of 89.6 mg (1.0 mmol) of copper(I) cyanide in 2 mL of THF was cooled to −30 °C, and 1.2 mL of *t*-BuLi (2.0 mmol, 1.7 M solution in pentane) was added dropwise. The mixture was stirred at −30 °C for 30 min, then cooled to −80 °C, and a solution of 0.9 mmol of the Michael acceptor (**6**: 162.2 mg; **9**: 185.7 mg) in 1 mL of THF was added dropwise. The red solution was stirred for 15 min at −80 °C and then ca. 3 mL was removed with a syringe, followed by addition of 0.2 mL of THF-d_8. The remaining solution was degassed by three freeze–pump–thaw cycles; during thawing the temperature was kept below −80 °C. The solution was transferred into the precooled (−80 °C) NMR tube which was sealed off under vacuum. By the same procedure, a NMR sample of the π-complex of 6,6-dimethyl-2-hepten-4-ynenitrile (119.9 mg, 0.9 mmol) with Me_2CuLi·LiI (from 190.4 mg = 1.0 mmol copper(I) iodide and 1.3 mL (2.0 mmol) of MeLi (1.5 M solution in diethyl ether)) was prepared with diethyl ether as solvent.

^{13}C-NMR data, obtained with a Bruker WM-300 spectrometer at 75.5 MHz.

6 ($CDCl_3$ as solvent and internal standard (δ = 77.05)): δ 14.2 (+, $CO_2CH_2CH_3$), 28.3 (x, C-6), 30.6 (+, $C(CH_3)_3$), 60.5 (−, CO_2CH_2), 76.5 (x, C-4), 108.4 (x, C-5), 126.1 (x, C-3), 129.1 (x, C-2), 166.1 (x, C-1).

7 (THF as solvent and internal standard (δ = 26.5), −80 °C): δ = 48.2/48.9 (+, C-2), 59.3/59.6 (−, CO_2CH_2), 60.7/61.7 (+, C-3), 84.7/84.9 (x, C-4/C-5), 89.3/89.5 (x, C-4/C-5), 159.2 (x, CN), 173.0/174.2 (x, C-1).

8 (THF as solvent and internal standard (δ = 26.5), −20 °C): δ 61.7 (−, CO_2CH_2), 64.1 (+, C-2), 94.9 (+, C-3), 120.4 (x, C-5), 149.5 (x, CN), 164.2 (x, C-1), 201.3 (x, C-4).

9 ($CDCl_3$ as solvent and internal standard (δ = 77.05)): δ 14.3 (+, $CO_2CH_2CH_3$), 28.3 (x, C-8), 30.8 (+, $C(CH_3)_3$), 60.4 (−, CO_2CH_2), 78.0 (x, C-6), 105.9 (x, C-7), 120.4 (+, C-5), 122.0 (+, C-2), 137.4 (+, C-4), 143.4 (+, C-3), 166.7 (x, C-1).

10 (THF as solvent and internal standard (δ = 26.5), −80 °C): δ 58.6/59.6 (−, CO_2CH_2), 59.6/59.8 (+, C-2), 70.3/70.8 (+, C-3), 81.2/81.3 (x, C-6), 93.9/94.0 (x, C-7), 172.0/173.0 (x, C-1).

11 (THF as solvent and internal standard (δ = 26.5), −20 °C): δ 59.8/60.1 (−, CO_2CH_2), 78.5 (+, C-2), 95.1 (+, C-3/C-5), 103.4 (+, C-3/C-5), 116.7 (x, C-7), 129.5 (+, C-4), 171.8/173.0 (x, C-1), 204.1 (x, C-6).

6,6-Dimethyl-2-hepten-4-ynenitrile ($CDCl_3$ as solvent and internal standard (δ = 77.05)): δ 28.4 (x, C-6), 30.3 (+, $C(CH_3)_3$), 75.9 (x, C-4), 107.2 (+, C-2), 111.0 (x, C-5), 117.2 (x, C-1), 131.9 (+, C-3).

π-Complex of 6,6-dimethyl-2-hepten-4-ynenitrile with Me_2CuLi·LiI (Et_2O as solvent and internal standard (δ = 14.6), −50 °C): δ 25.6 (+, C-2), 28.5 (x, C-6), 31.8 (+, $C(CH_3)_3$), 40.5 (+, C-3), 82.6 (x, C-4/C-5), 89.3 (x, C-4/C-5), 128.7 (x, C-1).

Acknowledgment. Financial support of this work by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie is gratefully acknowledged.

Abnormal Weiss–Cook Condensation of *cis*-6-Cyclodecene-1,2-dione with Dimethyl 1,3-Acetonedicarboxylate. The Consequences of Ring Strain Release

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The 2-fold condensation of dimethyl 1,3-acetonedicarboxylate (**2**) with α-dicarbonyl compounds, the Cook–Weiss reaction, has served very well as a vehicle for the rapid assembly of heavily functionalized diquinane frameworks under relatively mild conditions.[2] The extensive carbon–carbon bond construction that materializes has been formulated in terms of a sequence of aldol, Michael, and β-elimination reactions.[3] Aliphatic 1,2-dicarbonyl compounds enter effectively into this condensation; alicyclic analogues have proven more variable in their response. Thus, while [*n*.3.3]propellanes **3a** and **3c** are formed in good yield (>80%) under modestly acidic or basic conditions,[4] cyclodecane-1,2-dione (**1b**) has been reported to give **3b** inefficiently (30%) and only when strong basic catalysis is applied.[5]

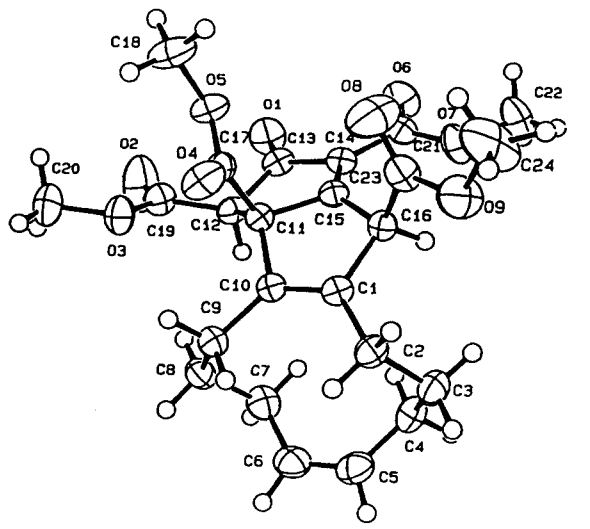
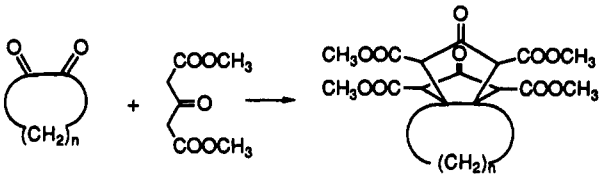


Figure 1. ORTEP diagram of **8**. The non-hydrogen atoms are represented by 50% probability thermal ellipsoids. The hydrogen atoms are drawn with an artificial radius.



1a, n = 6 **2** **3a**, n = 6
b, n = 8 **b**, n = 8
c, n = 10 **c**, n = 10

One might question whether the last observation is an indicator of a possible interrelationship between ring size and relative ease of cyclopentannulation. Certainly, the value of *n* is crucial to smooth operation of the Cook–Weiss process.

Our laboratory has been engaged in the synthesis of 1,5-biscyclooctatetraenophanes.[6] For the [2_2] derivative, early use is made of the conversion of **4** to **5** at pH 5.6.[7] The yield of this conversion peaks at 86%. In a more recent extension of this chemistry, *cis*-6-cyclodecene-1,2-dione (**6**)[8] failed to undergo detectable cyclocondensation

(1) Author to whom inquiries concerning the X-ray crystallographic analysis should be addressed.

(2) Gupta, A. K.; Fu, X.; Snyder, J. P.; Cook, J. M. *Tetrahedron* **1991**, *47*, 3665.

(3) Yang-Lan, S.; Mueller-Johnson, M.; Oehldrich, J.; Wichman, D.; Cook, J. M.; Weiss, U. *J. Org. Chem.* **1976**, *41*, 4053.

(4) (a) Yang, S.; Cook, J. M. *J. Org. Chem.* **1976**, *41*, 1903. (b) Mitschka, R.; Weiss, U.; Cook, J. M. *J. Am. Chem. Soc.* **1978**, *100*, 3973.

(5) Paquette, L. A.; Trova, M. P.; Luo, J.; Clough, A. E.; Anderson, L. B. *J. Am. Chem. Soc.* **1990**, *112*, 228.

(6) (a) Paquette, L. A.; Kesselmayer, M. A. *J. Am. Chem. Soc.* **1990**, *112*, 1258. (b) Paquette, L. A.; Kesselmayer, M. A.; Underiner, G. E.; House, S. D.; Rogers, R. D.; Meerholz, K.; Heinze, J. *J. Am. Chem. Soc.* **1992**, *114*, 2644.

(7) Mitschka, R.; Oehldrich, J.; Takahashi, K.; Cook, J. M.; Weiss, U.; Silverton, J. V. *Tetrahedron* **1981**, *37*, 4521.

(8) Cram, D. J.; Allinger, N. L. *J. Am. Chem. Soc.* **1956**, *78*, 2518.

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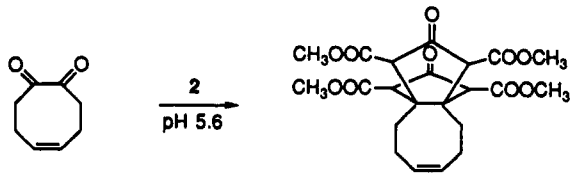
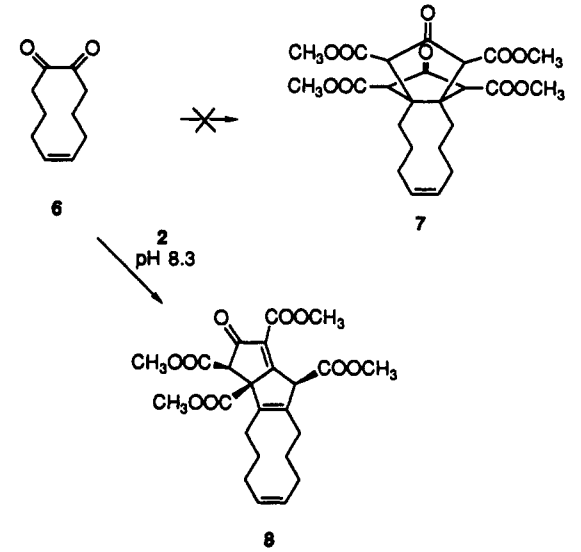


4 5

under comparably acidic conditions.[9] By contrast, stirring **6** with dimethyl 1,3-acetonedicarboxylate (**2**) in aqueous methanol at pH 8.3 for 3 days led to a single diastereomeric product, which clearly was not **7** because its NMR spectra were distinctively different from those of **3** and **5**. The



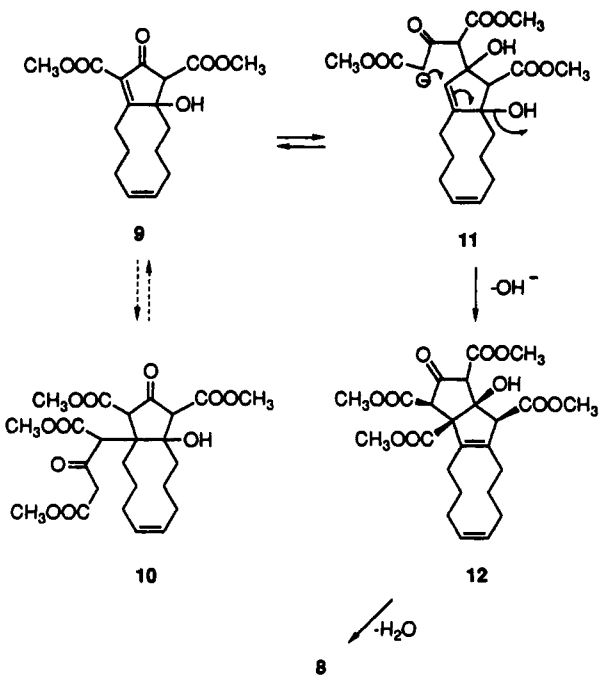
6 7 8

high crystallinity of this substance led to its examination by X-ray diffraction methods. As seen in Figure 1, the resultant bisadduct is a monoketo tetracarboxylate with a radically different diquinane part structure than the norm. In **8**, all three stereogenic centers carry carbomethoxy groups and these are fixed in an all-cis relationship.

Compound **8** presumably arises by initial conversion of **6** to **9** in customary fashion. Second-stage attack is now diverted away from the 1,4-addition that normally operates (Scheme I). Of course, the possibility exists that **10** does form,[10] but reverts uneventfully back to **9**. The logical alternative process is to form **11** by 1,2-addition, thereby setting the stage for ring closure to generate **12**, the penultimate precursor to **8**. Although several pathways exist for the conversion of **11** into **12**, that which is illustrated best accommodates the perceived thermodynamic advantages discussed below. Associated electronic and steric effects also likely contribute to the success of this condensation.

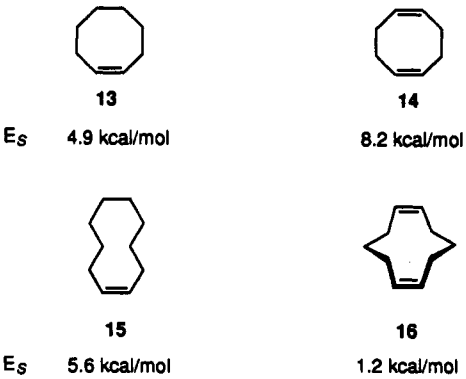
The evolution of **8** as the kinetically favored product is considered to be a response on the part of the cyclodecene ring to a more energetically rewarding pathway not exercised under normal circumstances. We are mindful of the fact that introduction of a second double bond into *cis*-cyclooctene (**13**) so as to generate 1,5-diene **14** increases the level of ring strain by more than 3 kcal/mol.[11,12]

Scheme I



9 11 10 12 8

Conversely, analogous modification of *cis*-cyclodecene (**15**) to give **16** is now *highly favorable* (~4.5 kcal/mol).[11] This remarkable crossover likely has its origins in the possible adoption by **16** of a ground-state lounge conformation[13,14] that lies ca. 1 kcal/mol below the boat form.[11,15-17] 1,5-Cyclooctadiene does not find it possible to exit as readily from a boat arrangement.[15-18]



13 14

E_S 4.9 kcal/mol 8.2 kcal/mol

15 16

E_S 5.6 kcal/mol 1.2 kcal/mol

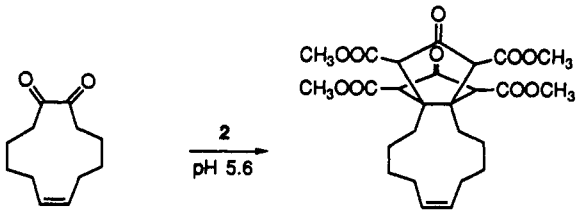
In light of this appraisal, the conversion of **11** to **12** has several favorable features, not the least of which is less energy-demanding passage to a *cis,cis*-1,6-cyclodecadiene framework. In the cyclooctene equivalent, this step would be disadvantaged relative to the Michael reaction that ultimately generates the propellane network. The very special character of cyclodecene/1,6-cyclooctadiene energetics does not carry over to larger ring systems. As expected, therefore, upon further probing of the reactivity

(9) The acid-catalyzed condensation of cyclododecane-1,2-dione with dimethyl 1,3-acetonedicarboxylate has been reported to proceed abnormally and to lead to a bicyclic furan derivative [Campos, O.; Cook, J. M. *J. Heterocycl. Chem.* **1977**, *14*, 711].

(10) Different levels of steric congestion are likely encountered during this Michael reaction as the size of the cycloalkene ring is varied. We do not rule out the possibility that the formation of **10** is perhaps made demanding because of somewhat higher levels of nonbonded steric compression.

(11) Turner, R. B.; Mallon, B. J.; Tichy, M.; Doering, W. v. E.; Roth, W. R.; Schröder, G. *J. Am. Chem. Soc.* **1973**, *95*, 8605.
(12) White, D. N. J.; Bovill, M. J. *J. Chem. Soc., Perkin Trans II* **1977**, 1610.
(13) Dale, J.; Ekeland, T.; Schaug, J. *Chem. Commun.* **1968**, 1477.
(14) Almenningen, A.; Jacobsen, G. G.; Seip, H. M. *Acta Chem. Scand.* **1969**, *23*, 1495.
(15) Anet, F. A. L.; Kozerski, L. *J. Am. Chem. Soc.* **1973**, *95*, 3407.
(16) Anet, F. A. L.; Anet, R. In *Dynamic Nuclear Magnetic Resonance Spectroscopy*; Cotton, F. A.; Jackman, L. M., Eds.: Academic Press: New York, 1975; p 571.
(17) Ermer, O. *J. Am. Chem. Soc.* **1976**, *98*, 3964.
(18) (a) Allinger, N. L.; Sprague, J. T. *Tetrahedron* **1975**, *31*, 21. (b) Allinger, N. L.; Tribble, M. T.; Sprague, J. T. *J. Org. Chem.* **1972**, *37*, 2423.

connection with 17,[19] the Cook-Weiss pathway was reestablished. This control experiment proceeded smoothly to deliver 18 in 70% yield.[20]



17 18

Other applications of medium-ring energetics to the control of chemical reactions can easily be envisioned. Recently, this principle was deployed so as to permit observation of the first reversible oxy-Cope rearrangement.[21]

Experimental Section

Tetramethyl (3*R*,3a*R*,12*S*)-2,3a,4,5,6,9,10,11-Octahydro-2-oxocyclodeca[*a*]pentalene-1,3,3a,12(3*H*)-tetracarboxylate (8). Dimethyl 1,3-acetonedicarboxylate (3.76 g, 21.2 mmol) was dissolved in aqueous $NaHCO_3$ solution (0.98 g, 11.7 mmol, 70 mL of water) and 6 (1.76 6, 10.6 mmol) was introduced followed by enough methanol to achieve dissolution (70 mL). After 3 days of stirring at rt, the homogeneous solution was cooled in ice and acidified to pH 1 with dilute HCl. The resultant precipitate was recrystallized from methanol to give large colorless prisms of 8 (2.07 g, 41%): mp 161-163 °C; IR ($CHCl_3$, cm^{-1}) 1755, 1680; ^1H NMR (300 MHz, $CDCl_3$) δ 5.38-5.25 (m, 2 H), 4.58 (s, 1 H), 3.84 (s, 3 H), 3.80 (s, 3 H), 3.642 (s, 3 H), 3.639 (s, 3 H), 3.46 (s, 1 H), 2.52-2.48 (br m, 3 H), 2.15-2.05 (br m, 1 H), 1.84 (m, 5 H), 1.53 (m, 2 H), 1.38 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 191.4, 181.8, 169.2, 167.4, 166.6, 161.4, 140.7, 138.2, 130.0, 129.5, 127.3, 67.4, 65.3, 52.8, 52.5, 52.4, 52.2, 24.7, 24.6, 24.3, 24.1, 24.0, 22.8; MS m/z (M^+) calcd 460.1733, obsd 460.1728.

Anal. Calcd for $C_{24}H_{28}O_9$: C, 62.59; H, 6.13. Found: C, 62.55; H, 6.11.

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Registry No. 2, 1830-54-2; 6, 99172-44-8; 8, 141119-96-2; 17, 141119-97-3; 18, 141119-98-4.

Supplementary Material Available: Crystallographic details, bond lengths, bond angles, torsion angles, positional parameters, anisotropic thermal parameters, and calculated positional parameters for the hydrogen atoms of 8 (12 pages). Ordering information is given on any current masthead page.

(19) Obtained by controlled catalytic hydrogenation (H_2, Pd-$BaSO_4$) of 7,8-diketocyclododecyne prepared according to ref 8.
(20) Underiner, G. E. Unpublished results.
(21) Elmore, S. W.; Paquette, L. A. *Tetrahedron Lett.* **1991**, *32*, 319.

Mechanism of Epoxidation of Vitamin K with Basic Hydrogen Peroxide

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Introduction

Vitamin K (1) has attracted attention because of its function as an obligatory cofactor in enzymic sequences central to blood clotting.[1,2] In a recent study of the mechanism of action of vitamin K, the role of molecular oxygen in the formation of vitamin K oxide (2) was explored.[2] A mechanism for this reaction has been suggested that is supported by the results of parallel ^{16}O-^{16}O and ^{18}O-^{18}O experiments in the oxygen-promoted oxidation of vitamin K hydroquinone and in the corresponding oxidation of the model systems, 2,4-dimethyl-1-naphthol and 2,3,4-trimethyl-1-naphthol.[2] Key features of this mechanism include (i) the formation of a dioxetane intermediate and (ii) the possibility that as many as two ^{18}O atoms are incorporated into vitamin K oxide (2) as a result of the molecular oxygen promoted oxidation process.[2]

Several years ago, Alder and co-workers[3a] reported that the enedione carbon-carbon double bond in *endo*-tricyclo[6.2.1.$0^{2,7}$]undeca-4,9-diene-3,8-dione (3) can be selectively epoxidized using basic hydrogen peroxide to yield the corresponding *exo*-4,5-epoxide 4.[3b,c] One possible mechanism that would account for the formation of 4 is shown in Scheme I as a 1,2-addition/rearrangement mechanism. This mechanism postulates formation of a dioxetane intermediate 5 and is analogous to the mechanism suggested for the oxygen-promoted oxidation of vitamin K hydroquinone to vitamin K oxide.[2] An alternative, equally plausible, mechanism for the selective epoxidation of 3 to 4 can be envisioned is also outlined in Scheme I. Rather than proceeding through a dioxetane intermediate, the alternative 1,4-addition mechanism focuses upon initial Michael addition of HOO^- to the enedione carbon-carbon double bond, which is activated toward nucleophilic attack by conjugation with the adjacent carbonyl groups.[3b]

In the present study, we have investigated both the reaction of 3 and of vitamin K with basic H_2O_2, using $Na^{18}OH/H_2O_2$ and $NaOH/H^{18}O$-^{18}OH in separate labeling experiments. The results of these experiments unambiguously differentiate between the mechanisms shown in Scheme I.

Results and Discussion

Treatment of vitamin K with $H^{18}O$-^{18}OH and sodium carbonate in either aqueous or anhydrous ethanol results in exclusive formation of the ^{18}O-labeled epoxide (Scheme II). This is most readily demonstrated by analysis of the mass spectrum of vitamin K oxide-^{18}O. In the aqueous ethanol experiments, the molecular ion is observed at m/z 468 and the ratio of the m/z 468, 469, 470 peaks is 100:33.3:6.9. The calculated values are 100:34.4:6.3.[4] The same result was obtained under anhydrous conditions. Thus, the peak at 470 is completely normal in intensity indicating that only one atom of ^{18}O has been incorporated into vitamin K oxide. Analysis of the fragmentation pattern establishes unambiguously that the label is located at the epoxide oxygen.[2a] Treatment of the ^{18}O-labeled epoxide with aqueous base resulted in no change in the mass spectral pattern showing that all the ^{18}O was incor-

(1) For a review of early studies of vitamin K, see: Wagner, A. F.; Folkers, K. *Vitamins and Coenzymes*; Interscience: New York, 1964; pp 407-434.
(2) (a) Dowd, P.; Ham, S. W.; Geib, S. J. *J. Am. Chem. Soc.* **1991**, *113*, 7734. (b) Ham, S. W.; Dowd, P. *J. Am. Chem. Soc.* **1990**, *112*, 1660. (c) Dowd, P.; Ham, S. W. *J. Am. Chem. Soc.* **1991**, *113*, 9403.
(3) (a) Alder, K.; Flock, F. H.; Baumling, H. *Chem. Ber.* **1960**, *93*, 1896. (b) See also: Weitz, E.; Scheffer, A. *Chem. Ber.* **1921**, *54*, 2327. Bunton, C. A.; Minkoff, G. J. *J. Chem. Soc.* **1949**, 655. (c) Fieser, L. F.; Campbell, W. P.; Fry, E. M.; Gates, M. D., Jr. *J. Org. Chem.* **1939**, *61*, 3216. For other examples of epoxidation with basic hydrogen peroxide see: Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*; Wiley: New York, 1967; Vol. 1, pp 466-467.
(4) Beynon, J. H. *Mass Spectrometry and its Applications to Organic Chemistry*; Elsevier: Amsterdam, 1960; p 524.

0022-3263/92/1957-3514$03.00/0