Unusual Acid-Catalyzed Rearrangement of a Tetracyclic Bicyclo[3.2.0]hept-6-en-2-one Derivative

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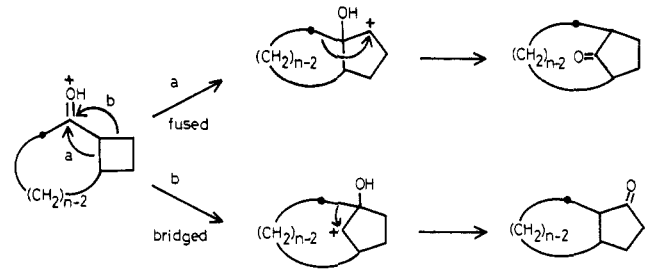
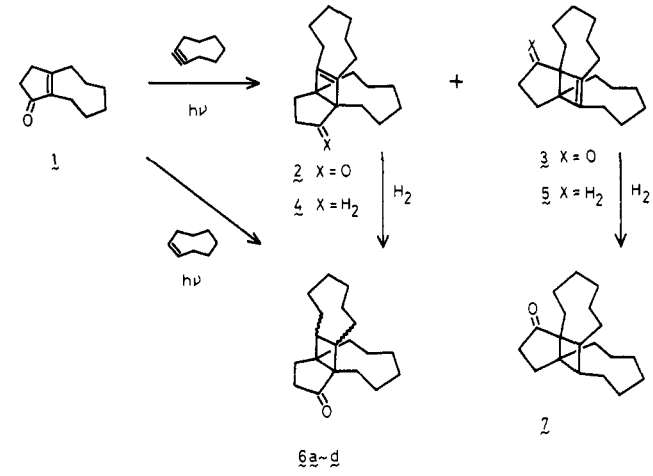
The acid-catalyzed rearrangement of cyclobutyl carbinyl ketones, especially that of bicyclo[*n*.2.0]alkanone derivatives (n = 3, 4), has been recognized as a useful method for the synthesis of important polycarbocyclic ring systems.[1] Concerning the acid-catalyzed rearrangement of bicyclo[*n*.2.0] systems, two migratory modes are possible: "fused" migration by the 1,2 alkyl shift of the internal cyclobutane bond (path a) and "bridged" migration by the 1,2 alkyl shift of the external cyclobutane bond (path b) as shown in Scheme I. Actually, in the cases of bicyclo[4.2.0]octanone derivatives, both types of migrations have been found, depending on the stereochemical features of the substrates.[1] On the other hand, only "fused" migration has been observed for bicyclo[3.2.0]heptenone systems[1a,2] except for the cases of the retro-aldol-type reactions of the ketones having an electron-donating substituent at the angular position.[1a] Moreover, the β,γ-unsaturated ketones consisting of the same ring systems occasionally undergo the well-known 1,3 acyl shift concurrently.[1a] We have found, however, that the tetracyclic bicyclo[3.2.0]heptenone derivative **3**, which was prepared by the photochemical 1,3 acyl shift[3] of the [2 + 2] photocycloadduct (**2**) of the bicyclic α,β-unsaturated ketone **1** to cyclooctyne,[4] undergoes unusual "fused" migration of the internal bond, predominantly leading to the interesting norbornen-7-one derivative **8** in good yield.

The irradiation of **1** and 2 equiv of cyclooctyne in ether gave the [2 + 2] cycloadduct **2** (mp 59–60 °C) and the 1,3 acyl shift product **3** (mp 46–47 °C) in 44% and 29% yields, respectively. By monitoring the course of the photoreaction by GLC, it was deduced that **2** was initially formed by the [2 + 2] photocycloaddition and that **3** was derived from **2** by the photochemical 1,3 acyl shift. The structures of **2** and **3** were further confirmed by the following results from the reactions of **2** and **3** (Scheme II): (i) The Wolff–Kishner reduction of **3** and the related reaction of **2** gave the corresponding unsaturated hydrocarbons (**5** and **4**).[5] Both **4** and **5** showed ten ^{13}C NMR signals involving two singlets (**4**, δ 141.4 and 55.9; **5**, δ 142.4 and 57.6), which indicate the presence of the plane of symmetry in **4** and **5**. (ii) The catalytic hydrogenation of **2** afforded the ketones composed of three kinds of stereoisomers (**6a–c**). They were identical with respect to GLC retention times and mass spectra with the three stereoisomers of the four cycloadducts **6a–d**, which were given by the [2 + 2] photocycloaddition of **1** to cyclooctene.[6] (iii) The similar hydrogenation of **3**, however, gave the ketone **7** which was distinct from any of the cycloadducts **6a–d**. (iv) The irradiation of either **2** or **3** in ether resulted in a photo-

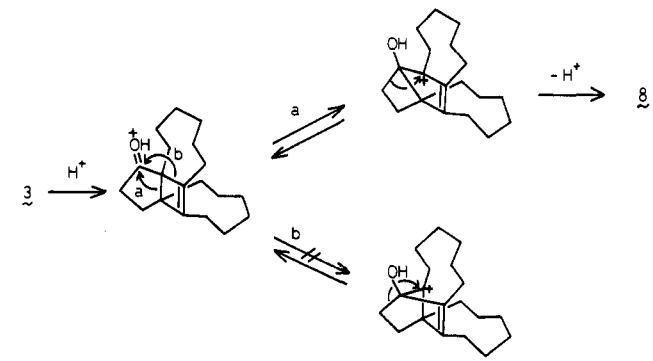
Scheme I



Scheme II



Scheme III



(1) (a) Cargill, R. L.; Jackson, T. E.; Peet, N. P.; Pond, D. M. *Acc. Chem. Res.* **1974**, *7*, 106. (b) Duc, D. K. M.; Fetizon, M.; Lazare, S. *J. Chem. Soc., Chem. Commun.* **1975**, 282. (c) Duc, D. K. M.; Fetizon, M.; Kone, M. *Tetrahedron* **1978**, *34*, 3513. (d) Yanagiya, M.; Kaneko, T.; Kaji, T.; Matsumoto, T. *Tetrahedron Lett.* **1979**, 1761. (e) Duc, D. K. M.; Fetizon, M.; Hanna, I.; Olesker, A. *J. Chem. Soc., Chem. Commun.* **1980**, 1209. (f) Eaton, P. E.; Jobe, P. G.; Nyi, K. *J. Am. Chem. Soc.* **1980**, *102*, 6636. (g) Pirrung, M. C. *Ibid.* **1981**, *103*, 82. (h) Smith, A. B., III; Jerris, P. J. *Ibid.* **1981**, *103*, 194.

(2) For the solvolytic rearrangements of bicyclo[3.2.0]hept-2-yl derivatives see: (a) Yano, K.; Isobe, M.; Yoshida, K. *J. Am. Chem. Soc.* **1978**, *100*, 6166 and references cited therein. (b) Tobe, Y.; Hayauchi, Y.; Sakai, Y.; Odaira, Y. *J. Org. Chem.* **1980**, *45*, 637.

(3) For a review of the photochemical 1,3 acyl shift of β,γ-unsaturated ketones see: (a) Houk, K. N. *Chem. Rev.* **1976**, *76*, 1. The photochemical 1,3 acyl shift of the related systems has been extensively investigated by Cargill and his co-workers: (b) Cargill, R. L.; Beckham, M. E.; Siebert, A. E.; Dorn, J. *J. Org. Chem.* **1965**, *30*, 3647. (c) Peet, N. P.; Cargill, R. L. *Ibid.* **1973**, *38*, 4281. (d) Cargill, R. L.; Sears, A. B. *Tetrahedron Lett.* **1972**, 3555.

(4) The photocycloaddition of the enone **1** with cyclohexene has been examined by us: Tobe, Y.; Doi, A.; Kunai, A.; Kimura, K.; Odaira, Y. *J. Org. Chem.* **1977**, *42*, 2523.

(5) Since the Wolff–Kishner reduction of **2** under similar conditions to that of **3** with hydrazine appeared unfruitful, the reduction of **2** was carried out by the lithium aluminum hydride reduction of the tosylhydrazone of **2** (see Experimental Section).

(6) In principle, the formation of four stereoisomers of the cycloadducts is possible. Though the stereochemistry of the obtainable cycloadducts **6a–d** has not been determined, it may be reasonable to consider that the major adduct **6c** has a cis-anti-trans configuration in view of the results on the photocycloaddition of **1** and related enones to olefins.[4,7]

(7) Tobe, Y.; Hoshino, T.; Kawakami, Y.; Sakai, Y.; Kimura, K.; Odaira, Y. *J. Org. Chem.* **1978**, *43*, 4334.

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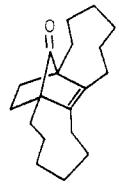
stationary state involving **2** and **3** in a ratio of 3:2.[8]

The treatment of the tetracyclic β,γ-unsaturated ketone **3** with *p*-toluenesulfonic acid (1 equiv) in benzene at 60 °C gave, after chromatography on silica gel, the norbornen-7-one derivative **8** (mp 70–72 °C) in 71% isolated



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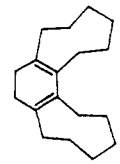

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yield along with a small amount (3%) of the 1,3 acyl shift product **2**. The structure of **8** was elucidated on the basis of spectroscopic considerations: the carbonyl absorption in the IR spectrum was at 1760 cm^{-1}, characteristic of norbornan-7-one derivatives.[2b,9] The ^{13}C NMR spectrum comprised nine signals involving three singlets at δ 212.4, 140.6, and 54.1. Moreover, the fact that the decarbonylation of **8** by pyrolysis during GLC (10% FFAP, 200 °C) took place readily to afford the diene **9** (mp 29–31 °C) confirmed the norbornen-7-one structure of **8**.

Interestingly, the acid-catalyzed reaction of the tetracyclic propellanone **2** under similar conditions also yielded **8** as the major product (51%), presumably via **3** formed by the acid-catalyzed 1,3 acyl shift of **2**, together with some unidentified products.

Evidently, the formation of **8** from **3** involves "fused" migration (path a) of the internal cyclobutane bond (Scheme III); this is, to our knowledge, the first example of this type migration of bicyclo[3.2.0]heptenone systems. Although "bridged" migration (path b) of **3** seems to be kinetically favored because it would lead to the formation of a cation intermediate having 7-norbornenyl system,[10] thermodynamically less favorable bicyclo[3.2.0]heptenone system[11] or a highly strained bridgehead diene[12] would be formed by the subsequent 1,2 alkyl shift–deprotonation or deprotonation from the adjacent carbon atom, respectively. On the other hand, although "fused" migration of **3** seems to be kinetically disfavored, the product **8** formed by the subsequent 1,2 alkyl shift–deprotonation is thermodynamically more favorable than those derived from path b.[11] By analogy, it is reasonable to consider that 1,3 acyl shift of **3** to **2** under acidic conditions may be unfavorable in view of the greater thermodynamic stability of norbornane over bicyclo[3.2.0]heptane.[11] Thus it may be deduced that **8** was formed predominantly because of its greater stability than the products derived from the other paths under thermodynamic control of the acid-catalyzed rearrangement in nonnucleophilic media such as the *p*-toluenesulfonic acid–benzene system.[1a]

Experimental Section[13]

Preparation of 2 and 3. A solution of 2.71 g (16.5 mmol) of **1** and 3.6 g (33 mmol) of cyclooctyne[14] in 50 mL of ether was irradiated in a Pyrex tube under nitrogen at room temperature for 10 h. The course of the reaction was monitored by GLC (column A, 200 °C). After evaporation of the solvent and excess cyclooctyne, the residue was chromatographed on silica gel. Elution with 5% ether–petroleum ether gave 3.30 g (71%) of a mixture of **2** and **3** in a ratio of 3:2 (by GLC). Pure samples of **2** and **3** were obtained by repeated chromatography by elution with 3% ether–petroleum ether.

2: mp 59–60 °C; IR 1705 cm^{-1}; mass spectrum, *m/e* 272 (M^+); ^1H NMR (CCl_4) δ 0.8–2.9 (m); ^{13}C NMR ($CDCl_3$) δ 218.8 (s), 149.2 (s), 142.2 (s), 63.1 (s), 54.0 (s), 35.2 (t), 30.3 (t), 26.9, 26.3, 25.8, 25.5, 24.8, 24.3 (3 C), 24.1 (2 C), 23.6, 20.8 (t); UV (EtOH) 307 nm (ε 301); semicarbazone, mp 219–220 °C. Anal. Calcd for $C_{20}H_{31}ON_3$: C, 72.90; H, 9.48; N, 12.76. Found: C, 72.50; H, 9.52; N, 12.39.

3: mp 46–47 °C; IR 1705 cm^{-1}; mass spectrum, *m/e* 272 (M^+); ^1H NMR (CCl_4) δ 1.0–2.8 (m); ^{13}C NMR ($CDCl_3$) δ 219.3 (s), 150.2 (s), 143.3 (s), 64.6 (s), 56.3 (s), 35.1 (t), 33.4 (t), 29.3 (t), 28.3 (t), 26.1 (2 C), 25.7, 25.5 (2 C), 25.3, 25.1, 22.9, 22.1, 21.7; UV (EtOH) 307 nm (ε 334); semicarbazone, mp 190–192 °C. Anal. Calcd for $C_{20}H_{31}ON_3$: C, 72.90; H, 9.48; N, 12.76. Found: C, 72.72; H, 9.49; N, 12.96.

Wolff–Kishner Reduction of 3. Compound **3** (243 mg, 0.89 mmol), 1.2 g (20 mmol) of potassium hydroxide, and 5 mL of 80% hydrazine hydrate in 18 mL of diethylene glycol was heated at 120 °C for 3 h, and then excess hydrazine was distilled off. The solution was heated at 200 °C for 3 h and cooled. After neutralization with hydrochloric acid, the solution was extracted with ether. The extracts were washed with saturated sodium chloride solution and then dried over anhydrous sodium sulfate (Na_2SO_4). The solvent was evaporated, and the residue was chromatographed on silica gel. Elution with petroleum ether gave 62 mg (27%) of **5** as oil: IR 2900, 1440 cm^{-1}; mass spectrum, *m/e* 258 (M^+); ^1H NMR (CCl_4) δ 0.7–2.4 (m); ^{13}C NMR ($CDCl_3$) δ 142.4 (s, 2 C), 57.6 (s, 2 C), 32.2 (t, 2 C), 32.0 (t, 2 C), 28.6 (t, 2 C), 25.9 (2 C), 25.8 (2 C), 24.3 (t, 2 C), 23.3 (t), 23.1 (t, 2 C). Anal. Calcd for $C_{19}H_{30}$: C, 88.30; H, 11.70. Found: C, 87.96; H, 11.66.

Tosylhydrazone Reduction of 2. Since reduction of **2** under conditions similar to those above resulted in the recovery of unreacted **2**, it was reduced by the lithium aluminum hydride reduction of its tosylhydrazone.

A solution of 103 mg (0.37 mmol) of **2** and 74 mg (0.40 mmol) of tosylhydrazine in 3 mL of methanol was refluxed for 5 h. After the mixture cooled to room temperature, the precipitates were collected by filtration and recrystallized from methanol to give 121 mg (74%) of the tosylhydrazone; mp 200–203 °C dec; IR 3200, 1590, 1340, 1150, 680 cm^{-1}. Anal. Calcd for $C_{26}H_{36}O_2N_2S$: C, 70.87; H, 8.24; N, 6.36; S, 7.28. Found: C, 70.51; H, 8.07; N, 6.31; S, 6.99.

To a solution of 741 mg (1.68 mmol) of the tosylhydrazone in 20 mL of THF was added 255 mg (6.7 mmol) of lithium aluminum hydride portionwise, and the mixture was stirred and refluxed for 20 h. Water was added carefully followed by 1 N hydrochloric acid, and the organic layer was separated. The aqueous layer was extracted with ether, and the combined extracts were washed with saturated sodium chloride solution and then dried (Na_2SO_4). Evaporation of the solvent and subsequent chromatography on silica gel afforded 272 mg of products composed of two hydro-

(8) In connection with the study on the synthesis of pentacyclic propellanes (Tobe, Y.; Kimura, K.; Odaira, Y. *J. Org. Chem.* **1978**, *43*, 3776), we have found that the oxidation of **3** and **5** with *m*-chloroperbenzoic acid gave the corresponding epoxides (mp 90–92 and 60–62 °C, respectively) having a novel pentacyclic skeleton involving an octasubstituted cyclobutane ring. Work on this subject is now being undertaken.

(9) (a) Lewis, S. C.; Whitham, G. H. *J. Chem. Soc. C* **1967**, 274. (b) Cargill, R. L.; Beckham, M. E.; Damewood, J. R.; Pond, D. M.; Bundy, W. A. *J. Org. Chem.* **1972**, *37*, 78.

(10) Although this cation intermediate contains a bridgehead carbonium ion center as well as a bridgehead double bond, it seems to be unstrained because both the carbonium ion and double bond are involved in a large bicyclic system: (a) Parker, W.; Tranter, R. L.; Watt, C. I. F.; Chang, L. W. K.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1974**, *96*, 7121. (b) Maier, W. F.; Schleyer, P. v. R. *Ibid.* **1981**, *103*, 1891.

(11) Engler, E. M.; Andose, J. D.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1973**, *95*, 8005.

(12) Shea, K. J. *Tetrahedron* **1980**, *36*, 1683.

(13) Melting points are uncorrected. IR spectra were recorded with a JASCO IR-G spectrometer. ^1H and ^{13}C NMR spectra were obtained on JEOL JNM-PS-100 and JEOL JNM-FX-60S spectrometers, respectively, with tetramethylsilane as an internal standard. Mass spectra were measured with a Hitachi RMU-6E spectrometer. Analytical GLC was carried out on a Hitachi 163 gas chromatograph, and preparative GLC separation was conducted on a Varian Aerograph 920 chromatograph using columns A, 10% FFAP, and B, 5% SE-30. The irradiation was carried out with an Eikosha PIH-500 high-pressure mercury lamp (500 W).

(14) Lalezari, I.; Shafiee, A.; Yalpani, M. *J. Heterocycl. Chem.* **1972**, *9*, 1141.

carbons in a ratio of 3:1 (by GLC on column B). On the basis of the mass spectra of the samples separated by GLC (major, m/e 256, and minor, m/e 258), it was suggested that the major product was the diene derived by the Bamford–Stevens reaction and that the minor one was the desired olefin **4**. Therefore, the mixture of the above olefins (161 mg), 2 mL of 90% hydrazine hydrate, and 100 mg of cupric sulfate in 20 mL of ethanol was stirred at room temperature for 12 h (monitored by GLC) while air was bubbled through a syringe. The mixture was diluted with water and extracted with ether. The extracts were washed with 1 N hydrochloric acid and water, and then dried (Na_2SO_4). After evaporation of the solvent, the residue was chromatographed on silica gel to afford 124 mg of **4**: IR 2900, 1450 cm^{-1}; mass spectrum, m/e 258 (M^+); ^1H NMR ($CDCl_3$) δ 0.9–2.1 (m); ^{13}C NMR ($CDCl_3$) δ 141.4 (s, 2 C), 55.9 (s, 2 C), 28.5 (t, 2 C), 27.1 (t, 2 C), 26.2 (t, 2 C), 26.0 (t, 2 C), 25.3 (t, 2 C), 24.9 (t, 2 C), 23.4 (t, 2 C), 23.1 (t). Anal. Calcd for $C_{19}H_{30}$: C, 88.30; H, 11.70. Found: C, 88.14; H, 11.91.

Photocycloaddition of 1 with Cyclooctene. Compound **1** (492 mg, 3.0 mmol) and 3.3 g (30 mmol) of cyclooctene were irradiated in a Pyrex tube for 7 h. The excess cyclooctene was evaporated and the residue distilled under reduced pressure [180 °C, bath temperature (1 mmHg)] to afford 760 mg of products which solidified on standing. The products were analyzed by GLC [the retention times of **6a–d** (column A, 200 °C) are given below] and separated by preparative GLC. All of **6a–d** showed the carbonyl absorptions at 1710 cm^{-1} in the IR spectra, a weak parent peak at m/e 274 with a base peak at m/e 165 in the mass spectra, and only aliphatic proton multiplets at δ 0.8–2.8 in the ^1H NMR spectra. Retention times and yields are as follows: **6a**, 10.3 min, 1%; **6b**, 11.5 min, 6%; **6c**, 12.6 min, 84% (mp 76–78 °C); **6d**, 14.6 min, 2%. Anal. Calcd for $C_{19}H_{30}O$: C, 83.15; H, 11.02. Found: C, 83.21; H, 10.88.

Hydrogenation of 2. Compound **2** (95 mg) and a catalytic amount of 5% palladium carbon in 20 mL of ethyl acetate was heated at 65 °C under a 5-atm pressure of hydrogen in a stainless-steel pressure bottle for 4 days. The catalyst was filtered and the solvent evaporated to give 91 mg of products which were composed of three isomers: **6a** (65%), **6b** (28%), and **6c** (7%). The GLC retention times and the mass spectra of these products, which were separated by preparative GLC, were identical with those of **6a–c** obtained as described above.

Hydrogenation of 3. Compound **3** (95 mg) was hydrogenated as above to give 85 mg of **7**: GLC retention time (column A, 200 °C) 15.2 min; IR 1710 cm^{-1}; mass spectrum, m/e 274 (M^+); ^1H NMR (CCl_4) δ 1.0–2.4 (m). Anal. Calcd for $C_{19}H_{30}O$: C, 83.15; H, 11.02. Found: C, 83.12; H, 10.98.

Acid-Catalyzed Rearrangement of 3. Compound **3** (63 mg, 0.23 mmol) and 40 mg (0.23 mmol) of *p*-toluenesulfonic acid in 15 mL of benzene were heated at 60 °C for 18 h. The solution was washed with sodium bicarbonate solution and saturated sodium chloride solution and then dried (Na_2SO_4). After evaporation of the solvent, the residue was chromatographed on silica gel. Elution with 2% ether–petroleum ether afforded 45 mg (71%) of **8** and with 3% ether–petroleum ether afforded 2 mg (3%) of **2**.

For **8**: mp 70–72 °C; IR 1760 cm^{-1}; mass spectrum, m/e 272 (M^+); ^1H NMR ($CDCl_3$) δ 1.0–2.6 (m); ^{13}C NMR ($CDCl_3$) δ 212.4 (s), 140.6 (s, 2 C), 54.1 (s, 2 C), 31.3 (t, 2 C), 30.9 (t, 2 C), 26.8 (t, 2 C), 25.7 (t, 2 C), 25.6 (t, 4 C), 23.8 (t, 2 C). Anal. Calcd for $C_{19}H_{28}O$: C, 83.77; H, 10.36. Found: C, 83.71; H, 10.45.

Acid-Catalyzed Rearrangement of 2. Compound **2** (81 mg, 0.30 mmol) and 50 mg (0.29 mmol) of *p*-toluenesulfonic acid in 20 mL of benzene were heated at 60 °C for 42 h. A workup as above gave 51% of **8** as well as some minor products which were not determined.

Decarbonylation of 8. By preparative GLC of 67 mg of **8** on column A at 200 °C there was obtained 22 mg (36%) of **9**: mp 29–31 °C; IR 2900, 1460 cm^{-1}; mass spectrum, m/e 244 (M^+); ^1H NMR ($CDCl_3$) δ 1.04–1.96 (m, 16 H), 1.98 (s, 4 H), 2.04–2.48 (m, 8 H). Anal. Calcd for $C_{18}H_{28}$: C, 88.45; H, 11.55. Found: C, 88.07; H, 11.54.

Registry No. **1**, 38262-50-9; **2**, 79172-23-9; **2** semicarbazone, 79172-24-0; **2** tosylhydrazone, 79172-25-1; **3**, 79172-26-2; **3** semicarbazone, 79172-27-3; **3** epoxide, 79172-28-4; **4**, 79172-29-5; **5**, 79172-30-8; **5** epoxide, 79190-79-7; **6** (isomer 1), 79172-31-9; **6** (isomer 2), 79200-21-8; **6** (isomer 3), 79200-22-9; **6** (isomer 4), 79200-23-0; **7**, 79172-32-0; **8**, 79172-33-1; **9**, 79172-34-2; cyclooctyne, 1781-78-8; cyclooctene, 931-88-4.

Benzaldehyde plus Potassium Hydride—Benzoyl Anion?[1]

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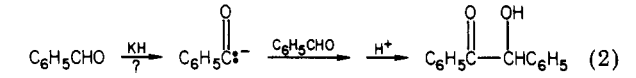
Removal of the CHO proton of an aldehyde would lead to an acyl anion which would allow the addition of electrophiles directly to the carbonyl. Unfortunately, this deprotonation reaction does not occur,[2] so a vast effort has resulted in the development of indirect methods for accomplishing this by using so-called acyl anion equivalents.[3] This "umpolung"[4] has allowed many useful synthetic conversions.

In connection with another project involving the anion of substituted cyclopropanes,[5] benzaldehyde was allowed to react with potassium hydride in the presence of 18-crown-6. After 48 h at room temperature, three products were isolated, benzyl alcohol (14%), benzoic acid (10%), and benzoin (47%) (eq 1). This last product attracted our

$$C_6H_5CHO \xrightarrow[\text{18-crown-6}]{KH} C_6H_5CH_2OH + C_6H_5COOH + C_6H_5C(OH)HC(O)C_6H_5 \quad (1)$$

attention as possibly arising via benzoyl anion (eq 2).



(2)

Potassium hydride has been used to effect nearly miraculous alkylations,[6] and so, in the absence of any complications from aldol condensations, this is not as strange as one might initially imagine.

Several attempts were made to trap the proposed benzoyl anion. The reaction of eq 1 was allowed to proceed in the presence of methyl iodide; however, only benzyl methyl ether (53%) and benzyl alcohol (33%) were formed.[7] No evidence for the formation of acetophenone was obtained. Similarly, no benzil was isolated from the benzaldehyde/potassium hydride/crown ether reaction when run in the presence of methyl benzoate. This latter reaction gave benzoin, benzyl benzoate, and benzoic acid. These negative trapping attempts argue against the intermediacy of benzoyl anion in the reaction of eq 1.

An examination of the product distribution from this reaction as a function of time is very revealing. It is most striking that benzyl benzoate is observed as a product when shorter reaction times are used (see Table I). The amount of benzoin appears to increase with increasing reaction time at the expense of benzyl benzoate. In addition, the product distribution is affected by the amount of crown ether at low levels (see Table II), and no benzoin is produced when the weaker base sodium hydride is used. For example, after 10 h only 9% benzoin is obtained when 50 mg (1.0 mol %) of 18-crown-6 is used. In the presence of

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