with stirring. Iodine monobromide (3.3 g, 0.016 mole) in 12.5 ml of solvent was added slowly with stirring. An adapter containing both an addition funnel with a nitrogen inlet and a gas outlet leading to a drying tube was attached. Pivalaldehyde hydrazone (0.4 g, 0.0038 mole) in 15 ml of solvent was added dropwise, with stirring, to the ice-cooled pyridine–halogen addition complex. Gas evolution was evident. The reaction was stirred for 1 hr after addition was complete.

The mixture was then washed, in series, with three, ice-cold, 30-ml portions each of saturated sodium sulfite, dilute hydrochloric acid, and water. The solvent layer was dried with anhydrous sodium sulfate and the solvent was removed on a rotary evaporator. Separation of 2 and 4 was carried out by preparative-scale vpc.

The reactions in dimethylformamide, ethyl alcohol, and pyridine were mixed with water and extracted with dichloromethane before washing; the dichloromethane layer contained the halide.

The nmr spectrum of 2 consisted of singlets at τ 4.50 and 8.81, relative areas 1:9.

Anal. Calcd for $C_5H_{10}BrI$: C, 21.68; H, 3.64; I, 45.82. Found: C, 21.87; H, 3.84; I, 45.73.

1-Iodo-1-chloroneopentane (3).—The procedure was the same as that used for preparation of 2. Iodine monochloride (2.6 g, 0.016 mole) was used except in expt 12, where 0.65 g (0.004 mole) was used. The nmr spectrum of 3 consisted of singlets at τ 4.38 and 8.85, relative areas 1:9.

Anal. Calcd for $C_5H_{10}ClI$: C, 25.83; H, 4.34; I, 54.59. Found: C, 25.91; H, 4.34; I, 54.35.

Preparative-Scale Synthesis of 1-Bromo-1-iodoneopentane (2).—Two grams of hydrazone and proportionate quantities of iodine monobromide and other chemicals were treated as above. The product was distilled through a 10-cm column packed with glass helices. 1-Bromo-1-iodoneopentane (2) was distilled with slight decomposition at 100° (35 mm), yielding 1.71 g (30%).

Registry No.—1, 10235-67-3; 2, 10199-23-2; 3, 10199-24-3.

Acknowledgments.—Dr. William R. Dolbier, Jr., and Professor M. J. Goldstein kindly communicated their experimental results to us before publication and granted permission to quote from the doctoral dissertation of W. R. D. J. N. C. was the recipient of a 1966 Wesleyan University Summer Study Grant. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

The Reaction of the Magnesium Salt of N-Cyclohexylcyclohexylimine with Epoxides[1]

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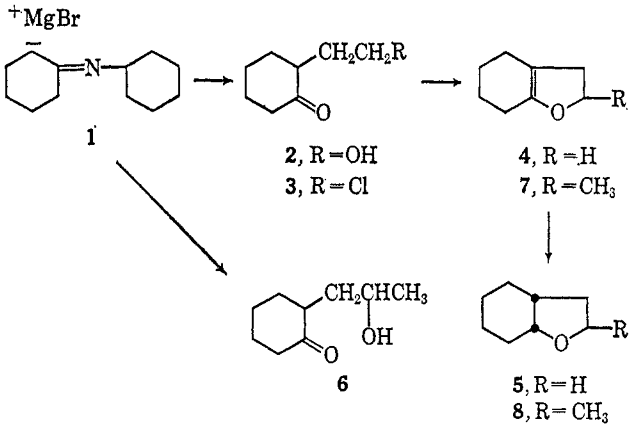
Received December 21, 1966

Enamines react with electrophilic olefins or with reactive halides to give, after hydrolysis, α-substituted carbonyl compounds.[2] We considered that reaction of an enamine derived from a cyclohexanone with an epoxide might provide a convenient route to 2-[2′-hydroxyalkyl]cyclohexanones which were required in connection with the synthesis of degradation products of fumagillin.[3]

N-Cyclohex-1-enylpyrrolidine (cyclohexanone pyrrolidine enamine) was recovered unchanged after treatment with ethylene oxide in benzene solution at 80° in a sealed tube for 18 hr, but the more reactive magnesium salt of N-cyclohexylcyclohexylimine (1)[4] (Scheme I), reacted readily at 0° in tetrahydrofuran. When the resulting solution was hydrolyzed with hydrochloric acid and worked up in the usual manner,[4] the product was not the expected 2-(2′-hydroxyethyl)cyclohexanone (2), but contained halogen and, although not obtained pure, appeared to consist mainly of 2-(2′-chloroethyl)cyclohexanone (3). However, if the reaction mixture resulting from the treatment of the magnesium salt with ethylene oxide was decomposed with ice and ammonium chloride, and the product so obtained was hydrolyzed at room temperature with dilute hydrochloric acid, the required hydroxy ketone was obtained, in fair yield, and could be distilled at pressures below 1 mm. 2-(2′-Hydroxyethyl)cyclohexanone is mentioned, without details, in the patent literature;[5] we identified it by its spectral properties and by conversion to the known[6] 2,4-dinitrophenylhydrazone, acetate, and acetate 2,4-dinitrophenylhydrazone. An attempted preparation[6] of the hydroxy ketone by hydrolysis of 2-(2′-ethylenedioxycyclohexyl)ethanol yielded only mixtures of "unsaturated cyclization products" possibly because on distillation at a pressure of approximately 10 mm, the hydroxy ketone loses water to form 2,3,4,5,6,7-hexahydrobenzofuran (4). This substance, which could be obtained from the imine–ethylene oxide reaction without isolation of the hydroxy ketone, showed strong infrared absorption at 1710 cm^{-1} (enol ether) and the nuclear magnetic resonance (nmr) spectrum showed a triplet (2 H) centered at τ 5.73 due to the protons on C-2 which were coupled to the allylic protons on C-3. The latter two protons gave rise to a triplet (2 H) centered at τ 7.49; spin decoupling experiments confirmed these assignments. Hydrogenation of the hexahydrobenzofuran gave *cis*-octahydrobenzofuran (5).[7,8]

Scheme I



Analogous treatment of the magnesium salt of N-cyclohexylcyclohexylimine with propylene oxide gave

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(1) Aided by Grant AI06328 from the National Institutes of Health.

(2) G. Stork, R. Terrell, and J. Szmuszkovicz, *J. Am. Chem. Soc.*, **76**, 2029 (1954); G. Stork and H. Landesman, *ibid.*, **78**, 5128 (1956); G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *ibid.*, **85**, 207 (1963). For review, see J. Szmuszkovicz, *Advan. Org. Chem.*, **4**, 1 (1963).

(3) D. S. Tarbell, *et al.*, *J. Am. Chem. Soc.*, **83**, 3096 (1961).

(4) G. Stork, and S. R. Dowd, *ibid.*, **85**, 2178 (1963).

(5) W. W. Prichard, U. S. Patent 2,549,520; *Chem. Abstr.*, **45**, 8553 (1951).

(6) A. Segre, R. Viterbo, and G. Parisi, *J. Am. Chem. Soc.*, **79**, 3503 (1957).

(7) N. I. Shuikin, I. I. Demitriev, and T. P. Dobrynina, *J. Gen. Chem. USSR*, **10**, 967 (1940); *Chem. Abstr.*, **35**, 2508 (1941).

(8) S. E. Cantor and D. S. Tarbell, *J. Am. Chem. Soc.*, **86**, 2902 (1964).

the known[9] 2-(2′-hydroxypropyl)cyclohexanone (**6**), which was converted into 2-methyl-2,3,4,5,6,7-hexahydrobenzofuran (**7**), and thence into *cis*-2-methyloctahydrobenzofuran (**8**).[8] No evidence was obtained that **8** was a mixture of diastereoisomers, which implies that the reduction of the hexahydrobenzofuran **7** proceeds stereospecifically.

The hexahydrobenzofurans are rather unstable compounds which appear to polymerize slowly and, in the presence of moisture, revert partially to the hydroxy ketones. This is indicated by changes in the infrared spectrum and by the fact that the hydroxy ketone can be distilled at low pressure from the hexahydrobenzofurans which have been exposed to moisture. It appears that an equilibrium exists between the hydroxy ketones on the one hand and the hexahydrobenzofurans and water on the other.

Experimental Section[10]

2-(2′-Hydroxyethyl)cyclohexanone (**2**).—N-Cyclohexylcyclohexylimine[11] (98 g, 0.5 mole) in tetrahydrofuran (150 ml) was added dropwise with stirring during 2 hr to a boiling solution of ethylmagnesium bromide (0.5 mole) in tetrahydrofuran (200 ml). Heating was continued until evolution of ethane ceased, then the solution was cooled to 0°. The colorless precipitate which separated dissolved as ethylene oxide (22 g, 0.5 mole) was passed in with stirring, and the resulting light brown solution was set aside overnight, concentrated under reduced pressure to remove most of the tetrahydrofuran, diluted with ether, and poured onto a mixture of ice (400 g) and ammonium chloride (100 g). The aqueous layer was separated and extracted three times with ether and the combined ether solutions were washed twice with water, dried (Na_2SO_4), and concentrated to yield a pale brown oil (83 g). The oil was stirred vigorously at room temperature with 1 *N* hydrochloric acid (600 ml, 0.6 mole) for 1.5 hr. The resulting mixture was extracted four times with ether, and the combined extracts were washed with 1 *N* HCl, with water, and with sodium bicarbonate solution, and were then dried and concentrated. Distillation under reduced pressure gave, after a small forerun of cyclohexanone, 2-(2′-hydroxyethyl)cyclohexanone, bp 68–70° (0.25 mm), n^{25}D 1.4815 (21 g, 30%).

Anal. Calcd for $C_8H_{14}O_2$: C, 67.6; H, 9.9. Found: C, 67.6; H, 9.6.

The infrared spectrum showed a broad band at 3450 cm^{-1} (OH) and strong bands at 1705 (C=O), 1448, 1070, 1000, and 940 cm^{-1}. The nmr spectrum showed a broad multiplet at τ 6.3 (2 H, CH_2O) and a broad singlet at τ 6.85 (1 H, OH) which disappeared when the sample was shaken with D_2O. The 2,4-dinitrophenylhydrazone formed orange plates (from ethanol), mp 148–149°, (lit.[6] mp 145–146.5°.

The acetyl derivative had n^{25}D 1.4615 (lit.[6] n^{27}D 1.4565) and showed strong bands in the infrared spectrum at 1740 (ester carbonyl), 1710 (keto carbonyl), 1370, 1235 (acetate), and 1035 cm^{-1}. The nmr spectrum showed a sharp triplet at τ 5.90 (2 H, J = 6.5 cps, CH_2OAc).

The acetate 2,4-dinitrophenylhydrazone formed yellow needles (from ethanol), mp 111–112°, lit.[6] mp 109–111°.

2,3,4,5,6,7-Hexahydrobenzofuran (**4**). A.—2-(2′-Hydroxyethyl)cyclohexanone was distilled at 10-mm pressure (oil bath at 140°) giving water and the hexahydrobenzofuran [bp 56° (10 mm), n^{25}D 1.4864] in almost quantitative yield.

Anal. Calcd for $C_8H_{12}O$: C, 77.4; H, 9.7. Found: C, 77.3; H, 9.6.

The infrared spectrum showed strong bands at 1708 (enol ether C=C) 1440, 1380, 1283, 1260, 1200 (C=CO), 1190, 1090, 980, 940, and 885 cm^{-1}. The nmr spectrum showed a sharp triplet at τ 5.73 (2 H, J = 9 cps, CH_2O) and a broad triplet at τ 7.49 (2 H, J = 9 cps, allylic protons).

B.—The magnesium salt of N-cyclohexylcyclohexylimine was treated with ethylene oxide as above, but the resulting solution was decomposed at 0° with 4 *N* sulphuric acid (700 ml), and the mixture was boiled with stirring for 2 hr. The product was collected with ether as before and distilled from a bath at 150° giving 2,3,4,5,6,7-hexahydrobenzofuran (28 g, 45%) identical with the material obtained by method A.

On standing, the hexahydrobenzofuran slowly polymerized, and in presence of moist air partly reverted to 2-(2′-hydroxyethyl)cyclohexanone.

The hexhydrobenzofuran gave 2,4-dinitrophenylhydrazone (mp 149–150°) shown by its X-ray powder pattern to be identical with the 2,4-dinitrophenylhydrazone from 2-(2′-hydroxyethyl)cyclohexanone.

On gas chromatography (15-ft column, 10% Apiezon L on Chromosorb P, 180°), 2,3,4,5,6,7-hexahydrobenzofuran gave a single peak. 2-(2′-Hyroxyethyl)cyclohexanone also gave a single peak with the same retention time, and collection of the material responsible for this peak and determination of the infrared spectrum showed that it was the hexahydrobenzofuran which presumably was formed by decomposition of the hydroxy ketone in the injection port or on the column.

2-(2′-Chloroethyl)cyclohexanone (**3**).—The magnesium salt of N-cyclohexylcyclohexylimine (0.25 mole) in tetrahydrofuran (200 ml) was treated with ethylene oxide as described above. The resulting solution was set aside overnight, then hydrochloric acid (375 ml, 4 *N*, 1.5 moles) was added slowly, and the solution was boiled with stirring for 2 hr. The cooled solution was extracted three times with ether and the combined ether extracts were washed until no longer acid, dried (Na_2SO_4), and concentrated. Distillation gave a small amount of cyclohexanone, followed by material [bp 80–83° (6 mm), n^{25}D 1.4830, 17 g], consisting of 2-(2′-chloroethyl)cyclohexanone containing probably a small amount of 2,3,4,5,6,7-hexahydrobenzofuran.

Anal. Calcd for $C_8H_{13}ClO$: C, 59.8; H, 8.2; Cl, 22.1. Found: C, 61.2; H, 8.7; Cl, 18.5.

This material reacted rapidly with sodium hydroxide solution to liberate chloride ion and decomposed on attempted gas chromatography (15-ft column, 10% Apiezon L on Chromosorb P, 180°) since it gave rise to a single peak shown by comparison of its retention time, and by collection, to be due to 2,3,4,5,6,7-tetrahydrobenzofuran.

The infrared spectrum of the chloro compound showed no OH band, a strong band at 1710 cm^{-1} (carbonyl) and also weak bands at 1200, 1260, and 1283 cm^{-1} which appeared to correspond to strong bands in the spectrum of 2,3,4,5,6,7-hexahydrobenzofuran.

***cis*-Octahydrobenzofuran** (**5**).—2,3,4,5,6,7-Hexahydrobenzofuran in ethyl acetate was shaken with hydrogen at 1 atm in the presence of 10% palladium–charcoal catalyst. Removal of the catalyst and distillation gave *cis*-octahydrobenzofuran, bp 66° (15 mm), n^{25}D 1.4639 [lit.[8] bp 66–68° (15 mm), n^{24}D 1.4648].

Anal. Calcd for $C_8H_{14}O$: C, 76.1; H, 11.2. Found: C, 75.8; H, 11.0.

The infrared spectrum had no OH or carbonyl bands but showed strong absorption at 1450, 1180, 1160, 1120, 1080, 1020, 930, 880, and 805 cm^{-1}. The nmr spectrum showed a broad multiplet at approximately τ 6.15 (3 H, $CHOCH_2$).

2-(2′-Hydroxypropyl)cyclohexanone (**6**).—Propylene oxide (29 g, 0.5 mole) was added dropwise with stirring to an ice-cold suspension of the magnesium salt of N-cyclohexylcyclohexylimine (0.5 mole) in tetrahydrofuran (400 ml). The resulting mixture was set aside overnight, boiled under reflux for 1 hr, then cooled and worked-up as described above for the analogous reaction with ethylene oxide, giving 2-(2′-hydroxypropyl)cyclohexanone [(28 g), bp 73–75° (0.2 mm), n^{25}D 1.4760] having infrared and nmr spectra identical with those of an authentic sample.[9]

2-Methyl-2,3,4,5,6,7-hexahydrobenzofuran (**7**).—Slow distillation of 2-(2′-hydroxypropyl)cyclohexanone at 30-mm pressure (oil bath at 120°) gave water and the 2-methylhexahydrobenzofuran in almost quantitative yield. It had bp 85–86° (30 mm), n^{25}D 1.4770.

Anal. Calcd for $C_9H_{14}O$: C, 78.2; H, 10.2. Found: C, 77.9; H, 10.1.

The infrared spectrum showed strong bands at 1710 (enol ether C=C), 1445, 1375, 1282, 1204 (C=CO), 1150, 909, and

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[9] D. P. Brust and D. S. Tarbell, *J. Org. Chem.*, **31**, 1251 (1966).

[10] Analyses were performed by Dr. A. D. Campbell and associates, University of Otago, Dunedin, New Zealand. Infrared spectra were recorded for liquid films using a Perkin-Elmer Model 421 spectrophotometer; nmr spectra were determined with Varian A-60 and Varian HR-60 instruments on deuteriochloroform solutions, using tetramethylsilane (TMS) as internal standard, under the direction of Dr. L. D. Colebrook. An Aerograph A90-P-2 gas chromatograph was used.

[11] E. D. Bergmann, E. Zimkin, and S. Pinchas, *Rec. Trav. Chim.*, **71**, 168 (1952).

818 cm^{-1}. The nmr spectrum showed a doublet centered at τ 8.57 (3 H, J = 6 cps, CH_3) and a multiplet at approximately τ 5.28 (1 H, CHO).

When the methylhexahydrobenzofuran was set aside with access of moist air, it slowly became more viscous, the infrared spectrum showed hydroxyl absorption, and, on distillation, 2-(2'-hydroxypropyl)cyclohexanone was obtained (identified by infrared and nmr spectra); a resinous residue remained.

cis-**2-Methyloctahydrobenzofuran** (**8**).—2-Methyl-2,3,4,5,6,7-hexahydrobenzofuran in ethyl acetate was shaken with hydrogen at 1-atm pressure in the presence of reduced platinum oxide. Absorption of hydrogen was rapid and ceased after the uptake of 1 mole of hydrogen. Removal of the catalyst, and distillation gave, in quantitative yield, *cis*-2-methyloctahydrobenzofuran, bp 70–71° (20 mm), n^{25}D 1.4570 [lit.[8] bp 63° (16 mm), n^{25}D 1.4548].

The infrared spectrum was identical with that of an authentic sample. The nmr spectrum showed a sharp doublet centered at τ 8.71 (3 H, J = 6 cps, CH_3) and a broad multiplet at approximately τ 6.1 (2 H, CHOCH]. There was no indication of other peaks which could be attributed to methyl protons, and the material, therefore, probably consists of a single isomer since Cantor and Tarbell[8] record the presence of two methyl doublets in the spectrum of material considered to be a mixture of diastereoisomers. Gas chromatography (15-ft column, 4% Dow 11 on Chromosorb G, 100°) showed only one peak, thereby establishing the fact that the material was free of the *trans* isomer.

Registry No.—**1**, 10198-26-2; **2**, 10198-27-3; **3**, 2402-57-5; **4**, 10198-28-4; **5**, 10198-29-5; **6**, 6126-52-9; **7**, 10198-31-9; **8**, 10198-32-0; acetyl derivative of **2**, 10198-33-1.

Concerning the Structure of the $(C_4H_4O)^{+\cdot}$ Ion from the Electron Impact Induced Fragmentation of 2-Pyrone

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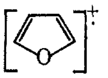
Received January 17, 1967

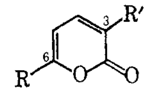
One of the fundamental and most difficult problems in mass spectrometric investigations is the assignment of structures to the various ions encountered. A classic attack on this problem has resulted in the elucidation of the structure of $C_7H_7^+$ ion by S. Meyerson and co-workers.[1b]

For want of positive structural evidence, many workers simply assign ionic structures which correspond to well known energy minimization criteria used in the ground state (*e.g.*, tertiary carbonium ions > secondary > primary). Another common practice may be termed the "external standard method."[2] The latter involves making a qualitative correlation between peaks of lower m/e values than a fragment ion, with peaks derived from a standard molecular ion of identical elemental composition. The observation of such a correspondence often prompts the claim that the fragment ion and the molecular ion (assumed to be unrearranged) possess the same structure.

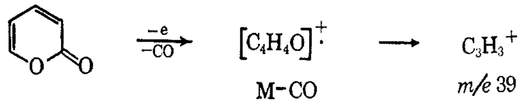
The "external standard method" has found wide use in the assignment of structure to ions formed by direct loss of carbon monoxide from various aromatic systems on electron impact.[2a–c,g–i] Recently, the application of this technique in the assignment of a cyclic furan structure (I) to the M–CO species produced in the fragmentation of 2-pyrones (reaction 1) has been questioned and rejected.[3] Pirkle has proposed[3] that if a cyclic furan radical ion (I) were an intermediate in the fragmentation of 2-pyrone (II), the distinction between carbon atoms three and six would be lost. Therefore, specific deuteration at C-3 (III) and C-6 (IV) would lead to the same isotopic distribution in peaks derived from the proposed furan intermediate I, *i.e.*, mainly m/e 39, which is the base peak in the spectrum of both furan and 2-pyrone. The spectra of 3-*d*-2-pyrone (III) and 6-*d*-2-pyrone (IV) were obtained,[3] and in the former the m/e 39 peak is preferentially shifted to m/e 40, while in the latter the m/e 39 peak largely remains unshifted. It was, therefore, concluded[3] that the C_4H_4O radical ion cannot have a furan structure (I).



I



II, R = R' = H
III, R = H; R' = D
IV, R = D; R' = H



(1)

We wish to show in this communication that the intermediacy of furan radical ion I is still an open question in these systems, since the differences of isotopic distribution in the mass spectra of III and IV can equally well be explained by multiple[4] pathways to m/e 39.

In fact, a second pathway which does not proceed through the intermediacy of an $[M-CO]^{+\cdot}$ ion has been clearly demonstrated[5] in the mass spectral fragmentation of various substituted 2-pyrones. This process (reaction 2) is supported[5] by the presence of an appropriate metastable peak, and involves specific loss of the C-6 substituent[6] in the first step (V → aa). Exactly the same situation obtains in the mass spectra of deuterium labeled 2-pyrones,[3] since III exhibits only an M − 1 ion, while IV shows solely an M − 2 ion. These results strongly suggest that formation of $C_3H_3^+$ (m/e 39) in 2-pyrone proceeds at least in part *via* the C-6 cleavage pathway (reaction 2). Since

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[1] (a) To whom correspondence should be addressed: Department of Chemistry, The University of Michigan, Ann Arbor, Mich. 48104. (b) For a summary of this work, see H. M. Grubb and S. Meyerson in "Mass Spectrometry of Organic Ions," F. W. McLafferty, Ed., Academic Press, Inc., New York, N. Y., 1963, p 453.

[2] For applications of this procedure, see (a) J. H. Beynon, G. R. Lester, and A. E. Williams, *J. Phys. Chem.*, **63**, 1861 (1959); (b) C. S. Barnes and J. L. Occolowitz, *Australian J. Chem.*, **17**, 975 (1964); (c) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Structure Elucidation of Natural Products by Mass Spectrometry," Vol. II, Holden-Day, Inc., San Francisco, Calif., 1964, Chapter 29; (d) P. Funke, K. G. Das, and A. K. Bose, *J. Am. Chem. Soc.*, **86**, 2527 (1964); (e) K. G. Das, P. T. Funke, and A. K. Bose, *ibid.*, 3729 (1964); (f) P. Brown and C. Djerassi, *ibid.*, **88**, 2469 (1966); (g) G. Spiteller and M. Spiteller-Friedman, *Monatsh. Chem.*, **93**, 1395 (1962); (h) J. D. McCollum and S. Meyerson, *J. Am. Chem. Soc.*, **85**, 1739 (1963); (i) J. M. Wilson, M. Ohashi, H. Budzikiewicz, C. Djerassi, S. Itô, and T. Nozoe, *Tetrahedron*, **19**, 2247 (1963); (j) C. E. Brion and L. D. Hall, *J. Am. Chem. Soc.*, **88**, 3661 (1966).

[3] W. H. Pirkle, *ibid.*, **87**, 3022 (1965).

[4] We should point out that in principle the demonstration of more than one pathway to m/e 39 in itself invalidates the conclusions drawn in ref 3.

[5] H. Nakata, Y. Hirata, and A. Tatematsu, *Tetrahedron Letters*, 123 (1965).

[6] H. Budzikiewicz, J. I. Brauman, and C. Djerassi [*Tetrahedron*, **21**, 1855 (1965)] report the mass spectrum of 4-methoxy-6-phenyl-2-pyrone, which also suffers characteristic cleavage of the 6-phenyl substituent.