^2 -carbon centers.

Problem 1.12 Is the hydrogenation of carbon monoxide into formaldehyde a feasible reaction provided that a suitable catalyst is available to catalyze this reaction?

Answer

This reaction is endergonic ($\Delta_r G^\circ = \Delta_r H^\circ - T\Delta_r S^\circ$) since it has an exothermicity ($\Delta_r H^\circ$) of only $-1.3 \text{ kcal mol}^{-1}$, which is not enough to compensate for the cost of entropy of condensation ($-T\Delta_r S^\circ = -298(-26.1) = 6.5 \text{ kcal mol}^{-1}$) at room temperature ($T = 298 \text{ K}$). Nevertheless, formaldehyde (methanal) may form in small amounts at equilibrium and then be trimerized into 1,3,5-trioxane (metaformaldehyde), a reaction that brings an exothermicity of $-28.2 \text{ kcal mol}^{-1}$ at 25°C and under one atmosphere. This is not enough to pay for the entropy cost of the hydrogenation of carbon monoxide (three times $6.5 \text{ kcal mol}^{-1}$) and that of the trimerization of formaldehyde ($298(88.8) = 26.4 \text{ kcal mol}^{-1}$). If one considers the overall process $\Delta_r G^\circ(3\text{CO} + 3\text{H}_2 \rightleftharpoons 1,3,5\text{-trioxane}) = \Delta_r H^\circ(3\text{CO} + 3\text{H}_2 \rightleftharpoons 1,3,5\text{-trioxane}) - T\Delta_r S^\circ(3\text{CO} + 3\text{H}_2 \rightleftharpoons 1,3,5\text{-trioxane}) = -111.3 - 3(-26.4) - 298(52.3 - 3(31.2)) - 3(47.2) = -32.1 - 298(-157.6) = -32.1 + 46.9 = 14.8 \text{ kcal mol}^{-1}$, a highly endergonic process at 25°C and under one atmosphere. On lowering the temperature of the reaction, it becomes less endergonic. Increasing pressure will help shift the equilibrium in favor of 1,3,5-trioxane. In theory, and for an ideal solution, the equilibrium constant $K(3\text{CO} + 3\text{H}_2 \rightleftharpoons 1,3,5\text{-trioxane})$ approaches unity ($\Delta_r G^\circ = 0$) when $T\Delta_r S^\circ = \Delta_r H^\circ$. In this case, one estimates $T = -32\,100/(-157.6) = 203.7 \text{ K} \approx -94^\circ\text{C}$. As 1,3,5-trioxane is a solid, it could be eliminated from the reaction mixture by precipitation or crystallization (shifting of the equilibrium, Section 1.14.1). For such a process to be possible, one would have to find a suitable catalyst allowing one to run the condensation at low temperature and high pressure.

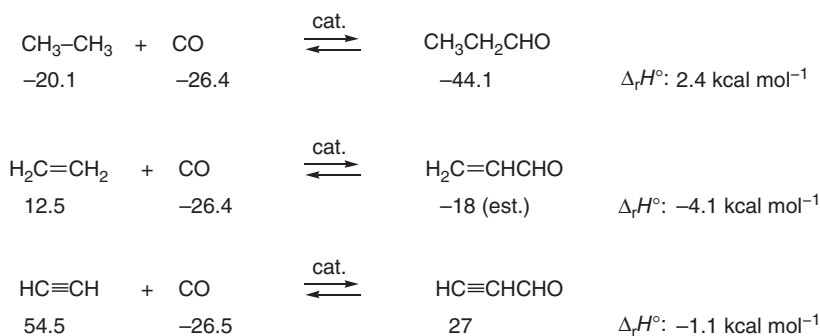


Formaldehyde is produced in the industry by catalyzed oxidation of methanol ($2\text{MeOH} + \text{O}_2 \rightleftharpoons 2\text{H}_2\text{CO} + 2\text{H}_2\text{O}$). In the "former process" the reaction occurs between 250 and 400°C and uses a solid catalyst made of iron oxide combined with molybdenum or/and vanadium oxides.

Hydrogenation of carbon monoxide is used to produce methanol in the industry. Under one atmosphere the overall reaction $\text{CO} + 2\text{H}_2 \rightleftharpoons \text{MeOH}$ has an exothermicity of $-22.6 \text{ kcal mol}^{-1}$. Several catalysts have been developed for this reaction, which is run under high pressure and temperatures above 200°C [6]. Under one atmosphere and at 200°C the entropy cost ($-T\Delta_r S^\circ(\text{CO} + 2\text{H}_2 \rightleftharpoons \text{MeOH}) = -473(54 - 47.2 - 2(31.2)) = 26.3 \text{ kcal mol}^{-1}$; it is not compensated by the exothermicity of the reaction. Nevertheless, pressure insures the formation of methanol. For instance, under 100 bars the reaction occurs between 275 and 325°C in the presence of Pt/Co/SiO₂ catalysts [7].

Problem 1.13 Are the hydrocarbations of carbon monoxide by alkanes, alkenes, or alkynes (or carbonylations of alkanes, alkenes, and alkynes) possible reactions provided suitable catalysts are available?

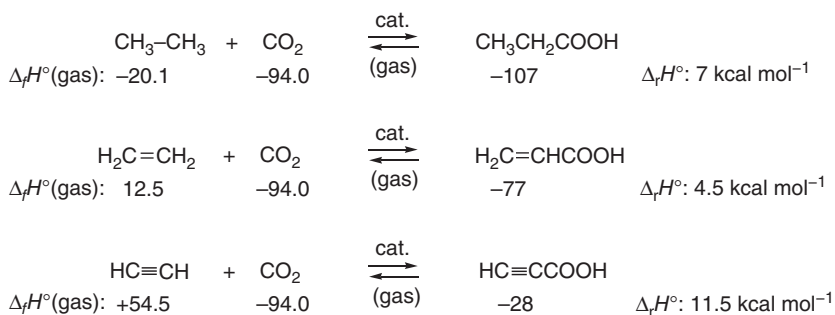
Answer



None of these reactions would be exergonic at room temperature (condensations with an entropy cost $-T\Delta_r S$ of $7\text{--}10 \text{ kcal mol}^{-1}$). However, in the case of the formation of unsaturated compounds their polymerizations are exothermic enough ($< -20 \text{ kcal mol}^{-1}$; see Problem 1.14) to pay for the entropy cost and thus displace the reaction in the sense of polycondensations.

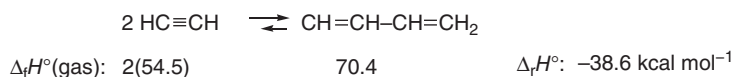
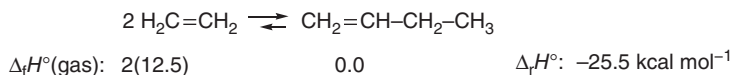
Problem 1.14 Are the hydrocarbations of carbon dioxide possible for alkanes, alkenes, and alkynes provided suitable catalysts are available to catalyze them?

Answer

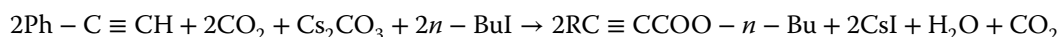


The three reactions are endothermic and they all have negative entropies, being condensations. Based on their heat of reaction they are more difficult than the corresponding carbonylation (Problem 1.13). They are impossible at room temperature and under 1 atm. Under low temperature and high pressure the second reaction (formation

of acrylic acid) might become feasible if a suitable catalyst is available. If the unsaturated carboxylic acids that form in the second and third reaction would undergo polymerization the polycondensation might occur since each new C—C bond generated is accompanied by a substantial exothermicity (better than 20 kcal mol^{-1}) that can compensate for the endothermicity of the hydrocarbations of CO_2 and the entropy cost ($-T\Delta_r S$) of the latter reactions and of the polymerization reactions.



One way to make the C—H carboxylation working is to quench the initial carboxylic product (RCOOH) in an exothermic reaction such as neutralization with a base to form the corresponding carboxylate salt (RCOOH + B: \rightleftharpoons RCOO⁻BH⁺). An example is given below with the CuI/Ph₃P-catalyzed carboxylation of phenylacetylene at 80 °C under one atmosphere (solvent: ethylene carbonate) and which converts the carboxylate salt into its *n*-butyl ester (overall yield: 99%). The base used is Cs₂CO₃ [8].

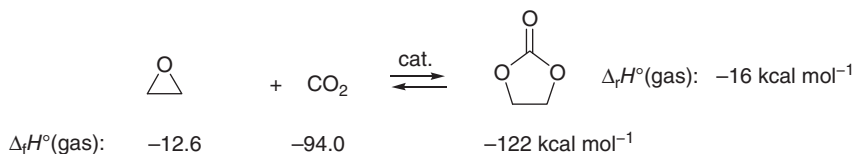
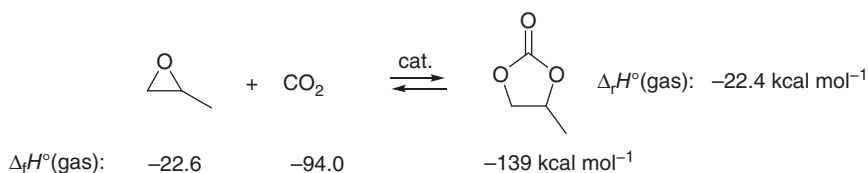


Another way to have the carboxylation of alkenes and acetylenes working is to couple them with the hydrogenation of the α,β -unsaturated carboxylic that forms initially [9].

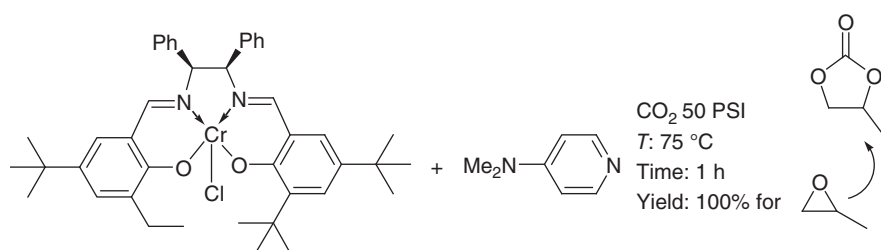
Problem 1.15 Can one fix CO_2 with epoxides? What products are expected (catalysts: mixed Mg/Al oxides, dimethylformamide [DMF] as solvent) to be formed at 100 °C?

Answer

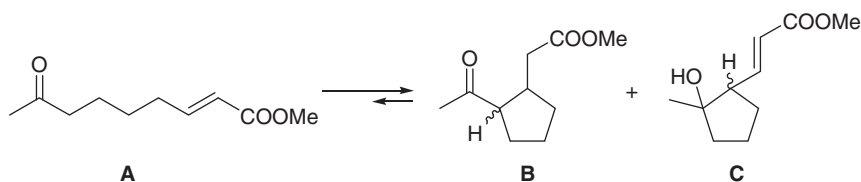
The thermochemical data shows that the condensations of CO_2 with methyl oxirane and oxirane can occur at 100 °C. Assuming an entropy of condensation of -40 eu , the entropy cost of these reactions at 100 °C amounts to $-T\Delta_r^\ddagger S = 373(-40 \text{ eu}) \approx 15 \text{ kcal mol}^{-1}$. Depending on the reaction conditions the vinylidene carbonates obtained can be polymerized into polycarbonates [10].



An example of catalyst for the carboxylation of methyloxirane is the Cr(III)salen complex represented below associated with 4-dimethylaminopyridine [11].

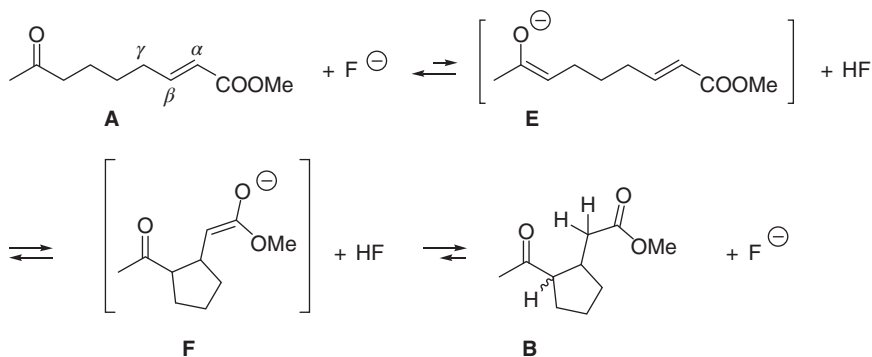


Problem 1.16 Which of the two products **B** and **C** is the favored product of cyclization of **A** catalyzed by $\text{Bu}_4\text{N}^+\text{F}^-$ (base catalyst) in DMF.

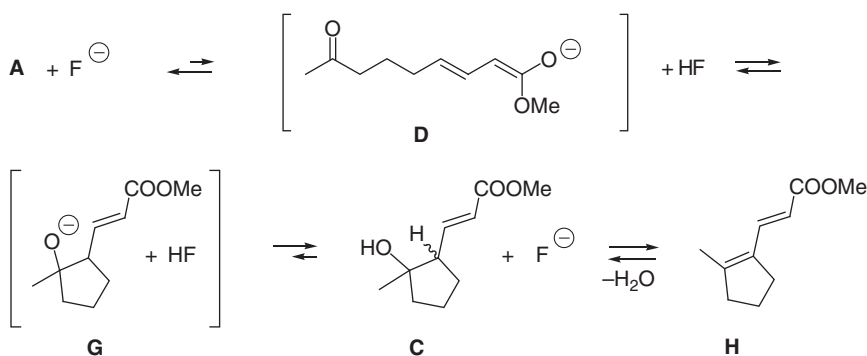


Answer

Under the action of the base (fluoride anion) ketone **A** equilibrates with two enolates (see Table 1.A.24 for pK_a values in dimethylsulfoxide [DMSO]). The ketone enolate **E** undergoes an intramolecular Michael addition onto the acrylic moiety of **E** generating the ester enolate **F**, which equilibrates with **B**, the main product of the reaction.



Alternatively, the acrylic ester **A** could also be deprotonated and be equilibrated with the dienolate intermediate **D**. An intramolecular 1,2-addition of **D** onto its methyl ketone moiety would generate alcoholate **G** that could equilibrate with the tertiary alcohol **C**. Since the hydrocarbation of a ketone is much less exothermic than the hydrocarbation of an alkene, this latter reaction might not be seen at room temperature. Product **C** could form under kinetic control (would form faster than **B**). On heating in the presence of the base it would equilibrate into the more stable product **B**. Both the intramolecular hydrocarbations are reversible reactions at high temperature because of their entropies of cyclization (Section 2.10) that make their exergonicity to diminish on raising temperature.



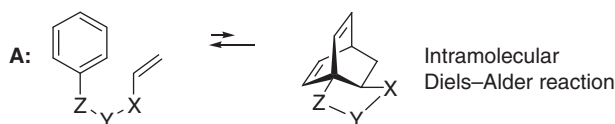
Problem 1.17 Are the Diels–Alder reactions ((4+2)-cycloadditions) of benzene with ethylene, acetylene, and allene thermodynamically possible at room temperature? Are the intramolecular versions possible? [12–15]

Answer

Using the standard heats of formation given in Tables 1.A.2 and 1.A.3 one can estimate the following standard heats of reaction:



$\Delta_r H^\circ(\text{benzene} + \text{ethylene} \rightleftharpoons \text{bicyclo[2.2.2]octa-2,5-diene}) = \Delta_f H^\circ(\text{bicyclo[2.2.2]octa-2,5-diene}) - \Delta_f H^\circ(\text{benzene}) - \Delta_f H^\circ(\text{ethylene}) = 34 - 19.8 - 12.5 = 1.7 \text{ kcal mol}^{-1}$. This condensation has a negative entropy of reaction similar to the Diels–Alder reaction of butadiene + ethylene giving cyclohexene (-44.8 eu , Section 1.4.4). Thus $\Delta_r G^\circ(\text{benzene} + \text{ethylene} \rightleftharpoons \text{bicyclo[2.2.2]octa-2,5-diene}) = 1.7 - 298(-0.045) = 1.7 + 13.4 = 15.1 \text{ kcal mol}^{-1}$, a very endergonic reaction. This intermolecular cycloaddition will not occur at room temperature under standard conditions. If benzene and ethylene would be attached through a tether as in **A**, and assuming the negative entropy of cyclization (blocking rotation about σ bonds of the tether) would be small, the intramolecular process will remain endergonic as it is highly endothermic.



For the intermolecular cycloaddition of benzene with acetylene that would equilibrate with bicyclo[2.2.2]octa-2,5,7-triene one estimates

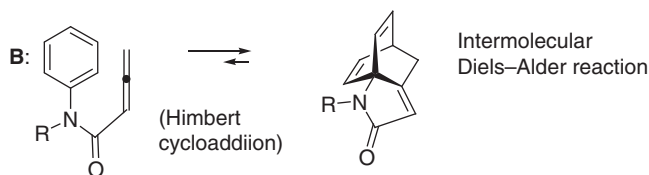


$\Delta_r H^\circ(\text{benzene} + \text{acetylene} \rightleftharpoons \text{bicyclo[2.2.2]octa-2,5,7-triene}) = \Delta_f H^\circ(\text{barrelene}) - \Delta_f H^\circ(\text{benzene}) - \Delta_f H^\circ(\text{acetylene}) = 73 - 19.8 - 54.2 = -1 \text{ kcal mol}^{-1}$. The situation is slightly better than for the cycloaddition of benzene to ethylene, but this exothermicity is not enough to compensate for the entropy cost ($10\text{--}13 \text{ kcal mol}^{-1}$) of condensation. As for the hydrocarbations and the dihydrogenation, the cycloadditions of alkynes are at least $10\text{--}15 \text{ kcal mol}^{-1}$ more exothermic than the cycloadditions of alkenes. For instance, for butadiene + acetylene \rightarrow cyclohexa-1,4-diene one estimates the exothermicity $-55.8 \text{ kcal mol}^{-1}$ to be compared with $-39.9 \text{ kcal mol}^{-1}$ for the cycloaddition of butadiene + ethylene \rightarrow cyclohexene. It is because of the electronic strain present in barrelene (the barrelene effect, Sections 2.9 and 4.7.6) that the intermolecular Diels–Alder reaction of benzene with acetylene (or an alkyne) is not possible. For an intramolecular version, the formation of tricyclic cycloadducts (strain increase) and the cost of entropy for blocking rotation about the σ bonds of the tether make the equilibrium favor the reactants (cycloaddents), not the product (cycloadduct).



For the cycloaddition of benzene to allene one estimates

$\Delta_r H^\circ(\text{benzene} + \text{allene} \rightleftharpoons \text{7-methylidenebicyclo[2.2.2]octa-2,5-diene}) = \Delta_f H^\circ(\text{7-methylidenebicyclo[2.2.2]octa-2,5-diene}) - \Delta_f H^\circ(\text{benzene}) - \Delta_f H^\circ(\text{allene}) = 55 - 19.8 - 45.5 = -10.3 \text{ kcal mol}^{-1}$, just enough exothermicity to compensate the entropy cost of condensation at 25°C under one atmosphere or an ideal solution under one atm. Alternatively, if the benzene and allene moiety are tethered as in **B**, the intramolecular version of this Diels–Alder addition is feasible at room temperature and above. It is called the Himbert cycloaddition [16, 17].



As the standard heat of formation of 7-methylidenebicyclo[2.2.2]octa-2,5-diene is not available, we can estimate it in the following way: $\Delta_f H^\circ(7\text{-methylidenebicyclo[2.2.2]octa-2,5-diene}) = \Delta_f H^\circ(\text{bicyclo[2.2.2]octa-2,5-diene}) + \Delta_f H^\circ(2\text{-methylidenebicyclo[2.2.2]octane}) - \Delta_f H^\circ(\text{bicyclo[2.2.2]octane}) = 34 - 2 + 23 = 55 \text{ kcal mol}^{-1}$.

Contrary to barrelene, 7-methylidenebicyclo[2.2.2]octa-2,5-diene is not destabilized electronically. Since allenes have the same relative stability as isomeric alkynes ($\Delta_f H^\circ(\text{allene}) = 45.5 \text{ kcal mol}^{-1}$, $\Delta_f H^\circ(\text{propyne}) = 44.2 \text{ kcal mol}^{-1}$) the heat of their cycloadditions is similar to those of alkynes.

Problem 1.18 Interpret the relative electron affinities of HO^\cdot , HS^\cdot , and HSe^\cdot . Interpret the relative electron affinities of halide radicals. What makes the trends observed?

Answer

Table 1.A.13 gives $-\text{EA}(X^\cdot) = -78.4, -83.4, -77.6,$ and $-70.5 \text{ kcal mol}^{-1}$ for F^\cdot , Cl^\cdot , Br^\cdot , and I^\cdot , respectively. $-\text{EA}(X^\cdot) = \Delta_f H^\circ(X^-) - \Delta_f H^\circ(X^\cdot)$. The trend observed for Cl^\cdot , Br^\cdot , and I^\cdot is consistent with the fact that Cl is more electronegative than Br, and Br is more electronegative than I. One thus would have expected for fluorine atom $-\text{EA}(\text{F}^\cdot) < -\text{EA}(\text{Cl}^\cdot)$, which is not the case. In the gas phase anions are stabilized by the electronegativity of the atom that bears the negative charge and by the polarizability of this atom. Polarizability is the property that chemical species and atoms have to delocalize the charge, and thus stabilize the anion or cation. This is done by the formation of induced dipole, π -conjugation and hyperconjugation (σ/π -interactions) for polyatomic species. The larger the atoms that constitute the charged species under examination, the larger their number, and the larger the number of bonds, the more the anion or cation is stabilized (electrostatic theory of substituent effects on charge species: dipole/charge stabilization or destabilization: $V_C = \pm q\mu|\cos \theta|/\epsilon r^2$; stabilization due to the induced dipole $V_I = -q^2\alpha/2\epsilon r^4$; q , the charge; ϵ , the dielectric constant of the medium; θ , the angle that the dipole μ makes with the electrostatic field line; α , the polarizability; r , the distance between the substituent and the charged center). For monoatomic anions and cations, their polarizability is the ability of all electrons circulating about the nucleus to follow deformed trajectories and thus to generate induced dipoles that stabilize the charge by charge/dipole interactions. Since fluoride anion is smaller (has fewer electrons) than chloride anion, its negative charge cannot be stabilized by polarizability as well as in chloride anion. There is a competition between stabilization of the charge by electronegativity (attractive interaction between the charge and the nucleus) and formation of induced dipoles due to electron trajectory deformations that stabilize the charge.

Table 1.A.13 gives $-\text{EA}(X^\cdot) = -42, -52.7,$ and $-51 \text{ kcal mol}^{-1}$ for HO^\cdot , HS^\cdot , and HSe^\cdot , respectively. Based on the greater electronegativity for oxygen than for sulfur one would have expected $-\text{EA}(\text{HO}^\cdot) < -\text{EA}(\text{HS}^\cdot)$, which is not the case. Stabilization by electronegativity (attraction of the negative charge of the anion by the nucleus) competes with the stabilization of the anion by its polarizability. Thus the larger the atom ($\text{Se} > \text{S} > \text{O}$), the more the anion is stabilized by polarizability. The data for HS^\cdot and HSe^\cdot are consistent with the greater electronegativity of S compared with that of Se.

Problem 1.19 Why is the hydride anion more stable than hydrogen radical in the gas phase?

Answer

Table 1.A.13 gives $\text{IE}(\text{H}^\cdot) = 313.6 \text{ kcal mol}^{-1}$, $\Delta_f H^\circ(\text{H}^+) = 365.2 \text{ kcal mol}^{-1}$, $\Delta_f H^\circ(\text{H}^\cdot) = \frac{1}{2}DH^\circ(\text{H}^\cdot/\text{H}^\cdot) = 52.1 \text{ kcal mol}^{-1}$, and $\Delta_f H^\circ(\text{H}^-) = 34.7 \text{ kcal mol}^{-1}$.

Hydride anion enjoys stabilization with respect to hydrogen radical due to the filling of its valence shell (doublet of electrons instead a single valence electron).

Problem 1.20 Interpret the differences in electron affinities between alkyl, alkenyl, and alkynyl radicals.

Answer

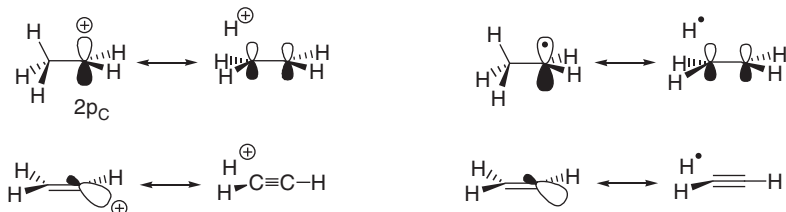
Tables 1.A.8 and 1.A.13 give $DH^\circ(\text{Et}^\cdot/\text{H}^\cdot) = 100.7$, $DH^\circ(\text{CH}_2=\text{CH}^\cdot/\text{H}^\cdot) = 110.6$, and $DH^\circ(\text{CH}\equiv\text{C}^\cdot/\text{H}^\cdot) = 111.9$ kcal mol⁻¹.

Table 1.A.13 gives $DH^\circ(\text{Et}^-/\text{H}^+) = 420.1$, $DH^\circ(\text{CH}_2=\text{CH}^-/\text{H}^+) = 406$, and $DH^\circ(\text{CH}\equiv\text{C}^-/\text{H}^+) = 377$ kcal mol⁻¹.

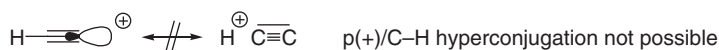
Table 1.A.14 gives $DH^\circ(\text{Et}^+/\text{H}^-) = 270$, $DH^\circ(\text{CH}_2=\text{CH}^+/\text{H}^-) = 291$ kcal mol⁻¹.

The latter data demonstrate that the positive charge is better supported by an sp³-hybridized carbon center than by an sp²-hybridized carbon center. The greater the s-character the more the positive charge that approaches the protons of the nucleus, and the less stable is the carbocation. The situation is reversed for carbanions. The greater the s-character of the doubly occupied orbital of the anion, the more these two electrons are stabilized by attraction by the protons of the nucleus. Carbon-centered radicals are electron-deficient species since they lack one electron to fulfill the octet rule. One thus expects a parallelism between the relative stabilities of sextet carbocations (carbenium ions) and their radical analogs. Carbenium ions such as alkyl cations are stabilized by hyperconjugation. In the case of ethyl cation the positive charge is delocalized by three C—H bonds (Mulliken hyperconjugation, see Section 4.8.1). In vinyl cation, only one C—H bond can hyperconjugate with the cationic center, whereas in ethynyl cation hyperconjugation is not possible. Hyperconjugation is evidenced in radicals by the fine structure of their electron spin resonance (ESR) spectra that shows spin/spin coupling between the electron and the nearby C—H protons.

For simple alkyl cations their relative stabilities (as given by $DH^\circ(\text{R}^+/\text{H}^-)$) follow the sequence: methyl cation < primary < secondary < tertiary cations. The more β $\sigma(\text{C—H})$ bonds are available to interact (hyperconjugate) with the empty 2p⁽⁺⁾ orbital localized at the electro-deficient carbon center, the more stable is the carbocation. A similar, but very much attenuated trend is observed for the corresponding alkyl radicals as given by $DH^\circ(\text{R}^\cdot/\text{H}^\cdot)$. This has been attributed also to hyperconjugation (interaction between 2p and β $\sigma(\text{C—H})$ bonds) as suggested by the ESR spectra of the radicals that demonstrate delocalization of the spin onto their β H atoms. However, steric destabilizing interactions in the precursor (R—H) that are reduced in the radical R[·] might be the origin of this stability trend (see Section 4.8.5).



sp²: s-character, brings the positive charge closer to the C nucleus. This destabilizes the vinyl cation but stabilizes the vinyl anion relatively to ethyl anion.



sp¹: more s-character, brings the positive charge closer to the C nucleus



sp¹: more s-character, brings the negative charge closer to the C nucleus: terminal alkynes are more acidic than terminal alkenes, and alkenes are more acidic than alkanes.

Problem 1.21 Why is there no linear relationship for the homolytic bond dissociation enthalpies $DH^\circ(\text{Me}^\cdot/\text{Me}^\cdot) = 89$ kcal mol⁻¹, $DH^\circ(t\text{-Bu}^\cdot/\text{Me}^\cdot) = 81.8$ kcal mol⁻¹ and $DH^\circ(t\text{-Bu}^\cdot/t\text{-Bu}^\cdot) = 68.8$ kcal mol⁻¹?

Answer

Alkane *t*-Bu-*t*-Bu is destabilized by front strain (F-strain) and back strain (B-strain) (steric repulsion between the methyl groups, see Section 2.5.1), thus rendering its homolysis less endothermic than expected ($DH^\circ(t\text{-Bu}^\cdot/t\text{-Bu}^\cdot) = 89 - 2(7.2) = 74.6$ kcal mol⁻¹ instead of the observed $DH^\circ(t\text{-Bu}^\cdot/t\text{-Bu}^\cdot) = 68.8$ kcal mol⁻¹) on the basis of the relative stability of the radical fragments formed in the homolysis. Both F- and B-strains are relieved in the two *t*-butyl radicals.

Problem 1.22 Why is the homolytic dissociation enthalpy of HF higher than that of HCl?

Answer

H—F bond is stronger than H—Cl bond because of the greater electronegativity difference between H/F pair of atoms than between H/Cl pair of atoms and shorter H—F bond than H—Cl bond.

Problem 1.23 Why are oxygen-centered radicals more reactive than analogous carbon-centered radicals?

Answer

Oxygen-centered radicals such as R—O and Ph—O· are more reactive than alkyl radicals such as R—CH₂· and Ph—CH₂ because they form alcohols (R—O—H) and phenols (Ph—O—H) in which the O—H bonds are significantly stronger than the corresponding C—H bonds in the corresponding hydrocarbons (R—CH₂—H, Ph—CH₂—H). This is a manifestation of the electronegativity difference, which is larger between atom pair H/O than between atomic pair H/C.

Problem 1.24 Give an interpretation for the better stabilizing effect of 4-amino group than of 4-CN and 4-nitro group in 4-substituted phenoxy radicals.

Answer

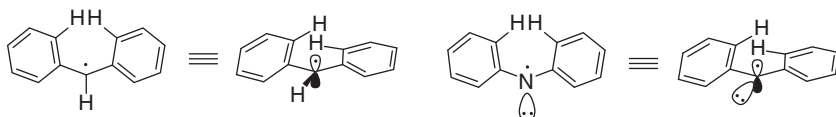
Table 1.A.11 gives $DH^\circ(\text{PhO}\cdot/\text{H}\cdot) = 90.4$, $DH^\circ(4\text{-H}_2\text{N-C}_6\text{H}_4\text{O}\cdot/\text{H}\cdot) = 77.3$, $DH^\circ(4\text{-O}_2\text{N-C}_6\text{H}_4\text{O}\cdot/\text{H}\cdot) = 94.7$ and $DH^\circ(4\text{-NC-C}_6\text{H}_4\text{O}\cdot/\text{H}\cdot) = 94.2$ kcal mol⁻¹ (in DMSO). Phenoxy radical is electrophilic (electron-poor) because of its tendency to take an electron from its neighborhood, a manifestation of the electronegativity of oxygen that is greater than that of carbon. Thus, the oxy radical pulls on the π -electrons of the phenyl ring, making it electron poor at position C(4). As a consequence, a 4-amino substituent, which is a strong electron-releasing group, better stabilizes the phenoxy radical than any electron-withdrawing 4-substituents such as CN and NO₂.

Problem 1.25 Compare the N—H homolytic bond dissociation enthalpies of amines (Table 1.A.11) and explain the non-additivity of phenyl substitution on the stability of nitrogen-centered radical.

Answer

Table 1.A.11 gives $DH^\circ(\text{H}_2\text{N}\cdot/\text{H}\cdot) = 108$ kcal mol⁻¹ (gas phase) and $DH^\circ(\text{PhNH}\cdot/\text{H}\cdot) = 88$ kcal mol⁻¹ (gas phase), indicating stabilizing effect of 20 kcal mol⁻¹ by a phenyl substituent on the nitrogen-centered radical. This is significantly higher than for the phenyl substituent effect (14.5 kcal mol⁻¹) measured for the corresponding carbon-centered radical (methyl radical) as given (Table 1.A.7) by comparing $DH^\circ(\text{H}_3\text{C}\cdot/\text{H}\cdot) = 104.2$ kcal mol⁻¹ (gas phase) and $DH^\circ(\text{PhCH}_2\cdot/\text{H}\cdot) = 89.7$ kcal mol⁻¹ (gas phase).

Table 1.A.11 gives also $DH^\circ(\text{PhNH}\cdot/\text{H}\cdot) = 92$ kcal mol⁻¹ and $DH^\circ(\text{Ph}_2\text{N}\cdot/\text{H}\cdot) = 87.5$ kcal mol⁻¹ in DMSO solution. A comparison of the two latter values shows a much weaker phenyl substituent effect of 4.5 kcal mol⁻¹ on the stabilization of the phenylaminy radical. In the case of related carbon-centered radicals, $DH^\circ(\text{PhCH}_2\cdot/\text{H}\cdot) = 89.7$ kcal mol⁻¹ (gas phase) and $DH^\circ(\text{Ph}_2\text{CH}\cdot/\text{H}\cdot) = 81.4$ kcal mol⁻¹ (gas phase) are measured. This gives a phenyl substituent stabilizing effect of 8.3 kcal mol⁻¹ on the benzyl radical, almost twice as much as the phenyl substituent effect on the stabilization of PhNH·. The difference between the nitrogen and carbon-centered radical arises from the fact that nitrogen is more electronegative than carbon. The electron demand of radical H₂N· is higher than that of H₃C·. As a consequence, the electron-rich and highly polarizable phenyl substituent responds more when substituting H₂N· instead of H₃C·. The spin is more delocalized in PhNH· than in PhCH₂·. This represents a first hypothesis to explain the smaller phenyl stabilizing effect on PhNH· than on PhCH₂·. Once the spin is delocalized by the phenyl substituent a second phenyl substituent cannot stabilize as much as the first one. A second hypothesis is to invoke the non-planarity of the two phenyl rings in Ph₂CH· and Ph₂N·. Because of gauche interactions between the two geminal phenyl rings in these radicals, conjugation between the radicals and the π -systems is reduced compared with PhCH₂· and PhNH·, respectively. Because of the shorter C—N bond (between Ph and N) compared with the C—C bond (between Ph and CH₂·) the two phenyl rings in Ph₂N· are closer to each other than in Ph₂CH·. Consequently, deviation from planarity might be larger in Ph₂N· than in Ph₂CH·. The above discussion ignores the error on the phenyl substituent effect considered. If it should be $\pm 2\text{--}3$ kcal mol⁻¹, more hypotheses should be examined!



Problem 1.26 Calculate the standard gas phase heat of reaction of the following additions:

- $R' + CO \rightleftharpoons RCO'$ for $R = \text{Ph}, \text{Me}, t\text{-Bu}$
- $\text{Et}' + \text{MeCOMe} \rightleftharpoons \text{EtC}(\text{Me})_2\text{C}-\text{O}'$
- $\text{Et}' + \text{acetone} \rightleftharpoons \text{EtO}-\text{C}(\cdot)\text{Me}_2$
- $\text{Et}' + \text{cyclopentene} \rightleftharpoons 2\text{-ethylcyclopentyl}'$

Answer

Heats of formation of radicals are taken from Table 1.A.7.

- $\Delta_f H^\circ(\text{Ph}' + \text{CO} \rightleftharpoons \text{PhCO}') = 26 (\pm?) - 81 (\pm 2.0) - (-26.4 \pm 0.04) = -28.8 \pm 3.$
 $\Delta_f H^\circ(\text{Me}' + \text{CO} \rightleftharpoons \text{MeCO}') = -2.9(\pm 0.7) - 34.8(\pm 0.2) - (-26.4 \pm 0.04) = -10.2 \pm 1.$
 $\Delta_f H^\circ(t\text{-Bu}' + \text{CO} \rightleftharpoons t\text{-BuCO}') = \Delta_f H^\circ(t\text{-BuCO}') - 11.0(\pm 0.7) - (-26.4 \pm 0.04) = X.$
 Since $\Delta_f H^\circ(t\text{-BuCO}')$ is not given in the table, we can estimate $\Delta_f H^\circ(t\text{-Bu}' + \text{CO} \rightleftharpoons t\text{-BuCO}') = \Delta_f H^\circ(\text{Me}' + \text{CO} \rightleftharpoons \text{MeCO}') +$ correction for the stability difference between $t\text{-Bu}'$ and Me' that is given by the comparison of $DH^\circ(\text{Me}'/\text{H}') = 104.7$ with $DH^\circ(t\text{-Bu}'/\text{H}') = 95.2 \text{ kcal mol}^{-1}$, i.e.: $9.5 \pm 2.0 \text{ kcal mol}^{-1}$, taking $\pm 1.0 \text{ kcal mol}^{-1}$ for the average standard error on the homolytic bond dissociation enthalpies given in Table 1.A.7. Assuming that the t -butyl group of $t\text{-BuCO}'$ radical does not stabilize the radical more than the methyl group in MeCO' (which must be the case since $DH^\circ(\text{MeCH}_2'/\text{H}') = 100.7$ and $DH^\circ(\text{PhCH}_2'/\text{H}') = 89.7$, but $DH^\circ(\text{MeCO}'/\text{H}') = 86$ and $DH^\circ(\text{PhCO}'/\text{H}') = 87 \text{ kcal mol}^{-1}$, Table 1.A.7), one estimates $\Delta_f H^\circ(t\text{-Bu}' + \text{CO} \rightleftharpoons t\text{-BuCO}') = -10.2(\pm 1.0) + 9.5(\pm 2.0) = -0.7 \pm 3.0 \text{ kcal mol}^{-1}$. This reaction is not exothermic enough to compensate for the entropy cost (condensation). Pivalyl radical ($t\text{-BuCO}'$) might be formed as an intermediate by addition of t -butyl radical to carbon monoxide. This intermediate might give a stable product such as $t\text{-BuCO}-t\text{-Bu}$ by reaction with a t -butyl radical, or form pivaldehyde ($t\text{-BuCHO}$) by hydrogen atom transfer from $t\text{-Bu}'$.

Disproportionation reaction: $t\text{-BuCO}' + t\text{-Bu}' \rightleftharpoons t\text{-BuCHO} + \text{isobutylene}$

But the latter reactions compete with a more frequent reaction that is the disproportionation $2 t\text{-Bu}' \rightleftharpoons \text{isobutylene} + \text{isobutane}$.

At room temperature, the concentration of $t\text{-BuCO}'$ remains always much lower than that of $t\text{-Bu}'$.

- Since $\Delta_f H^\circ(\text{Me}_2(\text{Et})\text{C}-\text{O}')$ is not given in the tables, one assumes
 $\Delta_f H^\circ(\text{Et}' + \text{Me}_2\text{CO} \rightleftharpoons \text{Me}_2(\text{Et})\text{CO}') = \Delta_f H^\circ(\text{Me}' + \text{Me}_2\text{CO} \rightleftharpoons \text{Me}_3\text{CO}') +$ correction for the difference in relative stability between methyl and ethyl radicals, which is given on comparing $DH^\circ(\text{Me}'/\text{H}') = 104.7$ with $DH^\circ(\text{Et}'/\text{H}') = 100.7 \text{ kcal mol}^{-1}$, i.e. $4.0 \pm 2.0 \text{ kcal mol}^{-1}$, taking $\pm 1.0 \text{ kcal mol}^{-1}$ for the average standard error on the homolytic bond dissociation enthalpies given in Table 1.A.7. This implies that the relative stability of the alkyloxy radicals is the same irrespective of the size of the alkyl group. This is indeed the case as $DH^\circ(t\text{-BuO}'/\text{H}') = DH^\circ(\text{MeO}'/\text{H}') = 104\text{--}105 \text{ kcal mol}^{-1}$ (Table 1.A.13).

One finds the following data:

$$\Delta_f H^\circ(\text{Me}') = 34.8 \pm 0.2 \text{ (Table 1.A.7)}, \Delta_f H^\circ(\text{Me}_2\text{CO}) = -52.23 \pm 0.14 \text{ kcal mol}^{-1} \text{ (Table 1.A.4)}.$$

$$\Delta_f H^\circ(\text{Me}_3\text{C}-\text{O}') \text{ can be calculated from } DH^\circ(t\text{-BuO}'/\text{H}') = 105 \text{ kcal mol}^{-1} \text{ (Table 1.A.11):}$$

$$DH^\circ(t\text{-BuO}'/\text{H}') = 105 \pm 1.0 = \Delta_f H^\circ(t\text{-BuO}') + \Delta_f H^\circ(\text{H}') - \Delta_f H^\circ(t\text{-BuOH}) = \Delta_f H^\circ(t\text{-BuO}') + 52.1(\pm 0.001) - (-74.72 \pm 0.21), \text{ which leads to } \Delta_f H^\circ(t\text{-BuO}') = -21.8 \pm 2.0 \text{ (Table 1.A.13 gives } \Delta_f H^\circ(t\text{-BuO}') = -21.0)$$

This gives $\Delta_f H^\circ(\text{Me}' + \text{Me}_2\text{CO} \rightleftharpoons \text{Me}_3\text{CO}') = -21.8(\pm 2) - 34.8(\pm 0.2) - (-52.23 \pm 0.14) = -4.4 \pm 2.4 \text{ kcal mol}^{-1}$. Thus, $\Delta_f H^\circ(\text{Et}' + \text{Me}_2\text{CO} \rightleftharpoons \text{Me}_2(\text{Et})\text{CO}') = -4.4 \pm (2.4) + 4.0 \pm (2.0) = -0.4 \pm 4.4 \text{ kcal mol}^{-1}$.

Alternatively, one can estimate $\Delta_f H^\circ(\text{Me}_2(\text{Et})\text{C}-\text{O}')$ from $\Delta_f H^\circ(\text{Me}_3\text{C}-\text{O}')$ by considering the difference $\Delta_f H^\circ(\text{Me}_2(\text{Et})\text{C}-\text{OH}) = -78.7$ and $\Delta_f H^\circ(\text{Me}_3\text{C}-\text{OH}) = -74.72 \pm 0.21 \text{ kcal mol}^{-1}$ (Table 1.A.4) of $-4.0 \pm 0.5 \text{ kcal mol}^{-1}$. This gives $\Delta_f H^\circ(\text{Me}_2(\text{Et})\text{C}-\text{O}') = \Delta_f H^\circ(\text{Me}_3\text{C}-\text{O}') - 4.0 \pm 0.5 \text{ kcal mol}^{-1} = -21.8(\pm 2.0) - 4.0(\pm 0.5) = -25.8 \pm 2.5 \text{ kcal mol}^{-1}$. Thus, $\Delta_f H^\circ(\text{Et}' + \text{Me}_2\text{CO} \rightleftharpoons \text{Me}_2(\text{Et})\text{CO}') = -25.8(\pm 2.5) - 28.4(\pm 0.5) - (-52.23 \pm 0.14) = -2.0 \pm 3.2 \text{ kcal mol}^{-1}$.

The more the alkyl radical is stable, the least exothermic is its addition to the carbon center of a ketone. This is the case because the oxygen-centered radicals that result from these reactions have the same relative stabilities since they are not affected (Table 1.A.13) by the different tertiary alkyl groups. Indeed, Table 1.A.13 gives $DH^\circ(\text{MeO}'/\text{H}') = DH^\circ(t\text{-BuO}'/\text{H}') = DH^\circ(\text{Me}_2(\text{Et})\text{CO}'/\text{H}') = 104\text{--}105 \text{ kcal mol}^{-1}$.

- $\Delta_f H^\circ(\text{Et}' + \text{Me}_2\text{CO} \rightleftharpoons \text{EtO}-(\text{Me})_2\text{C}') = \Delta_f H^\circ(\text{EtO}-(\text{Me})_2\text{C}') - \Delta_f H^\circ(\text{Et}') - \Delta_f H^\circ(\text{MeCOMe}) = \Delta_f H^\circ(\text{EtO}-(\text{Me})_2\text{C}') - 28.4(\pm 0.5) - (52.23 \pm 0.14).$

$\Delta_f H^\circ(\text{EtO}-(\text{Me})_2\text{C}^\cdot)$ is estimated from $\Delta_f H^\circ(\text{MeOCH}_2^\cdot) = -3 \text{ kcal mol}^{-1}$ (Table 1.A.7) by considering the exchange of a methoxy group for an ethoxy group (contribution X) and by converting the primary alkyl radical into a dimethylalkyl radical: contribution Y.

$X = \Delta_f H^\circ(\text{MeOEt}) - \Delta_f H^\circ(\text{MeOMe}) = -51.73(\pm 0.16) - (-44.0(\pm 0.12)) = -7.7 \pm 0.3 \text{ kcal mol}^{-1}$ (Table 1.A.4).
 $Y = \Delta_f H^\circ(\text{Et}(\text{Me})_2\text{C}^\cdot) - \Delta_f H^\circ(\text{EtCH}_2^\cdot) = (6.7 \pm 0.7) - (23.5 \pm 0.5) = -16.8 \pm 1.2 \text{ kcal mol}^{-1}$ (Table 1.A.7). One obtains $\Delta_f H^\circ(\text{EtO}-(\text{Me})_2\text{C}^\cdot) = \Delta_f H^\circ(\text{MeOCH}_2^\cdot) = -3.0 + X + Y = -3.0 - 7.7(\pm 0.3) - 16.8(\pm 1.2) = -27.5 \pm 2.5 \text{ kcal mol}^{-1}$.

Thus, $\Delta_f H^\circ(\text{Et}^\cdot + \text{Me}_2\text{CO} \rightleftharpoons \text{EtO}-(\text{Me})_2\text{C}^\cdot) = \Delta_f H^\circ(\text{EtO}-(\text{Me})_2\text{C}^\cdot) - \Delta_f H^\circ(\text{Et}^\cdot) - \Delta_f H^\circ(\text{Me}_2\text{CO}) = -27.5(\pm 2.5) - 28.4(\pm 0.5) - (52.23 \pm 0.14) = -3.7 \pm 3.1 \text{ kcal mol}^{-1}$

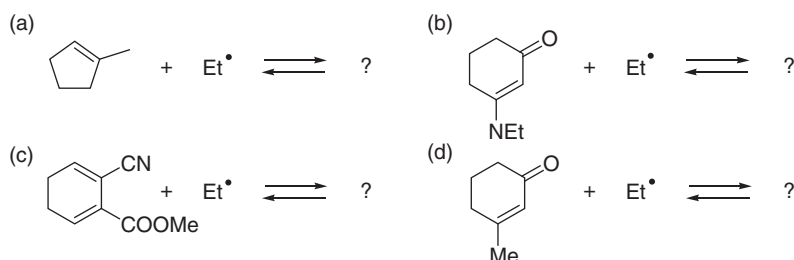
d) $\Delta_f H^\circ(\text{Et}^\cdot + \text{cyclopentene} \rightleftharpoons 2\text{-ethylcyclopent-1-yl}^\cdot) = \Delta_f H^\circ(2\text{-Et-cyclopentyl}^\cdot) - \Delta_f H^\circ(\text{Et}^\cdot) - \Delta_f H^\circ(\text{cyclopentene}) = \Delta_f H^\circ(2\text{-Et-cyclopentyl}^\cdot) - 28.4(\pm 0.5) - (8.5 \pm ?)$.

$\Delta_f H^\circ(2\text{-Et-cyclopentyl}^\cdot) = \Delta_f H^\circ(\text{cyclopentyl}^\cdot) + \text{difference } \Delta_f H^\circ(3\text{-Et-pentane}) - \Delta_f H^\circ(\text{pentane}) = 24.3(\pm ?) + W$ (Table 1.A.7).

$W = \Delta_f H^\circ(3\text{-Et-pentane}) - \Delta_f H^\circ(\text{pentane}) = -45.34(\pm 0.28) - (35.0 \pm 0.14) = -10.3 \pm 0.4 \text{ kcal mol}^{-1}$ (Table 1.A.2). One obtains $\Delta_f H^\circ(2\text{-Et-cyclopentyl}^\cdot) = 24.3 - 10.3 = 14.0 (\pm ?) \text{ kcal mol}^{-1}$. This leads to $\Delta_f H^\circ(\text{Et}^\cdot + \text{cyclopentene} \rightleftharpoons 2\text{-ethylcyclopent-1-yl}^\cdot) = 14.0 - 28.4 - 8.5 = -22.9 (\pm ?) \text{ kcal mol}^{-1}$.

The addition of alkyl radicals to alkenes is much more exothermic than the addition of the same alkyl radicals to ketones. This is due mostly to the greater C=O bond energies than C=C bond energies. The heats of alkyl radical additions to alkenes and carbonyl compounds parallel those of the corresponding hydrocarbocations (Section 1.7.1).

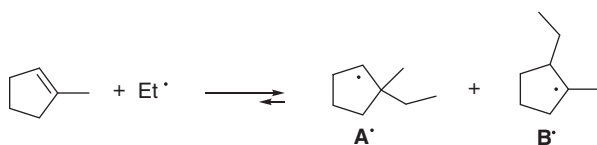
Problem 1.27 What is the preferred regioisomeric adduct of the following equilibria?



Answer

Under thermodynamic control (fully reversible reactions) the most stable regioisomeric adduct-radical should be preferred.

a) The two radicals **A** \cdot and **B** \cdot can form concurrently:



A \cdot is a secondary alkyl radical with a quaternary carbon center (doubly branched alkane); **B** \cdot is a tertiary alkyl radical with two monobranchings (branched hydrocarbons are more stable than their unbranched isomers; Section 1.6.4). One needs to consider the difference in standard heats of formation of the corresponding alkanes A-H and B-H and the corresponding homolytic bond dissociation enthalpies $DH^\circ(\text{A}^\cdot/\text{H}^\cdot)$ and $DH^\circ(\text{B}^\cdot/\text{H}^\cdot)$:

$\Delta_f H^\circ(\text{A}^\cdot \rightleftharpoons \text{B}^\cdot) = \Delta_f H^\circ(\text{B}^\cdot) - \Delta_f H^\circ(\text{A}^\cdot) = DH^\circ(\text{B}^\cdot/\text{H}^\cdot) - DH^\circ(\text{A}^\cdot/\text{H}^\cdot) - \Delta_f H^\circ(\text{A-H}) + \Delta_f H^\circ(\text{B-H}) = \Delta_f H^\circ(\text{B}^\cdot) + \Delta_f H^\circ(\text{H}^\cdot) - \Delta_f H^\circ(\text{B-H}) - \Delta_f H^\circ(\text{A}^\cdot) - \Delta_f H^\circ(\text{H}^\cdot) + \Delta_f H^\circ(\text{A-H}) - \Delta_f H^\circ(\text{A-H}) + \Delta_f H^\circ(\text{B-H})$.

Since $\Delta_f H^\circ(\text{A-H})$ and $\Delta_f H^\circ(\text{B-H})$ are not available $\Delta_f H^\circ(\text{A-H}) - \Delta_f H^\circ(\text{B-H})$ can be estimated to be similar to the difference $\Delta_f H^\circ(3,3\text{-dimethylpentane}) - \Delta_f H^\circ(2,3\text{-dimethylpentane}) = -48.17 (\pm 0.22) - (-47.62 \pm 0.30) = -0.55 \pm 0.52 \text{ kcal mol}^{-1}$.

$DH^\circ(\text{A}^\cdot/\text{H}^\cdot)$ and $DH^\circ(\text{B}^\cdot/\text{H}^\cdot)$ are not available. $DH^\circ(\text{cyclopentyl}^\cdot/\text{H}^\cdot) = 94.8 \text{ kcal mol}^{-1}$ (Table 1.A.7) but $DH^\circ(1\text{-alkylcyclopentyl}^\cdot/\text{H}^\cdot)$ is not available, which is required to estimate the difference in

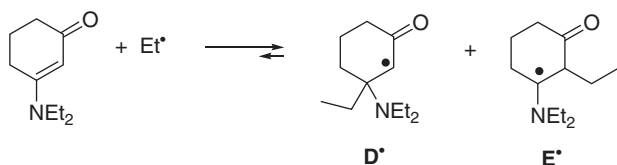
C—H bond energies between secondary and tertiary C—H bonds in alkylcyclopentanes. We thus need to turn to simpler model compounds for which this difference is available. Table 1.A.7 gives $DH^\circ(2\text{-methylbut-2-yl}/H^\cdot) = 95.3 \text{ kcal mol}^{-1}$ and $DH^\circ(\text{pent-2-yl}/H^\cdot) = 99.2 \text{ kcal mol}^{-1}$, a difference of c. 4 kcal mol^{-1} in favor of the tertiary C—H bond. The same difference is found with the comparison $DH^\circ(2\text{-methylprop-2-yl}/H^\cdot) = 95.2 \text{ kcal mol}^{-1}$ and $DH^\circ(n\text{-but-2-yl}/H^\cdot) = 99.1 \text{ kcal mol}^{-1}$. Accepting standard deviations of $\pm 1.0 \text{ kcal mol}^{-1}$ on published DH° values, one obtains:

$$\Delta_r H^\circ(\mathbf{A}^\cdot \rightleftharpoons \mathbf{B}^\cdot) = DH^\circ(\mathbf{B}^\cdot/H^\cdot) - DH^\circ(\mathbf{A}^\cdot/H^\cdot) - \Delta_f H^\circ(\mathbf{A}-\text{H}) + \Delta_f H^\circ(\mathbf{B}-\text{H}) = -4(\pm 2.0) + 0.55(\pm 0.52) = -3.5 \pm 2.5 \text{ kcal mol}^{-1}.$$

In this case the greater stability of the tertiary radical \mathbf{B}^\cdot with respect to isomeric secondary radical \mathbf{A}^\cdot overwhelms the relative small difference in stability of the alkyl skeletons due to changes in chain branching. Both radical \mathbf{A}^\cdot and \mathbf{B}^\cdot do not share any symmetry axis of rotation and have similar conformational flexibility. They are expected to have the same entropy, thus:

$$\Delta_r G^\circ(\mathbf{A}^\cdot \rightleftharpoons \mathbf{B}^\cdot) = \Delta_r H^\circ(\mathbf{A}^\cdot \rightleftharpoons \mathbf{B}^\cdot). \text{ Radical } \mathbf{B}^\cdot \text{ forms to a greater extent than radical } \mathbf{A}^\cdot.$$

- b) Ethyl radical adds to the C=C double bond, not to the C=O double bond (see Problem 1.26). Radicals \mathbf{D}^\cdot and \mathbf{E}^\cdot can form concurrently.



$$\Delta_r H^\circ(\mathbf{D}^\cdot \rightleftharpoons \mathbf{E}^\cdot) = \Delta_f H^\circ(\mathbf{E}^\cdot) - \Delta_f H^\circ(\mathbf{D}^\cdot) = DH^\circ(\mathbf{E}^\cdot/H^\cdot) - DH^\circ(\mathbf{D}^\cdot/H^\cdot) - \Delta_f H^\circ(\mathbf{D}-\text{H}) + \Delta_f H^\circ(\mathbf{E}-\text{H}).$$

The corresponding hydrocarbons $\mathbf{D}-\text{H}$ and $\mathbf{E}-\text{H}$ are isomers in which $\mathbf{D}-\text{H}$ contains a tertiary alkylamine whereas $\mathbf{E}-\text{H}$ contains a secondary alkylamine. The stability difference $\Delta_f H^\circ(\mathbf{D}-\text{H}) - \Delta_f H^\circ(\mathbf{E}-\text{H})$ can be taken, to a first approximation, similar to $\Delta_f H^\circ(\text{Me}_3\text{C}-\text{NH}_2) - \Delta_f H^\circ(\text{MeCH}(\text{NH}_2)\text{CH}_2\text{Me}) = -28.8(\pm 0.2) - (-23.6 \pm 0.13) = -5.2 \pm 0.33 \text{ kcal mol}^{-1}$ (Table 1.A.4).

$DH^\circ(\mathbf{D}^\cdot/H^\cdot)$ can be estimated from $DH^\circ(\text{MeCOCH}_2^\cdot/H^\cdot) = 98 \pm 2 \text{ kcal mol}^{-1}$ (Table 1.A.9) and by considering the fact that \mathbf{D}^\cdot is a secondary, not a primary alkyl radical. Thus, $DH^\circ(\mathbf{D}^\cdot/H^\cdot) = 98 - 2 = 96 \pm 3 \text{ kcal mol}^{-1}$.

$DH^\circ(\mathbf{E}^\cdot/H^\cdot)$ can be estimated from $DH^\circ(\text{Me}_2\text{NCH}_2^\cdot/H^\cdot) = 83.8 \pm 1.0 \text{ kcal mol}^{-1}$ (Tables 1.A.7 and 1.A.9) and corrected for the stability difference between a primary and a secondary substituted alkyl radical (c. 4 kcal mol^{-1}). Thus, $DH^\circ(\mathbf{E}^\cdot/H^\cdot) = 83.8 (\pm 1.0) - 4 = 79.8 \pm 1.0 \text{ kcal mol}^{-1}$.

This leads to $\Delta_r H^\circ(\mathbf{D}^\cdot \rightleftharpoons \mathbf{E}^\cdot) = \Delta_f H^\circ(\mathbf{E}^\cdot) - \Delta_f H^\circ(\mathbf{D}^\cdot) = DH^\circ(\mathbf{E}^\cdot/H^\cdot) - DH^\circ(\mathbf{D}^\cdot/H^\cdot) - \Delta_f H^\circ(\mathbf{D}-\text{H}) + \Delta_f H^\circ(\mathbf{E}-\text{H}) = 83.8 - 96 + 5.2 \approx -7 \text{ kcal mol}^{-1}$. Thus, radical \mathbf{E}^\cdot is highly preferred over radical \mathbf{D}^\cdot (two isomers with similar entropies).

- c) Ethyl radical adds to the alkene moieties forming the isomeric tertiary-allylic radicals \mathbf{F}^\cdot and \mathbf{G}^\cdot . Isomers \mathbf{H}^\cdot and \mathbf{I}^\cdot do not form as they are secondary alkyl radicals, not stabilized by allylic conjugation. Both radicals \mathbf{F}^\cdot and \mathbf{G}^\cdot have the same skeleton, the same degree of chain branching. They can be interconverted by exchange of their COOEt and CN groups.

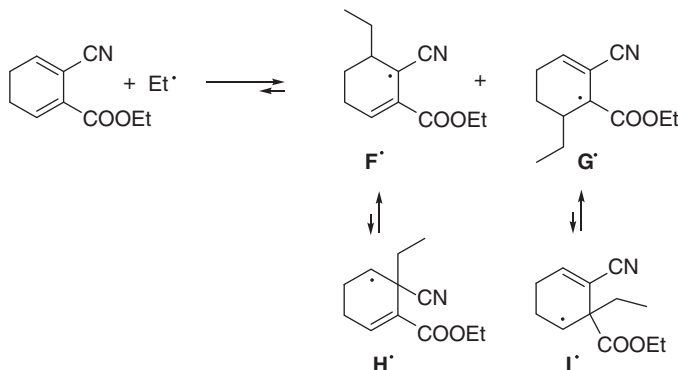
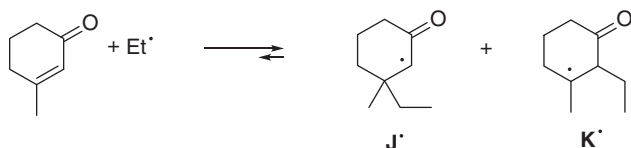


Table 1.A.9 gives the substituent effects on the relative stabilities of primary radicals (MeCOOC stabilizes by 9.7 ± 2.0 kcal mol⁻¹, and N≡C by 12 ± 2.7 kcal mol⁻¹). Assuming they are similar for tertiary allylic radicals, one predicts that radical **H'** will form to a greater extent than radical **G'**.

- d) Ethyl radical adds to 3-methylcyclohex-2-enone giving the regioisomeric radicals **J'** and **K'**. The former is a secondary alkyl radical stabilized by 7 ± 2 kcal mol⁻¹ (Table 1.A.9) through conjugation; the latter is a tertiary alkyl radical not stabilized by carbonyl conjugation, but intrinsically 2–4 kcal mol⁻¹ more stable than a secondary radical. As the difference in stability between an alkane containing a quaternary carbon center and an isomer containing two tertiary carbon centers is very small (see Problem 1.27a), one can predict that radical **J'** will form to a greater extent than radical **K'**.



Problem 1.28 If you had to propose good radical scavenging agents, which compounds listed in Table 1.A.11 would you choose?

Answer

Those compounds with the smallest homolytic bond dissociation enthalpies such as the conjugate base of hydroquinone (O—H bond: 73 kcal mol⁻¹) and (*t*-Bu)₂NO—H (O—H bond: 68.2 kcal mol⁻¹).

Problem 1.29 Compare the gas phase heterolytic bond dissociation energies $\text{ROH} \rightleftharpoons \text{RO}^- + \text{H}^+$ for methanol, ethanol, isopropanol, and *tert*-butanol. Is the trend the same in solution?

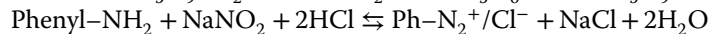
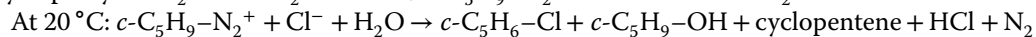
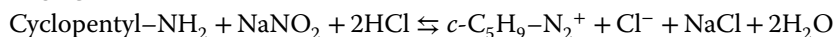
Answer

Table 1.A.13 gives $DH^\circ(\text{MeO}^-/\text{H}^+) = 380.5$, $DH^\circ(\text{EtO}^-/\text{H}^+) = 377.5$, $DH^\circ(i\text{-PrO}^-/\text{H}^+) = 375$, and $DH^\circ(t\text{-BuO}^-/\text{H}^+) = 374.5$ kcal mol⁻¹. The gas phase acidities of alcohols increases with the size of the alkyl group. The larger the alkyl group, the larger its polarizability, the more it stabilizes the alcoholate anion.

Bordwell's tables give pK_a values of 16.0, 18.8, and 19.9 for EtOH, *i*-PrOH, and *t*-BuOH in water (Table 1.A.24), and 29.0, 29.8, 30.3, and 32.2 for MeOH, EtOH, *i*-PrOH, and *t*-BuOH in DMSO (Table 1.A.25), respectively. In solution, the acidity of alcohols decreases with the size of the alkyl group. This arises from solvation that overwhelms the intrinsic stability of the alcoholate anions. The smaller the alcoholate anion, the better it is stabilized by interaction with the solvent molecules (charge/dipole interactions depend on the distance separating the charge from the solvent dipoles). In *t*-BuO⁻ the solvent molecules cannot get close to the oxide anion as in MeO⁻. There is a steric effect to solvation in large alcoholate anions.

Problem 1.30 Diazotization of primary alkyl amines with NaNO₂/HCl/H₂O at 0 °C leads to mixtures of alcohols, chlorides, and alkenes with the evolution of N₂. The same reaction with aniline and other aromatic primary amines generates at 0 °C persistent diazonium salts that decompose with N₂ evolution on heating above 60 °C. Why is there this difference in behavior between the diazonium salts resulting from alkyl and aryl primary amines?

Answer



At 20 °C, PhN₂⁺/Cl⁻ is stable.

Table 1.A.14 gives $DH^\circ(c\text{-pentyl}^+/\text{H}^-) = 249.8 \ll DH^\circ(\text{Ph}^+/\text{H}^-) = 287$ kcal mol⁻¹. Thus, the dissociation of *c*-pentyl-N₂⁺ into *c*-pentyl cation and N₂ is much easier than dissociation of Ph-N₂⁺ into phenyl cation + N₂.

Problem 1.31 Explain the difference in heterolytic bond dissociation enthalpies $DH^\circ(\text{cyclopent-2-enyl}^+/\text{H}^-)$, $DH^\circ(\text{cyclopentadienyl}^+/\text{H}^-)$ and $DH^\circ(\text{tropylium}^+/\text{H}^-)$.

Answer

Table 1.A.14 gives $DH^\circ(\text{cyclopent-2-enyl}^+/\text{H}^-) = 225$, $DH^\circ(\text{cyclopentadienyl}^+/\text{H}^-) = 255.6$ and $DH^\circ(\text{cycloheptatrienyl}^+/\text{H}^-) = DH^\circ(\text{tropylium cation}/\text{H}^-) = 194 \text{ kcal mol}^{-1}$. The smaller the hydride affinity, the more stable the carbenium ion. Cyclopent-2-enyl cation is a 1,3-dialkylallyl cation stabilized by allylic conjugation. Cyclopentadienyl cation would be stabilized twice by allylic conjugation, but it realizes a Hückel π -system with four electrons (Section 4.5.8) that is antiaromatic, thus destabilized electronically. In contrast, tropylium cation (Section 4.5.13) is a six electron Hückel system that is stabilized by aromaticity.

Problem 1.32 Ethyl cation and methylsilicenium ion are both primary cations. Explain the data of Table 1.A.16, in particular $\Delta_r H^\circ(\text{Et}^+ + \text{MeSiH}_3 \rightleftharpoons \text{MeSiH}_2^+ + \text{EtH}) = -20 \text{ kcal mol}^{-1}$. Why is this value not closer to zero?

Answer

In this equilibrium one exchanges one Si—H bond for a C—H bond. The latter is c. 14 kcal mol^{-1} more stable than the former as given by the comparison $DH^\circ(\text{CH}_3\cdot/\text{H}\cdot) = 104.7 \text{ kcal mol}^{-1}$ with $DH^\circ(\text{SiH}_3\cdot/\text{H}\cdot) = 90.3 \text{ kcal mol}^{-1}$ [18, 19]. This does not account totally for the 20 kcal mol^{-1} of exothermicity in favor of the silicenium cation. One needs to consider also the higher polarizability of the Si atom compared with that of the C atom. The Si atom has more electrons circulating about its nucleus than the C atom. The Si atom is thus more polarizable than the C atom. The positive charge in MeSiH_2^+ is better supported by the Si atom than by the carbon atom in MeCH_2^+ .

Problem 1.33 Compare the gas phase hydride affinities of the following primary alkyl cations: Et^+ , $n\text{-Pr}^+$ and $n\text{-Bu}^+$. Why are they not the same?

Answer

Table 1.A.14 gives $DH^\circ(\text{Me-CH}_2^+/\text{H}^-) = 270$, $DH^\circ(\text{Me-CH}_2\text{-CH}_2^+/\text{H}^-) = 267$, and $DH^\circ(\text{Me-CH}_2\text{-CH}_2\text{-CH}_2^+/\text{H}^-) = 265 \text{ kcal mol}^{-1}$.

In the absence of solvation, the larger the alkyl substituent, the larger its polarizability, the better it stabilizes the primary carbenium ion.

Problem 1.34 Calculate the heat of cyclopropanation of ethylene with CH_2 : (methylene).

Answer

$$\Delta_r H^\circ(\text{CH}_2 + \text{CH}_2=\text{CH}_2 \rightleftharpoons c\text{-C}_3\text{H}_6) = 12.74(\pm 0.14) - 62.9(\pm 0.6) - 12.54(\pm 0.1) = -62.7 \pm 0.85 \text{ kcal mol}^{-1}$$

Problem 1.35 Calculate the heat of the addition of trimethylenemethane to ethylene giving methylenecyclopentane.

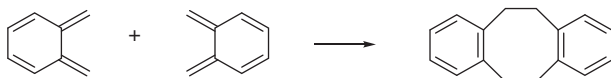
Answer

$\Delta_r H^\circ((\text{CH}_2)_3\text{C} + \text{CH}_2=\text{CH}_2 \rightleftharpoons \text{methylidenecyclopentane}) = 2.4 - 62 - 12.5 = \text{c. } -72 \text{ kcal mol}^{-1}$. The standard heat of formation of trimethylenemethane is estimated in the following way: $\Delta_f H^\circ(\text{trimethylenemethane}) = \Delta_f H^\circ(\text{isobutylene}) + 2DH^\circ(2\text{-methylallyl}/\text{H}\cdot) - DH^\circ(\text{H}\cdot/\text{H}\cdot) = -4.3 + 2(85.1) - 104.4 \approx 62 \text{ kcal mol}^{-1}$.

Problem 1.36 What is the major product of cyclodimerization of *o*-xylylene?

Answer

o-Xylylene is a highly reactive diene that searches to recover the aromatic stabilization of the benzene system. It can do that by entering into (4+2)- (Diels–Alder reactions) and (4+4)-cycloadditions. The cyclodimerization leading to the highest exothermicity is the [4+4]-cycloaddition forming dibenzocycloocta-1,5-diene.

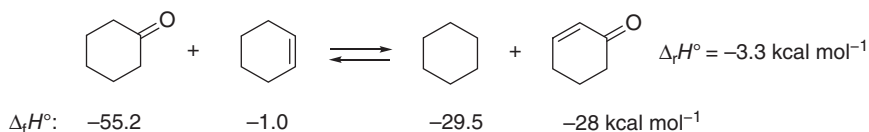


Problem 1.37 Estimate the equilibrium constant at 25°C for phenol \rightleftharpoons cyclohex-2,4-dien-1-one [20, 21].

Answer

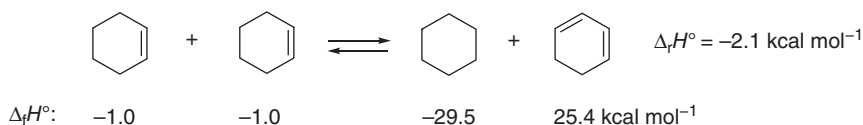
$\Delta_r H^\circ$ (phenol \rightleftharpoons cyclohex-2,4-dien-1-one) = gain of stability for enol \rightleftharpoons ketone ($-11 \text{ kcal mol}^{-1}$; Section 1.12.3), plus gain in stability for the π -conjugation in cyclohexa-2,4-dienone ($-5.4 \text{ kcal mol}^{-1}$; see below) and loss of aromaticity of phenol ($36.2 \text{ kcal mol}^{-1}$; see below) = $19.8 \text{ kcal mol}^{-1}$.

The following equilibrium gives a first estimate of the π -conjugation stabilization effect in cyclohex-2-enone ($-3.3 \text{ kcal mol}^{-1}$):



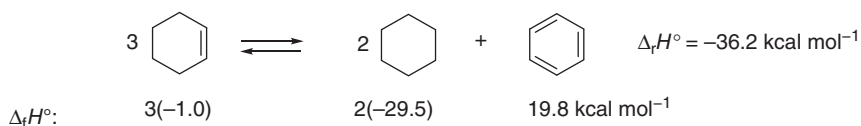
The above equilibrium compares the heats of hydrogenation of cyclohex-2-enone into cyclohexanone with the heat of hydrogenation of cyclohexene into cyclohexane. It ignores the differential hyperconjugation effects ($\sigma(\text{CH}_2)/\pi(\text{C}=\text{O})$ and $\sigma(\text{CH}_2)/\pi(\text{C}=\text{C})$ interactions) between products and reactants. In the products one counts two such interactions and four in the reactants. The difference of c. 2 kcal mol^{-1} in heat of formation of a terminal olefin (1-alkylethylene) with its 1,2-dialkylethylene isomers could be used as the stabilization introduced by one ($\sigma(\text{CH}_2)/\pi(\text{C}=\text{C})$) interaction. With the above equilibrium, one ignores also the differential ring strain effects between products and reactants.

Making the same simplifications (ignoring differential hyperconjugation effects and ring strain effects) the heat of the next equilibrium ($-2.1 \text{ kcal mol}^{-1}$) can be considered as the π -conjugation effect in cyclohexa-1,3-diene.



This leads to an estimate of $-3.3 - 2.1 = -5.4 \text{ kcal mol}^{-1}$ for the stabilization of cyclohexa-2,4-dien-1-one due to π -conjugation.

Stabilization by aromaticity in phenol is taken to be the same as that in benzene for which the following equilibrium gives a first estimate ($-36.2 \text{ kcal mol}^{-1}$, ignores differential hyperconjugation and ring strain effects):



One estimates $\Delta_r G^\circ$ (phenol \rightleftharpoons cyclohex-2,4-dien-1-one) = $\Delta_r H^\circ$ (phenol \rightleftharpoons cyclohex-2,4-dien-1-one) - $T\Delta_r S^\circ = 19\,800 - 298(\Delta_r S^\circ) \text{ cal mol}^{-1}$.

Phenol has one C_2 -axis whereas cyclohexadienone does not have any rotation axis. Thus $\Delta_r S^\circ$ (phenol \rightleftharpoons cyclohex-2,4-dien-1-one) = $R \ln 2 = 1.987 \ln 2 = 1.38 \text{ eu}$. This gives

$$\Delta_r G^\circ \text{ (phenol } \rightleftharpoons \text{ cyclohex-2,4-dien-1-one)} = 19\,800 - 298(1.38) = 19\,390 \text{ cal mol}^{-1}.$$

This leads to $\log K = -(\Delta_r G^\circ / RT) \cdot \log e = (-19\,390 / (1.987 \times 298)) \cdot 0.4343 = -14.22$, and $K = 0.6 \times 10^{-14}$.

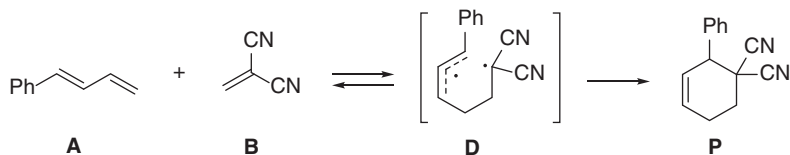
One can also use at 25°C $\log K = \Delta_r G^\circ \text{ (phenol } \rightleftharpoons \text{ cyclohex-2,4-dien-1-one)} / 1.36 = -14.25$ (see equation (1.8)).

Our estimated value of K (phenol \rightleftharpoons cyclohex-2,4-dien-1-one, gas phase) can be compared with the calculated (CBS-QB3) value $\kappa = 7.15 \times 10^{-14}$ reported by Zhu and Bozzelli, and with the gas phase (flash photolysis) experimental value $K = 10^{-13 \pm 1}$ [21].

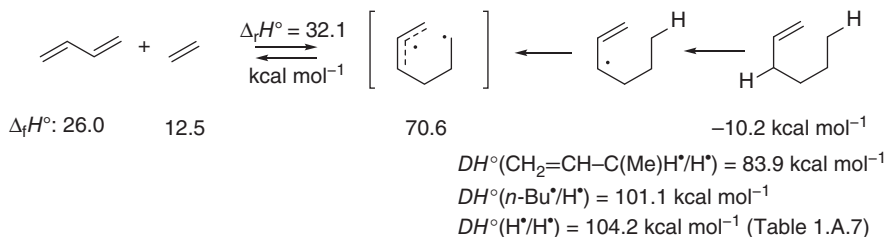
Problem 1.38 Can the Diels–Alder addition of methylenemalonodinitrile with 1-phenylbutadiene occur through a diradical intermediate? Which one?

Answer

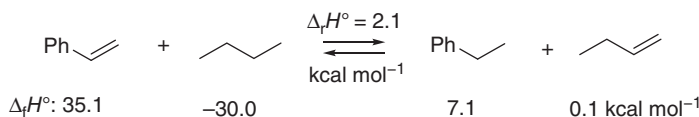
The most stable diradical resulting from the condensation of 1-phenylbutadiene with methylenemalonodinitrile possesses an allyl radical enjoying stabilization by the phenyl substituent and an alkyl radical doubly substituted by the two cyano substituents. Any other diradicals would not be as stable.



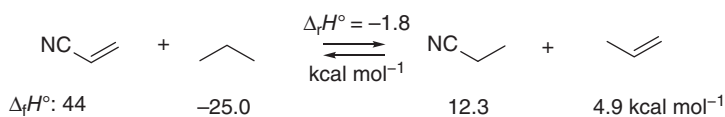
$\Delta_r H^\circ(\text{A} + \text{B} \rightleftharpoons \text{D})$ can be deduced from $\Delta_r H^\circ(\text{butadiene} + \text{ethylene} \rightleftharpoons \text{hex-2-en-1,6-diyl diradical}) = 32.1 \text{ kcal mol}^{-1}$ by considering π -conjugation stabilization of cycloaddends **A** and **B** introduced by their substituent with respect to butadiene and ethylene, and the phenyl and cyano substituent effect on the relative stability of the radicals they substitute. $\Delta_r H^\circ(\text{hex-2-en-1,6-diyl diradical}) = \Delta_r H^\circ(\text{hex-1-ene}) + DH^\circ(\text{but-3-en-2-yl}^\cdot/\text{H}^\cdot) + DH^\circ(\text{but-1-yl}^\cdot/\text{H}^\cdot) - DH^\circ(\text{H}^\cdot/\text{H}^\cdot) = -10.2 + 83.9 + 101.1 - 104.2 = 70.6 \text{ kcal mol}^{-1}$.



The stabilizing π -conjugation effect ($-2.1 \text{ kcal mol}^{-1}$) of the 1-phenyl substituent on butadiene can be evaluated by the standard heat of the following equilibrium, which compares the standard heats of hydrogenation of styrene and of propene.



With the next equilibrium one compares the heats of hydrogenation of the C=C double bond of but-1-ene with that of acrylonitrile. One finds that π -conjugation in acrylonitrile does not stabilize the system; in fact, the available data indicate a destabilization of c. 2 kcal mol^{-1} in acrylonitrile. This arises from the stabilizing $\sigma(\text{CH}_2)/\pi(\text{CN})$ hyperconjugative interaction in propionitrile, which is not present in acrylonitrile. This is not compensated by the stabilizing $\sigma(\text{CH}_3)/\pi(\text{C}=\text{C})$ hyperconjugation in propene, an interaction which is absent in propane.



Thus, it appears that the stabilizing effect introduced on the diene by the 1-phenyl substituent is compensated somewhat by a destabilization effect of the 1-cyano substituent effect in the dienophiles. The 1,1-dicyano substitution introduces an electrostatic repulsion effect due to the two geminal cyano dipoles, a repulsion effect that is probably similar to that in the diradical and cycloadduct. In the above analysis, one ignores the differential $\sigma(\text{CH}_2)/\pi(\text{C}=\text{C})$ hyperconjugation effects. The stabilization effects introduced by the phenyl group on diradical **D** must be a part of the phenyl substitution stabilizing effect on methyl radical (11 kcal mol^{-1} , Table 1.A.9) as the