

6.61-7.44 (m, 10 H), 7.98 (br, 1 H).

**2-[[4-(1-Methylethyl)phenyl]amino]-5-[6-(3-pyridinyl)hexyl]pyridine (24b)** was prepared similarly to **24a** above. From 10.3 g (0.025 mol) of **20b** there was obtained 8.5 g (92%) of **24b** suitable for use in the next step: IR (cm<sup>-1</sup>) (CHCl<sub>3</sub>) 3420 (w); MS, *m/e* (relative intensity) 373 (10), 277 (100); NMR (CDCl<sub>3</sub>) δ 1.25 (d, 6 H, *J* = 7 Hz), 1.3-1.75 (m, 8 H), 2.4-3.0 (m, 5 H), 6.38 (br, 1 H), 6.78-7.47 (m, 8 H), 7.99 (br, 1 H), 8.43 (br, 2 H).

**2-[[2-Bromo-4-(1-methylethyl)phenyl]amino]-5-[6-(1H-imidazol-1-yl)hexyl]pyridine (25a)**. A solution of 11.6 g (0.032 mol) of **24a** and 2.62 g (0.032 mol) of sodium acetate in 170 mL of acetic acid was held at room temperature with a water bath as 1.64 mL (0.032 mole of bromine was added over 10 min. After 1 h, the reaction mixture was evaporated to dryness and the residue was partitioned between ethyl acetate and dilute potassium carbonate. The organic layer was dried and evaporated, and the residue was purified by preparative HPLC eluting with 4:1:95 methanol-triethylamine-dichloromethane. The product-containing fractions were taken up in ethyl acetate, washed with water, dried, and evaporated to give 11.8 g (84%) of **25a** contaminated with a trace of dibrominated compound: MS, *m/e* (relative intensity) 442 (20), 440 (20); NMR (CDCl<sub>3</sub>) δ 1.20-1.95 (m, 14 H), 2.50 (m, 2 H), 2.86 (m, 1 H, *J* = 7 Hz), 3.91 (m, 2 H), 6.88 (br, 1 H), 7.06 (br, 1 H), 7.17-7.60 (m, 5 H), 7.97 (m, 1 H), 8.38 (m, 1 H).

**2-[[2-Bromo-4-(1-methylethyl)phenyl]amino]-5-[6-(3-pyridinyl)hexyl]pyridine (25b)** was obtained as above. With 7.6 g (0.020 mol) of **24b**, 1.6 g (0.020 mol) of sodium acetate, and 1.0 mL (0.020 mol) of bromine in 50 mL of acetic acid as starting material, there was obtained 4.3 g (48%): MS, *m/e* (relative intensity) 453 (11), 451 (11); high-resolution MS (molecular ion) calcd 451.1623, observed 451.1634; NMR (CDCl<sub>3</sub>) δ 1.21 (d, 6 H, *J* = 7 Hz), 1.3-1.75 (m, 8 H), 2.40-2.96 (m, 5 H), 6.64 (br, 1 H), 6.75 (d, 1 H, *J* = 9 Hz), 7.04-7.52 (m, 5 H), 7.82 (d, 1 H, *J* = 9 Hz), 8.04 (br, 1 H), 8.42 (br, 2 H).

**2-(1-Methylethyl)-8-[6-(1H-imidazol-1-yl)hexyl]-11H-pyrido[2,1-*b*]quinazolin-11-one (3a)** was prepared by carbonylation of **25a** as described above for **11**. From 11.8 g (0.0267

mol) of **25a**, 1.12 g (0.042 mole of triphenylphosphine, and 7.2 mL (0.03 mol) of tributylamine in 20 mL of *tert*-butyl alcohol and 1.1 mL of water, there was obtained, after preparative chromatography eluting with 2:1:97 methanol-triethylamine-dichloromethane and recrystallization from ethyl acetate-hexane, 3.66 g (35%) of **3a**: mp 77-82 °C; IR (cm<sup>-1</sup>) (CHCl<sub>3</sub>) 1682 (s), 1651 (s); MS, *m/e* (relative intensity) 388 (100); NMR (CDCl<sub>3</sub>) δ 1.30-1.95 (m, 14 H), 2.63 (m, 2 H), 3.11 (m, 1 H, *J* = 7 Hz), 3.83 (m, 2 H), 6.90 (br, 1 H), 7.05 (br, 1 H), 7.37-7.45 (m, 3 H), 7.75 (m, 2 H), 8.28 (br, 1 H), 8.64 (br, 1 H). Anal. Calcd for C<sub>24</sub>H<sub>28</sub>N<sub>4</sub>O: C, 74.20; H, 7.26; N, 14.42. Found: C, 74.12; H, 7.30; N, 14.52. Treatment with excess ethanolic hydrochloric acid, evaporation, and recrystallization from ethanol-ether afforded 4.17 g of the dihydrochloride salt, mp 251-256 °C. Anal. Calcd for C<sub>24</sub>H<sub>28</sub>N<sub>4</sub>O·2H<sub>2</sub>O: C, 62.47; H, 6.55; N, 12.14; Cl, 15.37. Found: C, 62.49; H, 6.35; N, 12.13; Cl, 15.09.

**2-(1-Methylethyl)-8-[6-(3-pyridinyl)hexyl]-11H-pyrido[2,1-*b*]quinazolin-11-one (3b)** was prepared from 4.0 g (8.84 mmol) of **25b**, 0.26 g (1.0 mmol) of triphenylphosphine, 0.35 g (0.5 mmol) of bis(triphenylphosphine) palladium dichloride, and 0.35 mL of water in 7 mL of *tert*-butyl alcohol as described above for **11**. The crude product was chromatographed over silica gel eluting with ethyl acetate and recrystallized from ethyl acetate-hexane to afford 2.27 g (65%): mp 62-64 °C; IR (cm<sup>-1</sup>) (CHCl<sub>3</sub>) 1683 (s), 1652 (s); MS, *m/e* (relative intensity) 399 (100); NMR (CDCl<sub>3</sub>) δ 1.20-1.80 (m, 14 H), 2.62 (m, 4 H), 3.10 (m, 1 H, *J* = 7 Hz), 7.08-7.73 (m, 6 H), 8.25 (br, 1 H), 8.40 (br, 2 H), 8.53 (br, 1 H). Anal. Calcd for C<sub>26</sub>H<sub>29</sub>N<sub>3</sub>O: C, 78.16; H, 7.32; N, 10.52. Found: C, 77.82; H, 7.34; N, 10.18.

**Acknowledgment.** We thank the members of the Physical Chemistry Department, Hoffmann LaRoche, Inc., for determining the spectra and microanalyses of the new compounds reported herein. We thank R. W. Kierstead for his support and encouragement during the course of these studies.

## Enones with Strained Double Bonds. 10. Use of Flash Vacuum Pyrolysis To Obtain Bicyclo[3.3.1]non-1-en-3-one<sup>1</sup>

Kay Ann Campbell,<sup>2a</sup> Herbert O. House,<sup>\*2a</sup> Bruce W. Surber,<sup>2b</sup> and Walter S. Trahanovsky<sup>\*2b</sup>

School of Chemistry, Georgia Institute of Technology, Atlanta, Georgia 30332, and Department of Chemistry, Iowa State University, Ames, Iowa 50011

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Pyrolysis of the furan adducts **3** in the gas phase at low pressure (10<sup>-4</sup> mm) formed a mixture of furan and the bicyclic enone **2a** with a bridgehead double bond that could be collected in a cold trap. NMR, IR, and UV spectra of this mixture were obtained. Although the enone **2a** reacted rapidly with methanol and more slowly with furan, efforts to find products from the reaction of the enone **2a** with either ground-state oxygen or one of several unsaturated compounds **9**, **11**, **12**, or **13** were unsuccessful. Instead, at temperatures above -40 °C the enone **2a** reacted with itself to form a mixture of the three dimers **4a**, **4b**, and **4c**.

In earlier studies<sup>3-5</sup> bicyclo[3.3.1]non-1-en-3-one (**2a**, Scheme I), prepared either by dehydrobromination of the

bromo ketone **1b** or by pyrolysis of the furan adduct **3** (a mixture of diastereoisomers), was found to undergo reaction with a variety of other materials such as nucleophiles or dienes. In the absence of other reagents, the enone **2a** reacted rapidly with itself even at room temperature in the

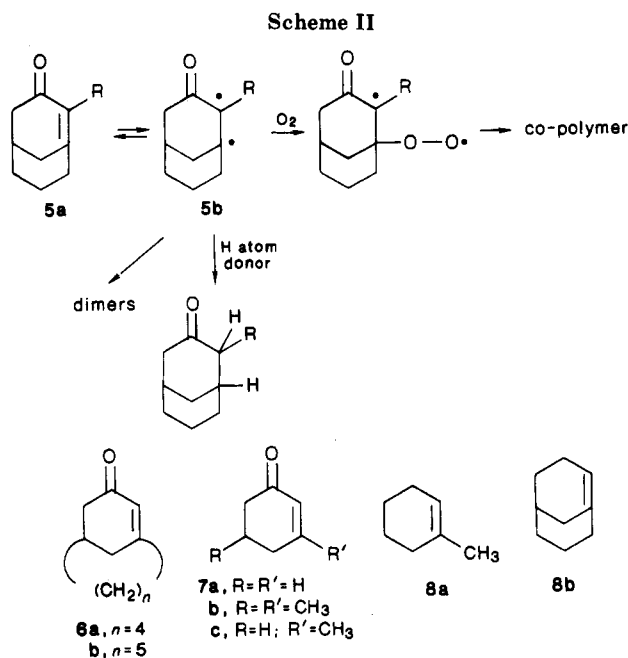
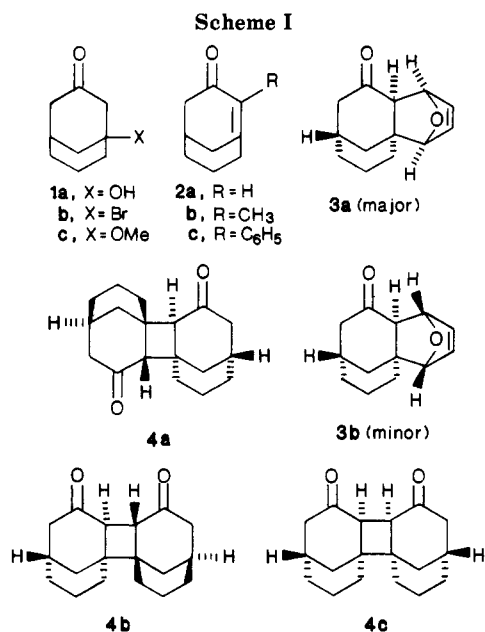
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(2) (a) School of Chemistry, Georgia Institute of Technology, Atlanta, GA 30332. (b) Department of Chemistry, Iowa State University, Ames, IA 50011.

(3) For recent work with bridgehead enones in other laboratories, see: (a) Magnus, P.; Gallagher, T.; Brown, P.; Huffman, J. C. *J. Am. Chem. Soc.* **1984**, *106*, 2105. (b) Kraus, G. A.; Hon, Y.-S. *J. Org. Chem.* **1986**, *51*, 116. (c) For recent reviews of bridgehead olefins, see: Shea, K. J. *Tetrahedron* **1980**, *36*, 1683. Becker, K. B. *Ibid.* **1980**, *36*, 1717.

(4) House, H. O.; DeTar, M. B.; VanDerveer, D. *J. Org. Chem.* **1979**, *44*, 3793.

(5) (a) House, H. O.; DeTar, M. B.; Sieloff, R. F.; VanDerveer, D. *J. Org. Chem.* **1980**, *45*, 3545. (b) House, H. O.; Outcalt, R. J.; Clifton, M. D. *Ibid.* **1982**, *47*, 2413. (c) House, H. O.; Outcalt, R. J.; Haack, J. L.; VanDerveer, D. *Ibid.* **1983**, *48*, 1654. (d) House, H. O.; Sieloff, R. F.; Lee, T. V.; DeTar, M. B. *Ibid.* **1980**, *45*, 1800. (e) House, H. O.; Lee, T. V. *Ibid.* **1979**, *44*, 2819. (f) For a review, see: House, H. O. In *Stereochemistry and Reactivity of Systems Containing π Electrons*; Watson, W. H., Ed.; Verlag Chemie International: Deerfield Beach, FL, 1983; pp 279-317.



dark to form a mixture of three isomeric 2 + 2 cycloadducts **4**. This cycloaddition could be retarded sterically by placing a methyl substituent at position 2 of the strained enone **2a** but then an alternative dimerization reaction, originally suggested to be a room temperature ene reaction, converted the 2-methyl enone **2b** into a different type of dimer.<sup>5a</sup> Finally, by placing a phenyl substituent at position 2 of the enone **2a**, we were able to isolate substituted bicyclo[3.3.1] enone **2c** that was stable at 25 °C in the absence of nucleophiles or molecular oxygen.<sup>5c</sup> Interestingly, this phenyl-substituted enone **2c** reacted with ground-state oxygen, even in the dark at -20 °C, to form a 1:1 oxygen-enone co-polymer. The enone **2c** also reacted with 1,3-butadiene at 100 °C to form a mixture of 2 + 2 and 2 + 4 cycloadducts.

A possible interpretation for the dimerization reactions, the reaction with oxygen, and certain other reactions observed with bicyclo[3.3.1]nonene systems involves the thermal excitation of a geometrically distorted ground state **5a** (Scheme II) to diradical state **5b**. The suggested diradical reactions of the bicyclo[3.3.1] system **5b** are analogous to the dimerization and H atom abstraction reactions observed when cyclohexenone (**7a**) is excited photochemically.<sup>6</sup> Failure to observe analogous reactions with the less highly distorted bicyclo[4.3.1]decenone **6a** and bicyclo[5.3.1]undecenone **6b** could be attributed to an energy difference between the less strained ground states and the diradical states that is too large for thermal excitation to be probable. To explore further the idea of diradical intermediate **5b**, we desired more information about the properties and reactions of the parent bicyclo[3.3.1] enone **2a**.

Because of the rapid reaction of the enone **2a** with itself, we concluded that the parent enone **2a** could be isolated only at low temperatures where the rate of dimerization would be retarded. We considered both the preparation of precursors<sup>5b</sup> that might be photolyzed to form the enone **2a** at low temperatures and the pyrolysis of the furan adduct **3** in the gas phase followed by condensation of the enone **2a** in a cold trap. When gas-phase pyrolysis of the furan adduct **3** was studied<sup>4</sup> at low concentrations in nitrogen at atmospheric pressure, most of the enone **2a** was converted to dimers **4** before the gas stream containing the

enone **2a** and a sizeable volume of nitrogen could be cooled sufficiently to trap the enone. Therefore, we turned to an alternative pyrolysis technique, flash vacuum pyrolysis (or thermolysis),<sup>7</sup> in which the furan adduct **3** at low pressure (10<sup>-4</sup> mm or less) was pyrolyzed at about 500 °C. The volatile products that escaped from the pyrolysis chamber could be chilled rapidly by collection in a trap cooled with liquid nitrogen.<sup>7,8</sup>

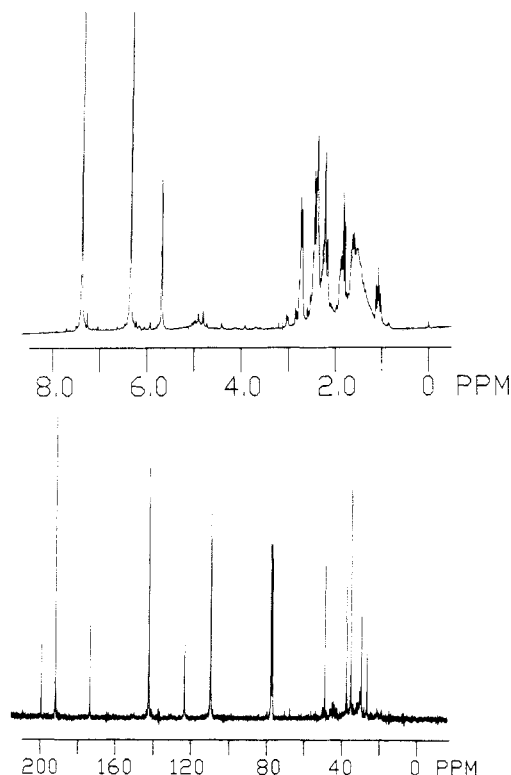
By adjusting the temperature of the sample inlet tube to control the rate of distillation of the furan adduct **3** into the pyrolysis chamber, we were able to find conditions (ca. 0.5 g of adduct **3** was passed through the apparatus during a 4–6-h period) where the volatile materials collected in the cold trap consisted of furan and the enone **2a** with little, if any, of the dimers **4** or the starting furan adduct **3**. Mixtures of the pyrolysis products (furan and enone **2a**) were dissolved in cold (-78 °C) hexane and the cold solution was allowed to warm slowly until precipitation of the hexane-insoluble dimers **4** was observed. These observations indicated that relatively rapid dimerization of the enone **2a** to form the dimers **4** began to occur as the hexane solution was warmed above -40 °C.

Cold (-60 to -40 °C) solutions of the enone-furan mixture in a mixture of CDCl<sub>3</sub> and CS<sub>2</sub> were used to measure the <sup>13</sup>C NMR and <sup>1</sup>H NMR spectra (Figure 1). When a cold (-78 °C) solution of the mixture in CH<sub>2</sub>Cl<sub>2</sub> was used to measure the IR spectrum (Figure 2), the C=O and C=C stretching vibrations of the enone **2a** were apparent. These spectra, especially the IR and <sup>13</sup>C NMR spectra, provide clear evidence that the material collected in the cold trap is a mixture of the enone **2a** and furan with no major byproducts. As the solution used for IR measurement was slowly warmed first to 0 °C and then to 20 °C, the two bands initially observed were replaced by the higher frequency saturated C=O stretching vibration of the dimers **4**.

(6) Pienta, N. J.; McKimmey, J. E. *J. Am. Chem. Soc.* **1982**, *104*, 5501.

(7) For recent reviews of flash vacuum thermolysis, see: (a) Wiersum, U. E. *Recl. Trav. Chim. Pays-Bas* **1982**, *101*, 317, 365. (b) Schiess, P.; Rutschmann, S. *Chimia* **1985**, *39*, 213–224. (c) Karpf, M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 414. (d) For a description of the apparatus used, see: Trahanovsky, W. S.; Ong, C. C.; Pataky, J. G.; Weitl, F. L.; Mullen, P. W.; Clardy, J. C.; Hansen, R. S. *J. Org. Chem.* **1971**, *36*, 3575.

(8) Commercial flash vacuum pyrolysis apparatus is available from Kontes Scientific Glassware; Vineland, NJ 08360.



**Figure 1.** The NMR spectra of the pyrolysis product from furan adduct **3** containing a mixture of furan and bicyclo[3.3.1]non-1-en-3-one (**2a**) dissolved in a mixture (1:1 v/v) of  $\text{CS}_2$  and  $\text{CDCl}_3$ . The upper curve is the  $^1\text{H}$  NMR spectrum measured at  $-40^\circ\text{C}$  and the lower curve is the  $^{13}\text{C}$  NMR spectrum measured at  $-60^\circ\text{C}$ . The peaks in the  $^{13}\text{C}$  NMR spectrum at 191.8 and 76–78 ppm are attributable to the solvents,  $\text{CS}_2$  and  $\text{CDCl}_3$ , respectively.

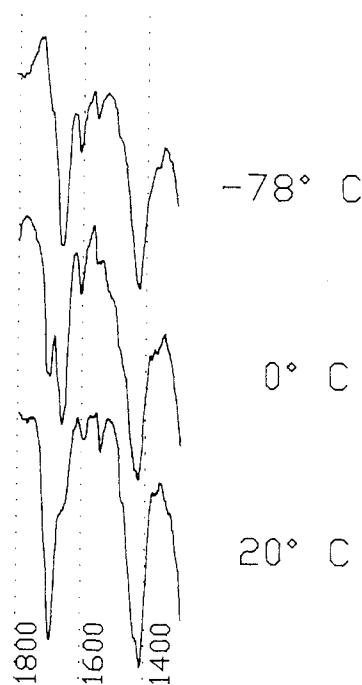
**Table I. Comparison of Infrared and Nuclear Magnetic Resonance Spectra for Various Cyclohexenone Derivatives**

cmpd	solvent	IR stretch, $\text{cm}^{-1}$		proton NMR vinyl CH signal, ppm	$^{13}\text{C}$ NMR signals, ppm	
		C=O	C=C		C=O	C=C
<b>7c<sup>a</sup></b>	$\text{CCl}_4$	1667	1633			
	$\text{CH}_2\text{Cl}_2$	1662	1628			
	$\text{CDCl}_3$ + $\text{CS}_2$			5.86	199.0	126.5, 162.2
<b>7b<sup>a</sup></b>	$\text{CCl}_4$	1671	1632	5.74		
	$\text{CH}_2\text{Cl}_2$	1665	1635			
	$\text{CDCl}_3$ + $\text{CS}_2$			5.86	197.5	125.2, 160.1
	$\text{CDCl}_3$			5.84	198.1	125.2, 160.7
<b>6b<sup>b</sup></b>	$\text{CCl}_4$	1673	1632	5.70		
	$\text{CDCl}_3$				198.9	126.4, 165.0
<b>6a<sup>c</sup></b>	$\text{CCl}_4$	1680+	1620	5.53		
		1667				
	$\text{CDCl}_3$				198.9	122.7, 164.1
<b>2a<sup>a</sup></b>	$\text{CH}_2\text{Cl}_2$	1663	1610			
	$\text{CDCl}_3$ + $\text{CS}_2$			5.67	199.5	123.0, 173.3
<b>2c<sup>a</sup></b>	$\text{CCl}_4$	1680				
	$\text{CDCl}_3$				199.6	137.9, 163.5
<b>8b<sup>d</sup></b>	none		1620			
	$\text{CCl}_4$			5.65		
	$\text{CDCl}_3$					125.1, 146.8
<b>8a<sup>a</sup></b>	$\text{CCl}_4$		1670	5.38		
	$\text{CDCl}_3$					121.0, 133.6

<sup>a</sup>Measurements obtained in this study. <sup>b</sup>Reference 5d.

<sup>c</sup>Reference 5e. <sup>d</sup>Becker, K. B. *Helv. Chim. Acta* 1977, 60, 81.

Table I compares the IR and NMR data for the series of bicyclic enones **2a**, **6a**, and **6b** with the two unstrained monocyclic enones **7b** and **7c**. Data for the bicyclic olefin



**Figure 2.** The 6- $\mu\text{m}$  regions in the IR spectra of the pyrolysis product from furan adduct **3** containing a mixture of furan and bicyclo[3.3.1]non-1-en-3-one (**2a**) dissolved in  $\text{CH}_2\text{Cl}_2$ . The top curve, measured at  $-78^\circ\text{C}$ , shows the C=O and C=C stretching vibrations for the enone **2a**. Subsequent curves at the middle (measured at  $0^\circ\text{C}$ ) and at the bottom (measured at  $20^\circ\text{C}$ ) of the figure show increasing amounts of C=O absorption attributable to the enone dimers **4** as the original cold ( $-78^\circ\text{C}$ ) solution was allowed to warm to room temperature in the IR cell.

**8b** and the monocyclic model **8a** are also included. The IR and NMR data for the C=O group and the  $\alpha$  CH group of the double bond are similar in the strained and in the unstrained compounds, supporting the predictions of MMPI molecular mechanics calculations<sup>5</sup> that these portions of the enones are not substantially altered by the presence of the bridgehead double bond. The  $^{13}\text{C}$  NMR signal for the  $\beta$  carbon of the enone system varied in some of the compounds, but no clear trend was apparent. The most consistent variation was a decreased frequency of the infrared C=C stretching (suggesting a weaker bond) with increasing double bond distortion.

Solutions of the pyrolysis products in either cold ( $-78^\circ\text{C}$ ) ether or cold ( $-40^\circ\text{C}$ )  $\text{CH}_3\text{CN}$  were used to measure the UV spectra. The relatively high freezing point of acetonitrile complicated measurement of the spectrum in this solvent because of concurrent dimerization during the measurement. Consequently, we were able to observe the more intense shorter wavelength transition at 264 nm in  $\text{CH}_3\text{CN}$  but not the weaker longer wavelength transition. In ether solution where lower temperatures could be maintained both peaks could be observed. Table II summarizes the UV data for the bicyclic enones **2a**, **6a**, and **6b** and the monocyclic models **7b** and **7c**. This table also includes the estimates (from MMPI molecular mechanics calculations<sup>5</sup>) of the C=C twisting deformation and the pyramidal distortion of each olefinic C atom along with the estimated distortion energy of each C=C group. The UV data for the enone **2a** followed a previously noted<sup>5d</sup> trend in which each increase in the distortion of the C=C results an additional shift of both the  $\pi-\pi^*$  and  $n-\pi^*$  maxima to longer wavelengths. We attribute both this change and related change in electrochemical reduction potentials<sup>5d</sup> to the idea that the highest occupied molecular orbital in both the photoexcited state and in the electro-

**Table II. Comparison of Ultraviolet Spectra, Calculated C=C Distortion Angles, and Calculated Distortion Energies for Various Cyclohexenone Derivatives**

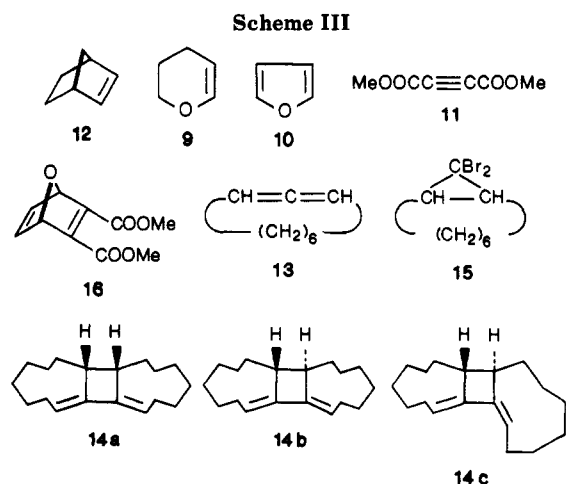
cmpd (solv)	$\pi-\pi^*$ band, nm ( $\epsilon$ )	$n-\pi^*$ band, nm ( $\epsilon$ )	est C=C twist angle, deg; pyr distn, deg <sup>a</sup>	est C=C distn energy, kcal/mol <sup>b</sup>
7c <sup>c</sup> (Et <sub>2</sub> O)	227 (13 900)	333 (28)		
7b <sup>d</sup> (CH <sub>3</sub> CN)	232 (13 800)	323 (25)	2.5 (2,4)	0.2
6b <sup>d</sup> (CH <sub>3</sub> CN)	240 (14 800)	335 (50)	4 (1, 9)	0.5
6a <sup>d</sup> (CH <sub>3</sub> CN)	250 (5070)	345 (92)	14 (14, 21)	4.7
2a <sup>c,e</sup> (CH <sub>3</sub> CN)	264 (-) e	e	21 (19, 37)	11.3
2a <sup>c</sup> (Et <sub>2</sub> O)	266 (ca. 7700)	355 (ca. 300)		

<sup>a</sup>The two values listed in parentheses are the calculated angles by which the substituents bound to each olefinic C atom deviate from planarity. <sup>b</sup>The C=C distortion energies were calculated from the twisting and pyramidal distortion angles by the relationship of Ermer, O. Z. Naturforsch. 1977, 32B, 837. <sup>c</sup>Measurement obtained in this study. <sup>d</sup>Reference 5d. <sup>e</sup>Experimental problems prevented us from obtaining a reliable wavelength value for the longer wavelength peak in acetonitrile solution and for determining the concentration of the enone 2a in the cell.

chemically generated radical anion has a node between the  $\alpha$  and  $\beta$  C atoms and consequently would not be destabilized by a twist in the molecule at this point. Thus, the C=C distortion destabilizes mainly the ground state leading to a smaller energy difference (and consequent longer wavelength UV absorption) between the ground and excited states.

When cold ( $-78$  °C) solutions of the pyrolysis products were mixed with either methanol or furan and then allowed to warm to room temperature, the enone 2a present was converted to either the methyl ether 1c or to the furan adducts 3. The yields of these products 3 or 1c, based upon the amount of starting furan adduct 3 pyrolyzed, were determined by adding a known weight of internal standard (borneol) and then analyzing the mixture with HPLC apparatus that had been calibrated with known mixtures of authentic materials. The yields of the products 3 or 1c were in the range 40–55%. A known mixture of the adducts 3 and an internal standard (dimethyl phthalate) was subjected to the usual pyrolysis procedure and the cold mixture of pyrolysis products was quenched with methanol to establish that the enone 2a formed in the pyrolysis chamber was not being lost mechanically by ineffective trapping or leakage. Although the yield of the methyl ether 1c (from enone 2a) was only 53%, 98% of the internal standard was collected in the cold trap. Therefore, we conclude that about half of the enone 2a or its precursor 3 is not escaping from the pyrolysis zone to be collected in the cold trap. Although the initial material formed may be the dimers 4 that are deposited on the walls of the quartz pyrolysis tube and beads, at the end of the pyrolysis none of the dimers 4 can be recovered by washing the pyrolysis tube and packing with either CH<sub>2</sub>Cl<sub>2</sub> or CHCl<sub>3</sub>, both of which are good solvents for the dimers 4. These observations indicate that the material deposited in the pyrolysis chamber is either insoluble initially or becomes insoluble after being heated to 500 °C for several hours.

With mixtures of the enone 2a and furan available, we explored the possible reaction of the enone 2a with ground-state oxygen and the possible cycloaddition reactions of the enone 2a with various unsaturated compounds. The unsaturated compounds studied included the electron-poor dimethyl acetylenedicarboxylate (11, Scheme III), the electron-rich dihydropyran 9, and two strained olefins, norbornene (12) and the cyclic allene 13. The cyclic allene 13 chosen is the one that dimerizes to form the dienes 14 when heated above 100 °C.<sup>9–11</sup> In all cases, the



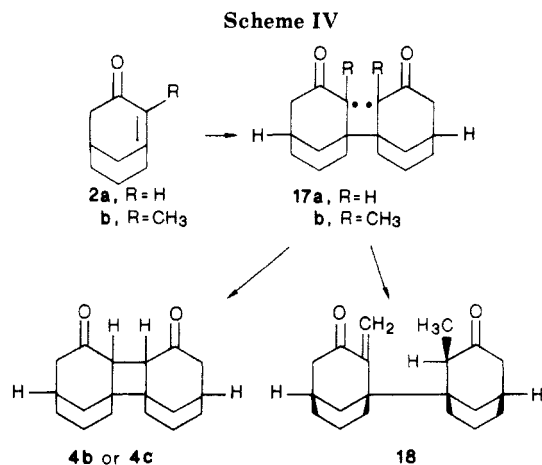
outcome of attempts to trap the enone 2a with these other reactants was the formation of the three dimers 4 accompanied in some cases by lesser amounts of the furan adducts 3. The thought that temperatures higher than  $-40$  °C might be required to promote some of the enone 2a to a diradical intermediate 5b prompted us to explore the possible reaction of the enone 2a, generated from the bromo ketone 1b and triethylamine at 25 °C, with strained olefins 12 and 13. Again only the usual dimers 4 were isolated and no adduct incorporating one of the olefins 12 or 13 was observed.

These observations force us to conclude that, although the phenyl-substituted enone 2c may be reacting as a diradical intermediate 5b, the parent enone 2a clearly is not. Furthermore, the fact that all three dimers 4 have stereochemistry corresponding to syn-syn and not syn-antarafacial cycloaddition indicates that the dimers are probably not formed by concerted 2 + 2 cycloaddition processes. Consequently, the most likely reaction path for the formation of the dimers 4 appears to be the reaction of two molecules of the enone 2a to form a dimeric di-

(9) For reviews of the properties of allenes, see: (a) Taylor, D. R. *Chem. Rev.* 1967, 67, 317. (b) Hopf, H. In *The Chemistry of Ketenes, Allenes, and Related Compounds*, Part 2; Patai, S., Ed.; Wiley: New York, 1980; Chapter 20, p 779. (c) Hopf, H. In *The Chemistry of the Allenes*, Vol. 2; Landor, S. R., Ed.; Academic Press: New York, 1982; p 525.

(10) Dimerization of the cyclic allene 13 occurs when a sample of the allene is heated to 135 °C in a sealed tube for 18 h. See: Skattebol, L.; Solomon, S. J. *Am. Chem. Soc.* 1965, 87, 4506.

(11) Moore, W. R.; Bach, R. D.; Ozretich, T. M. *J. Am. Chem. Soc.* 1969, 91, 5918.



radical, e.g. **17a** (Scheme IV), that can subsequently close to form a dimer (e.g. **4b**). In this process, the distortion energy associated with two molecules of the starting enone **2a** would be released as the intermediate **17a** was formed. We now believe that the reaction of the 2-methyl enone **2b** to form dimer **18** is also best explained via the formation of the 1,4-diradical **17b** that subsequently disproportionates. The failure of the less highly distorted enones **6a** and **6b** to undergo analogous reactions even at 200 °C<sup>5</sup> could be attributed to the substantially smaller amount of distortion energy that would be released if two of these less strained molecules formed a dimeric diradical.

### Experimental Section<sup>12</sup>

**Preparation of the Bromo Ketone 1b.** Following a modification of a previously described procedure,<sup>4</sup> a solution of 30.65 g (236 mmol) of ethyl acetoacetate and 21.9 g (228 mmol) of cyclohexenone in sodium methoxide (from 5.5 g or 239 mmol of Na and 250 mL of MeOH) was refluxed for 35 h and then cooled and treated with a solution of 31.4 g (477 mmol) of 85% KOH in 83 mL of water and 100 mL of MeOH. The resulting solution was refluxed for 12 h and then cooled, diluted with 100 mL of water, acidified to pH 3 by the addition of aqueous 3% HCl, and extracted with four 100-mL portions of methylene chloride. The combined organic extracts were dried and concentrated to leave 32.04 g (87%) of the crude ketol **1a** as colorless plates, mp 220–223 °C (lit.<sup>4</sup> mp 232–234 °C), that was identified with previously described samples by comparison of IR and NMR spectra. Reaction of 13.82 g (89.7 mmol) of the crude ketol **1a** with 9.56 g (35.4 mmol) of PBr<sub>3</sub> in 130 mL of anhydrous benzene as previously described<sup>4</sup> yielded 17.90 g (90%) of the bromo ketone **1b** as a colorless solid, mp 81.5–83 °C (lit.<sup>4</sup> mp 83.4–84.4 °C), that was identified with previous samples by comparison of IR, NMR, and mass spectra.

**Preparation of the Furan Adducts 3.** A solution of 17.0 g (79 mmol) of the bromo ketone **1b** in 50 mL of freshly distilled furan was treated with 22.3 g (220 mmol) of anhydrous triethylamine. The resulting solution, from which a colorless precipitate began to separate immediately, was stirred at 25 °C under a nitrogen atmosphere for 20 h and then partitioned between water

and methylene chloride. After the organic layer had been dried and concentrated, distillation of the residual yellow liquid (15.4 g) under reduced pressure separated 14.8 g (92%) of a mixture of the stereoisomeric furan adducts **3** as a colorless liquid, bp 117–122 °C (0.1 mm),  $n_D^{25}$  1.5315, [lit.<sup>4</sup> bp 117–120 °C (0.12 mm),  $n_D^{25}$  1.5323 (major stereoisomer)]. This material contained (NMR analysis) ca. 77% of the major isomer **3a** (NMR signal at 5.33 ppm) and ca. 23% of the minor isomer **3b** (NMR signal at 5.09 ppm).

**Pyrolysis of the Furan Adducts 3.** The pyrolysis apparatus utilized a commercial<sup>8</sup> quartz sample chamber and pyrolysis tube packed with 6-mm lengths of 6-mm o.d. quartz tubing and joined to a condenser and cold trap with an O-ring joint. This commercial apparatus is based on a previously published description.<sup>7</sup> The horizontally mounted pyrolysis tube was heated with a 600-W electric furnace while the temperature at the center of the furnace was monitored with a pyrometer. The actual temperature inside the pyrolysis tube was not measured. The sample chamber was warmed by placing it inside a 25 cm by 10 cm diameter aluminum cylinder that was heated with electrical tape and fitted with a thermometer to measure its temperature. The entire apparatus was evacuated with an oil diffusion pump to a pressure less than 10<sup>-4</sup> mm before each pyrolysis was begun. During the pyrolysis the differential pressure between the end of the pyrolysis chamber and the exit from the trap cooled with liquid nitrogen was measured with a MKS Baratron Pressure Meter, Type 144. During a typical pyrolysis experiment the electric furnace was held at 530 °C, the sample chamber was kept at 70–73 °C, and the differential pressure between the entrance and exit of the cold trap was 5 × 10<sup>-4</sup> mm. In typical experiments, a 450–500-mg (2.21–2.45 mmol) sample of the furan adducts **3** was used for each pyrolysis and the pyrolysis reaction was conducted over a period of approximately 5 h. The pyrolysate collected in the liquid nitrogen cooled trap was maintained under an N<sub>2</sub> atmosphere while it was warmed to -78 °C, then precooled solvents and/or reactants were added to the cold trap.

**Spectra of Pyrolysis Products. A. NMR Spectra.** The pyrolysate from 524 mg of adduct **3** was dissolved in 1.0 mL of a cold (-78 °C) mixture of CS<sub>2</sub> and CDCl<sub>3</sub> (1:1 v/v) and the <sup>13</sup>C NMR spectrum (75 MHz) was measured at -60 °C. In addition to solvent absorption, the following peaks were observed: 199.5 (1 C, C=O), 173.3 (1 C, vinyl C), 142.0 (2 C, furan), 123.0 (1 C, vinyl C), 109.2 (2 C, furan), 48.6 (1 C), 37.0 (1 C), 34.5 (2 C), 29.0 (1 C), 25.9 ppm (1 C). In a similar experiment, the pyrolysate from 541 mg of the adduct **3** was dissolved in 1.8 mL of a cold (-78 °C) mixture of CS<sub>2</sub> and CDCl<sub>3</sub> (1:1 v/v) and the <sup>1</sup>H NMR spectrum (300 MHz) was measured at -40 °C. The following absorptions were observed: δ 7.37 (2 H, m, furan CH), 6.33 (2 H, m, furan CH), 5.67 (1 H, s, vinyl CH), 1.0–3.0 (m, aliphatic CH, see Figure 1).

For comparison, solutions of 3-methylcyclohexenone (**7c**) in a mixture of CS<sub>2</sub> and CDCl<sub>3</sub> (1:1 v/v) were prepared for NMR measurement. The <sup>1</sup>H NMR spectrum (300 MHz) exhibited the following absorption: δ 5.86 (1 H, partially resolved multiplet, vinyl CH), 2.25–2.35 (4 H, m, aliphatic CH), 1.95–2.05 (5 H, m, aliphatic CH including a methyl singlet at 1.97). The <sup>13</sup>C NMR spectrum of the enone **7c** exhibited the following absorption: [CS<sub>2</sub> and CDCl<sub>3</sub> (1:1 v/v), multiplicity determined by a D(istortionless) E(nhancement) by P(olarization) T(ransfer)], 199.0 (s), 162.2 (s), 126.5 (d), 36.8 (t), 30.8(t), 24.1 (q), 22.5 ppm (t).

**B. IR Spectra.** The pyrolysate from 230 mg of adduct **3** was dissolved in 10 mL of cold (-78 °C) CH<sub>2</sub>Cl<sub>2</sub> and the solution was transferred to a precooled (-78 °C), variable-temperature IR cell.<sup>13</sup> The IR spectrum, measured at -78 °C, exhibits bands in the 6-μm region at 1663 (conjugated C=O) and 1610 cm<sup>-1</sup> (conjugated C=C). As illustrated in Figure 2, when this cold solution was allowed to warm, first to 0 °C and then to 20 °C, a new band at 1700 cm<sup>-1</sup>, attributable to the nonconjugated C=O stretching of

(12) All melting points are corrected and all boiling points are uncorrected. Unless otherwise noted, MgSO<sub>4</sub> was employed as a drying agent. The IR spectra were determined with either a Perkin-Elmer Model 299 or a Beckman Model 4240 infrared recording spectrophotometer fitted with a grating. The UV spectra were determined with either a Gilford response spectrophotometer or a Perkin-Elmer Model 202 recording spectrophotometer. The <sup>1</sup>H NMR spectra were determined at 60 MHz with a Varian Model T-60A NMR spectrometer or at 300 MHz with a Bruker Model WM-300 NMR spectrometer. The <sup>13</sup>C NMR spectra were determined at 75 MHz with a Bruker Model WM-300 NMR spectrometer. The NMR chemical shift values are expressed in ppm relative to a Me<sub>4</sub>Si internal standard. The mass spectra were obtained with either a Hitachi Perkin-Elmer Model RMU-7 or a Varian MAT Model 112S mass spectrometer. All reactions involving strong bases or reactive organometallic intermediates were performed under a nitrogen atmosphere.

(13) A variable-temperature infrared cell, Model VLT-2, was purchased from Research & Industrial Instruments Co., London, England. The cell, with NaCl windows and a 0.1-mm pathlength spacer, was attached to a hollow cylinder filled with liquid coolant and was contained within a metal Dewar fitted with NaCl windows. The temperature of the cell was measured with a thermocouple. Cold solutions were transferred to the precooled cell through ports connected to stainless steel tubing.

the dimers **4**, became the dominant feature in the 6- $\mu\text{m}$  region. For comparison, the IR spectrum of a  $\text{CH}_2\text{Cl}_2$  solution of the unstrained cyclic enone **7c** exhibits bands in the 6- $\mu\text{m}$  region at 1662 (conjugated  $\text{C}=\text{O}$ ) and 1628  $\text{cm}^{-1}$  (conjugated  $\text{C}=\text{C}$ ).

**C. UV Spectra.** The pyrolysate from 334 mg (1.64 mmol) of adduct **3** was dissolved in 2.0 mL of cold ( $-50^\circ\text{C}$ )  $\text{CH}_3\text{CN}$ . The resulting solution was warmed to  $-40^\circ\text{C}$  and transferred to a precooled ( $-40^\circ\text{C}$ ) variable-temperature IR cell (pathlength 0.1 mm).<sup>13</sup> The UV spectrum of enone **2a**, measured at  $-40^\circ\text{C}$ , exhibited the following absorption peaks, nm (absorbance): 330–360 (br, ca. 0.1, enone), 264 (0.77, enone), and 209 (1.16, furan). After the solution had been warmed to room temperature (with precipitation of the insoluble dimers **4**), the remaining solution exhibited a UV peaks at 209 nm (attributable to furan) and with weak absorption at 287 nm (attributable to the furan adducts **3** and/or the dimers **4**).

In another experiment, the pyrolysate from 206 mg (1.01 mmol) of adduct **3** was dissolved in 8.2 mL of cold ( $-78^\circ\text{C}$ )  $\text{Et}_2\text{O}$ . A 15.0  $\mu\text{m}$  aliquot of this solution was diluted to 3.41 mL with cold ether and then transferred to a precooled quartz UV cell (1.0 cm pathlength). The cold solution exhibited the following peaks, nm (absorbance): 266 (1.531), 356 (0.0589). When the solution was warmed to  $25^\circ\text{C}$  (with precipitation of the insoluble dimers **4**), the remaining solution exhibited weak absorption at 287 nm (attributable to the furan adducts **3** and/or the dimers **4**). A 4.0-mL aliquot of the original solution was allowed to warm to room temperature and then mixed with 22.0 mg of (+)-borneol for HPLC analysis to estimate the concentration of the enone **2a**. The calculated yields of products were 2.24 mg of dimer **4a**, 15.50 mg of dimer **4b**, and 6.68 mg of dimer **4c** corresponding to 0.022 mmol of dimers **4** or 0.045 mmol of enone **2a** per milliliter in the original solution. This value allows us to estimate the molecular extinction coefficients as 7700 and 300 for the peaks at 266 nm and 357 nm.

**Analysis of Products Formed in the Pyrolysis Experiments.** Weighed aliquots of the crude product mixtures were each mixed with a weighed sample of (+)-borneol as an internal standard. The resulting mixtures were analyzed with an HPLC apparatus equipped with a refractive index detector and fitted with two 25-cm columns each packed with 10- $\mu\text{m}$  silica gel. An  $\text{EtOAc}$ -hexane mixture (1:4 v/v) was employed as an eluent. Utilizing known mixtures of authentic samples, the following retention times and response factors were determined for the various components being analyzed: (+)-borneol (internal standard), 10.0 min, 1.00; bromo ketone **1b**, 8.9 min, 0.96; dimer **4a**, 14.3 min, 0.85; dimer **4b**, 29.4 min, 0.77; dimer **4c**, 34.1 min, 0.73; methyl ether **1c**, 25.9 min, 0.92; furan adducts **3** (isomers not resolved), 15.5 min, 0.91; dimethyl phthalate, 11.1 min, 1.03. The response factors for the two separate furan adducts (not resolved with the HPLC system used) were 1.08 for the major isomer **3a** and 0.81 for the minor isomer **3b**. With the same HPLC system, the retention times for other reactants studied were furan (**10**), 4.5 min; norbornene (**12**), 4.5 min; dihydropyran (**9**), 5.1 min; the allene **13**, 5.7 min; the allene dimers **14**, 11.6 (major isomer), 8.0, and 6.6 min. Under these HPLC conditions, the ketol **1a** was not eluted from the column. Throughout this manuscript, all HPLC retention time values are expressed relative to (+)-borneol having a value of 10.0 min.

In a related repetition of an earlier experiment,<sup>4</sup> a solution of 2.00 g (9.2 mmol) of the bromo ketone **1b** in 10 mL of anhydrous triethylamine was stirred at  $25^\circ\text{C}$  for 9 h and then partitioned between water and  $\text{CH}_2\text{Cl}_2$ . The organic phase was washed successively with aqueous  $\text{HCl}$  and with aqueous  $\text{NaCl}$  and then dried and concentrated to leave 1.59 g of crude product as a colorless solid. An aliquot of this material was mixed with a known weight of borneol (internal standard) for HPLC analysis. The calculated yields were 3% of dimer **4a**, 58% of dimer **4b**, and 19% of dimer **4c** (80% yield of dimers **4**).

Since the order of elution for the dimers **4** did not seem consistent with the TLC  $R_f$  values reported earlier,<sup>4</sup> we reexamined the TLC behavior of the dimers on plates coated with silica gel and eluted with  $\text{EtOAc}$ -hexane (4:1 v/v). Two of the previously reported  $R_f$  values had been interchanged in the earlier report; the correct  $R_f$  values for the three dimers are **4a**, 0.75; **4b**, 0.42; **4c**, 0.20.

**Reaction of Pyrolysis Products with Methanol.** The cold ( $-78^\circ\text{C}$ ) pyrolysate from 544 mg (2.67 mmol) of adduct **3** was diluted with 25 mL of cold ( $-78^\circ\text{C}$ )  $\text{MeOH}$ , and the resulting solution was allowed to warm to room temperature. This solution was concentrated under reduced pressure and the residual yellow liquid (281 mg) was mixed with 106 mg of (+)-borneol for HPLC analysis. The material contained borneol, the methyl ether **1c** (calculated yield 230 mg or 51%), and three minor unidentified peaks (19.5, 20.6, and 22.9 min). The major product was identified with an authentic sample<sup>4</sup> of the methyl ether **1c** by comparison of IR and NMR spectra as well as HPLC retention times.

A mixture of 364 mg (1.78 mmol) of the adduct **3** and 312 mg of dimethyl phthalate was pyrolyzed to demonstrate that the low yield (51%) of methyl ether **1c** was not attributable to the mechanical loss of enone **2a** from the pyrolysis apparatus. The crude pyrolysate was treated with cold ( $-78^\circ\text{C}$ )  $\text{MeOH}$  and then warmed to room temperature and concentrated. The residual pale yellow liquid (600 mg) was mixed with 97.5 mg of (+)-borneol for HPLC analysis. The crude liquid product contained 307 mg (97% recovery) of dimethyl phthalate and 160 mg (53%) of the methyl ether **1c**. Therefore, we conclude that approximately 50% of the enone **2a** is converted to some nonvolatile material in the pyrolysis chamber and does not reach the cold trap. Our repeated attempts to wash some soluble material from the walls of the pyrolysis chamber at the end of the pyrolysis with  $\text{CHCl}_3$  or  $\text{CH}_2\text{Cl}_2$  also have not yielded any soluble material. We therefore conclude that any material remaining in the hot pyrolysis chamber is converted to nonvolatile, insoluble material.

The cold ( $-78^\circ\text{C}$ ) pyrolysate from 540 mg (2.65 mmol) of adduct **3** was treated with 20 mL of cold ( $-78^\circ\text{C}$ ) mixture of  $\text{CHCl}_3$  and furan (1:1 v/v). After the resulting solution had been allowed to stand under an  $\text{N}_2$  atmosphere at  $-50^\circ\text{C}$  for 45 min, 20 mL of cold ( $-78^\circ\text{C}$ )  $\text{MeOH}$  was added and the resulting solution was allowed to warm to room temperature. The reaction solution was concentrated, and the residual yellow liquid (239 mg) was mixed with 129 mg of (+)-borneol and analyzed by HPLC. The products were 54% of the methyl ether **1c** (identified by its NMR spectrum), 3% of the furan adducts **3**, and 1% of a minor component with the retention time of the dimer **4b**. Thus, the enone **2a** is relatively stable both toward dimerization and toward reaction with furan at  $-50^\circ\text{C}$ .

**Dimerization of the Enone 2a in Hexane Solution.** The cold ( $-78^\circ\text{C}$ ) pyrolysate from 527 mg (2.58 mmol) of adduct **3** was dissolved in 15 mL of cold ( $-78^\circ\text{C}$ ) hexane and then allowed to warm to room temperature slowly. Precipitation of the hexane-insoluble dimers **4** began to occur in the temperature range  $-40$  to  $-30^\circ\text{C}$ . The resulting mixture was concentrated under reduced pressure, dissolved in a mixture of  $\text{EtOAc}$ , hexane, and  $\text{CHCl}_3$ , mixed with 46.9 mg of (+)-borneol, and analyzed by HPLC. The products were 6% of dimer **4a**, 32% of dimer **4b**, and 13% of dimer **4c** (total dimer **4**, 51%) accompanied by minor unidentified peaks at 7.7 and 28.0 min. A combination of preparative HPLC and fractional recrystallization from  $\text{CH}_2\text{Cl}_2$ -hexane mixtures separated 6 mg (2%) of dimer **4a**, mp  $222$ – $223^\circ\text{C}$ , 20 mg (6%) of dimer **4b**, mp  $229$ – $231^\circ\text{C}$ , and 12 mg (4%) of dimer **4c**, mp  $221$ – $222^\circ\text{C}$ . Each of these products was identified with an authentic sample<sup>4</sup> by a mixture melting point determination. In a second comparable experiment starting with 496 mg (2.4 mmol) of the adduct **3**, the calculated yields of products were 6% of dimer **4a**, 28% of dimer **4b**, and 6% of dimer **4c**.

**Treatment of the Enone 2a with Norbornene (12).** The cold ( $-78^\circ\text{C}$ ) pyrolysate from 516 mg (2.53 mmol) of adduct **3** was treated with a cold ( $-78^\circ\text{C}$ ) solution of 1.30 g (13.8 mmol) of norbornene (**12**) in 20 mL of hexane and the resulting solution was allowed to warm to room temperature. The resulting solution was concentrated under reduced pressure, mixed with 51.6 mg of (+)-borneol, and analyzed (HPLC). The products were the furan adducts **3** (3%), the dimer **4a** (9%), the dimer **4b** (11%), and the dimer **4c** (7%), accompanied by minor unidentified peaks at 7.7 and 26.4 min.

In a second experiment, the cold ( $-78^\circ\text{C}$ ) pyrolysate from 450 mg (2.21 mmol) of adduct **3** was treated with a cold ( $-78^\circ\text{C}$ ) solution of 1.30 g (13.8 mmol) of norbornene (**12**) in 20 mL of hexane. After the resulting solution had been warmed to  $-55^\circ\text{C}$  and kept at this temperature for 45 min, 10 mL of cold ( $-78^\circ\text{C}$ )  $\text{MeOH}$  was added, and the solution was allowed to warm to room

temperature. The reaction solution was concentrated under reduced pressure to leave 317 mg (85%) of the crude methyl ether **1c** as a yellow liquid that was identified by its NMR spectrum. This sample was mixed with 128.8 mg of (+)-borneol for HPLC analysis; from this analysis the calculated yield of the methyl ether **1c** was 65%.

A solution of 0.50 g (2.3 mmol) of the bromo ketone **1b** and 3.0 g (32 mmol) of the olefin **12** in 15 mL of  $\text{CH}_2\text{Cl}_2$  was treated with 0.57 g (5.6 mmol) of  $\text{Et}_3\text{N}$  and the resulting solution was stirred at room temperature to explore the possibility that norbornene (**12**) might react with the enone **2a** at room temperature. During this period a precipitate of  $\text{Et}_3\text{HNBr}$  separated slowly and analysis (TLC) indicated that all of the bromo ketone was gone after 48 h. The reaction mixture was partitioned between water and  $\text{CH}_2\text{Cl}_2$  and the organic layer was dried and concentrated. Fractional recrystallization of the residual yellow solid from either  $\text{CHCl}_3$ -hexane mixtures or  $\text{CH}_2\text{Cl}_2$ -hexane mixtures separated fractions of the dimers **4**, including 21 mg (7%) of the dimer **4a**, mp 223–224 °C (lit.<sup>4</sup> mp 222–224 °C) and 71 mg (23%) of the dimer **4b**, mp 229–230 °C (lit.<sup>4</sup> mp 231–232 °C). Both of these dimeric products were identified with authentic samples by comparison of NMR and mass spectra and by mixture melting point determinations. The NMR spectrum of the mother liquors from these fractional crystallizations also corresponded to the NMR spectra of the dimers **4**. Therefore, it is apparent that dimerization of the enone **2a** is more rapid than reaction of the enone **2a** with the excess norbornene (**12**) present.

**Treatment of the Enone 2a with Dihydropyran (9).** The cold (–78 °C) pyrolysate from 502 mg (2.46 mmol) of adduct **3** was dissolved in 15 mL of cold (–78 °C) dihydropyran (**9**), and the resulting solution was allowed to warm to room temperature. After the reaction solution had been concentrated under reduced pressure, the residual yellow liquid (320 mg) was mixed with 54.6 mg of (+)-borneol and analyzed (HPLC). The crude product contained 5% of the furan adducts **3**, 8% of the dimer **4a**, 13% of the dimer **4b**, and 8% of the dimer **4c**. Additional small unidentified peaks were present at 7.7 and 26.4 min. The crude products from two additional experiments (a total 1.043 g or 5.11 mmol of furan adduct **3** used) were combined and subjected to a series of preparative HPLC separations to separate 21 mg (3%) of dimer **4a**, mp 222–223 °C, 15 mg (2%) of dimer **4b**, mp 229–231 °C, and 5 mg (1%) of dimer **4c**, mp 221–222 °C. Each of these products was identified with an authentic sample<sup>4</sup> by a mixture melting point determination.

**Treatment of the Enone 2a with Dimethyl Acetylenedicarboxylate (11).** The cold (–78 °C) pyrolysate from 309 mg (1.51 mmol) of adduct **3** was diluted with a cold (–78 °C) solution of 2.30 g (16.2 mmol) of the acetylenic ester **11** in 25 mL of  $\text{CH}_2\text{Cl}_2$ , and the resulting solution was allowed to warm to room temperature. After the reaction solution had been concentrated under reduced pressure, the residual yellow liquid (350 mg) was mixed with 41.1 mg of (+)-borneol and analyzed (HPLC). The crude product contained 4% of the dimer **4a**, 18% of the dimer **4b**, and 4% of the dimer **4c**. A large peak at 8.4 min attributable to the acetylenic diester **11** was also present. None of the subsequently described furan adduct **16** was detected in this HPLC analysis. In a second comparable experiment, the calculated product yields were 4% of dimer **4a**, 15% of dimer **4b**, 5% of dimer **4c**, and 5% of the furan adducts **3**.

A freshly distilled sample of the acetylenic diester **11** was obtained as a colorless liquid, bp 100–105 °C (40 mm),  $n_D^{25}$  1.4448 [lit.<sup>14</sup> bp 95–98 °C (19 mm),  $n_D^{25}$  1.4444–1.4452]. A solution of 2.08 g (15 mmol) of the diester **11** in 2.0 g (29.3 mmol) of furan was refluxed for 20 h and then concentrated under reduced pressure. The residual orange liquid (1.5 g) was distilled in a short-path still to separate 1.0 g (27%) of the adduct **16** as a colorless liquid, bp 120 °C (0.5 mm),  $n_D^{25}$  1.4912 [lit.<sup>15</sup> bp 130 °C (1 mm)]; IR ( $\text{CCl}_4$ ) 1737, 1715  $\text{cm}^{-1}$  (conjugated ester C=O);  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.18 (2 H, d,  $J = 1.1$  Hz, vinyl CH), 5.64 (2 H, d,  $J = 1.1$  Hz, CHO), 3.78 (6 H, s, O-methyl); mass

spectrum,  $m/e$  (relative intensity), 210 (3,  $\text{M}^+$ ), 153 (32), 151 (17), 150 (22), 119 (38), 68 (100), 59 (17), 39 (18). Relative to the internal standard, borneol ( $t_R$  10.0 min), the HPLC retention times of the acetylenic diester **11** and the adduct **16** were 7.7 min and 17.8 min, respectively.

**Preparation of 9,9-Dibromo[6.1.0]nonane (15).** Following previously described<sup>16,17</sup> directions, a cold (0–5 °C) solution of 24.22 g (0.220 mol) of cyclooctene and  $\text{KO}t\text{-Bu}$  (from 10.4 g or 0.267 mol of potassium and 286 mL of  $t\text{-BuOH}$ ) was treated with 60.77 g (0.240 mol) of freshly distilled bromoform (bp 150–151 °C), and the resulting pink solution was stirred for 3 h. After the resulting reaction mixture had been partitioned between pentane and water, the organic phase was washed with aqueous NaCl and then dried and concentrated by distillation of the unchanged cyclooctene and bromoform (bp 40–45 °C at 40 mm). The residual brown liquid was distilled to separate 18.61 g (30%) of the dibromide **15** as a colorless liquid, bp 85–87 °C (0.1 mm),  $n_D^{25}$  1.5481 [lit. bp 62 °C (0.04 mm),<sup>16b</sup>  $n_D^{27}$  1.5105,<sup>16a</sup>  $n_D^{23}$  1.5493–1.5507<sup>16b</sup>]. Because of the large discrepancy in refractive index values, we obtained further characterization of our dibromide sample **15** to verify its composition and purity. The spectral properties of the dibromide **15** follow: IR ( $\text{CCl}_4$ ), no absorption corresponding to OH or C=O groups in the 3- or 6- $\mu\text{m}$  region;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  2.03 (2 H, dd,  $J = 3.1$  and 14 Hz, bridgehead CH), 1.4–1.7 (10 H, m, aliphatic CH), 1.0–1.4 (2 H, m, aliphatic CH);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ; multiplicity determined by off-resonance decoupling) 36.9 (s), 33.1 (d, 2 C), 27.8 (t, 2 C), 26.1 (t, 2 C), 25.2 ppm (t, 2 C); mass spectrum,  $m/e$  (E.I., relative intensity), 284 (M, 11), 282 (M, 24), 280 (M, 11), 214 (32), 212 (67), 210 (31), 121 (57), 96 (100), 93 (45), 81 (77), 79 (63), 77 (24), 68 (23), 67 (67), 65 (29), 55 (52), 54 (35), 41 (53), 39 (43).

Anal. Calcd for  $\text{C}_9\text{H}_{14}\text{Br}_2$ : C, 38.33; H, 5.00; Br, 56.67. Found: C, 38.39; H, 5.04; Br, 56.55.

**Preparation of the Allene 13.** Following a previously described<sup>16</sup> procedure, a cold (–30 to –40 °C) solution of 6.00 g (21.3 mmol) of the dibromide **15** in 50 mL of ether was treated with 280 mL of an ethereal solution containing 50.4 mmol of MeLi. After the resulting yellow solution had been allowed to warm to 25 °C, it was partitioned between water and ether and the organic layer was dried and concentrated. Distillation of the residual yellow liquid separated 2.58 g (99%) of the allene **13** as a colorless liquid, bp 62 °C (15 mm),  $n_D^{25}$  1.5025 [lit.<sup>9</sup> bp 62 °C (16 mm),  $n_D^{20}$  1.5060]. The spectral properties of the allene **13** follow: IR ( $\text{CCl}_4$ ), no absorption corresponding to OH or C=O groups in the 3- or 6- $\mu\text{m}$  region;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  5.2–5.3 (2 H, m, vinyl CH), 2.1–2.3 (4 H, m, allylic CH), 1.3–1.8 (10 H, m, aliphatic CH);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , multiplicity determined by off-resonance decoupling) 205.6 (s), 92.4 (d, 2 C), 28.0 (t, 2 C), 27.4 (t, 2 C), 25.4 ppm (t, 2 C); mass spectrum,  $m/e$  (C.I., relative intensity), 123 (M + 1, 92), 121 (46), 109 (69), 95 (51), 94 (31), 93 (100); UV absorption, nm (EtOH,  $\epsilon$ ) 203 (shoulder on end absorption, 2200).

**Dimerization of the Allene 13.** Following previously described procedures,<sup>10,11</sup> a 0.50-g (4.0 mmol) sample of the allene **13** was heated in a sealed tube at 150 °C for 70 min to leave material that crystallized as colorless needles upon cooling. Recrystallization from hexane afforded 0.43 g (88%) of the mixture of dimers **14a**, **14b**, and **14c** as colorless needles melting over the range 85–103 °C (lit.<sup>10,11</sup> **14b**, mp 80–83 °C; **14a**, 108–110 °C). A mixture of these dimers **14** with (+)-borneol exhibited HPLC peaks at 7.4 min (minor), 8.1 min (minor), and 11.6 min (major) relative to a retention time of 10.0 min for (+)-borneol. The spectral properties of the mixture of dimers **14** follow:  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  5.56 (2 H, m), 2.89 (2 H, m), 1.8–2.2 (22 H, m); mass spectrum,  $m/e$  (E.I., relative intensity) 244 ( $\text{M}^+$ , 53), 187 (29), 173 (33), 161 (32), 148 (48), 147 (48), 145 (33), 134 (38), 133 (52), 131 (37), 121 (31), 119 (48), 117 (39), 105 (62), 93 (54), 92 (30), 91 (100), 81 (40), 80 (30), 79 (68), 77 (34), 67 (51), 55 (44), 41 (82), 39 (30).

**Treatment of the Enone 2a with 1,2-Cyclononadiene (13).** The cold (–78 °C) pyrolysate from 499 mg (2.50 mmol) of adduct **3** was treated with a cold (–78 °C) solution of 2.90 g (23.8 mmol)

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of the allene **13** in 10 mL of  $\text{CH}_2\text{Cl}_2$ , and the resulting solution was allowed to warm to room temperature. The reaction solution was concentrated under reduced pressure, mixed with 48.6 mg of (+)-borneol, and analyzed (HPLC). The products were the furan adducts **3** (5%), the dimer **4a** (5%), the dimer **4b** (20%), and the dimer **4c** (12%), accompanied by 6% of the bromo ketone **1b** and minor unidentified peaks at 7.7 and 26.4 min. In addition, three minor peaks were observed that corresponded in retention times to the dimers **14** of the allene **13**.

In a second experiment designed to test the possibility that the enone **2a** might react with the allene at 25 °C, a solution of 321 mg (1.40 mmol) bromo ketone **1b** in 2.56 g (21 mmol) of the allene **13** was mixed with 10 mL (13.7 g, 138 mmol) of  $\text{Et}_3\text{N}$  and heated to 35 °C with stirring. A white precipitate separated from the initially clear solution as the reaction proceeded. After the mixture had been heated with stirring for 36 h, it was poured into aqueous 1 M HCl and extracted with  $\text{CH}_2\text{Cl}_2$ . The organic extract was washed with aqueous NaCl, dried, and concentrated under

reduced pressure. The residual yellow solid was mixed with 40.2 mg of (+)-borneol (an HPLC standard). The reaction mixture was subjected to preparative HPLC to separate 21 mg (7%) of the bromo ketone **1b**, 39.6 mg of borneol, 23.8 mg (12.5%) of dimer **4a**, and 154 mg (80.1%) of a mixture of dimers **4b** and **4c**. All products were identified with authentic samples by comparison of spectral data and/or by a mixture melting point determination.

**Treatment of the Enone 2a with Molecular Oxygen.** The cold (-78 °C) pyrolysate from 500 mg (2.45 mmol) of adduct **3** was dissolved in 25 mL of cold (-78 °C), anhydrous hexane and a stream of air (dried in a column packed with Drierite) was passed through the cold solution for 45 min. The resulting solution was allowed to warm to room temperature and then concentrated under reduced pressure and mixed with 45.5 mg of (+)-borneol for HPLC analysis. The crude product contained 2% of the furan adducts **3**, 2% of the dimer **4a**, 11% of the dimer **4b**, and 5% of the dimer **4c**. Additional small unidentified peaks were present at 7.8, 26.7, and 30.5 min.

## Nucleophilic Addition of the Pentafluoroethyl Group to Aldehydes, Ketones, and Esters

Paul G. Gassman\* and Neil J. O'Reilly

Department of Chemistry, University of Minnesota, Minneapolis, Minnesota 55455

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Pentafluoroethyl iodide reacts with methyllithium at -78 °C to produce (pentafluoroethyl)lithium. This halogen-metal exchange reaction can be carried out in the presence of aldehydes, ketones, and esters with no observable addition of methyllithium to the carbonyl derivative. The resultant (pentafluoroethyl)lithium adds to aldehydes and ketones in 80-100% yields to produce the corresponding secondary and tertiary carbinols. (Pentafluoroethyl)lithium adds to esters to give good yields of either ketones or tertiary carbinols. The nature of the product formed from the esters was a function of both the structure of the ester and the reaction conditions.

Recently, we communicated our results on the addition of (pentafluoroethyl)lithium to aldehydes and ketones.<sup>1a</sup> We now wish to provide the experimental details of this addition of (pentafluoroethyl)lithium<sup>1b</sup> to aldehydes and ketones and the extension of this nucleophilic addition to esters.

### Introduction

The introduction of a small perfluoroalkyl group into an organic molecule is highly desirable in connection with both biological studies<sup>2</sup> and physical organic studies. In the former area, the highly lipophilizing nature of the perfluorinated alkyl group may favorably alter in vivo transport and absorption rates of a drug, while its inherent stability may improve the analogue's stability and in vivo half-life. In addition, the strong electron-withdrawing nature of the perfluoroalkyl group can greatly alter the chemistry of the molecule. These factors make the incorporation of a small perfluoroalkyl group a powerful tool in drug modification. The electronic properties of these substituents have also attracted physical organic chemists, who have used them in studies of destabilized carboca-

tions<sup>3</sup> and reduced neighboring group participation by electron withdrawal.<sup>4</sup>

It was our interest in these latter areas which led us to look more closely at the methods currently available for the introduction of small perfluoroalkyl groups into organic molecules. In particular, we were interested in carbanionic-type additions to carbonyl containing functionalities. While the literature contains numerous reports of attempted introduction of a trifluoromethyl group using an organometallic reagent, there have been few successes.<sup>5-7</sup> Recent reports<sup>8</sup> utilizing transiently formed zinc reagents can be used with aldehydes, but the functionalization of ketones is much more problematic. (Trifluoromethyl)lithium<sup>6</sup> and Grignard<sup>7</sup> reagents are not synthetically useful as they decompose readily, apparently to difluorocarbene, even when formed at low temperature in the presence of a suitable electrophile. There is a marked increase in the stability of the organometallic with (heptafluoropropyl)lithium<sup>9</sup> and the heptafluoropropyl Grignard reagent.<sup>10,11</sup> While not entirely stable, these reagents

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