sive ammonium sulfate precipitations and calcium phosphate gel treatment produced an enzyme preparation in which the specific activity was 20-fold greater than previously reported.[1] To a cold (0°) solution of dehydroquinase (1.92 units/mg) in 5.0 ml of Tris buffer (pH 7.4, 0.03 M) was added 1.0 ml of 0.76 M sodium borohydride in water over a period of 30 min. The pH was maintained between 7.5 and 8.0 by the dropwise addition of 0.5 N acetic acid. After dialysis against Tris buffer, the activity of the enzyme was 1.65 units/mg. Another solution containing substrate 1[5] (0.735 mmol) and enzyme was treated with sodium borohydride in an identical manner. After dialysis the specific activity of the enzyme isolated from this solution was essentially inactive with a maximum activity of 0.0272 unit/mg.[6]

Deactivation of enzymes by sodium borohydride only in the presence of substrate is diagnostic of a Schiff base intermediate in enzymatic systems.[7-9] We therefore propose that the dehydration occurs via Schiff base formation between the enzyme and 1 as formulated below.
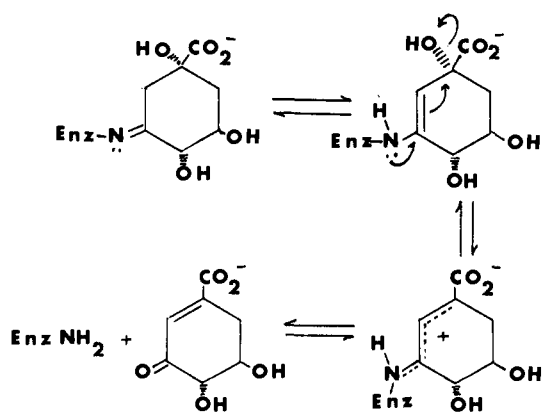
Acknowledgments. We thank Professors W. C. McDonald and J. R. Seed and Messrs. M. Dureau and M. Fontane for their help in growth and maintenance of bacteria. This research was supported in part by a National Institute of Health Biomedical Sciences Support Grant administered by Tulane University.

(5) E. Haslam, R. D. Haworth, and P. F. Knowles, *Methods Enzymol.*, 6, 498 (1963).

(6) Control experiments have shown that enzymatic activity is not lost when the enzyme is incubated with 0.735 mmol of substrate 1 in the absence of sodium borohydride.

(7) E. Grazi, T. Cheng, and B. L. Horecker, *Biochem. Biophys. Res. Commun.*, 7, 250 (1962).

(8) B. L. Horecker, S. Pontremoli, C. Ricci, and T. Cheng, *Proc. Nat. Acad. Sci. U. S.*, 47, 1949 (1961).

(9) Reference 3, p 335 ff.

(10) National Institutes of Health Career Development Award Recipient 1972-1977.

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Mechanism of the Base-Promoted Cyclodimerization of Cycloheptatriene

Sir:

Theoretical considerations suggest that the cycloheptatrienyl anion (1), one of the simplest "antiaromatic" carbocyclic π systems, will suffer Jahn–Teller distortion

from a triplet state of D_{7h} symmetry to one or more lower symmetry and lower energy singlet states.[1] Because of the possible availability of a variety of thermally accessible states, the chemical behavior of this highly reactive species represents an interesting problem.[2,3] We now report a remarkably rapid and highly regio- and stereoselective base-promoted cyclodimerization of cycloheptatriene and present evidence for the intermediacy of the cycloheptatrienyl anion (1) in this novel process.

When cycloheptatriene (2) is added to a 0.7 M solution of potassium amide in liquid ammonia at $-33°$ a deep red-brown color is formed immediately. Upon quenching into saturated aqueous ammonium chloride–pentane after 10 min a mixture of cycloheptatriene dimers consisting predominantly of 4 (81%) and 5 (16%) was obtained. Isolated yields were as high as

3

4 + **5**
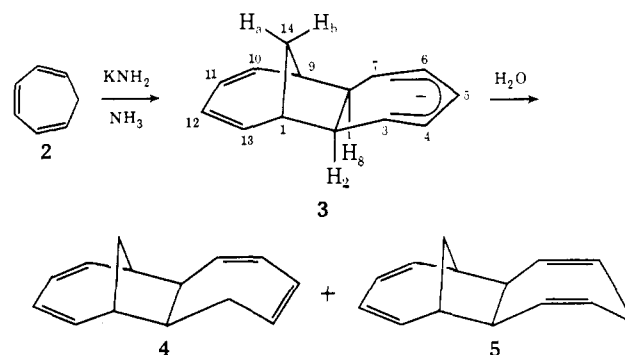
88%. The nmr spectrum of the initial red-brown solution, obtained at $-55°$ in ammonia-d_3,[4] is completely consistent with anion 3. The spectral parameters for 3 (Table I) are closely analogous to those for

Table I. Nmr Spectral Data for Tricyclo[7.4.1.0^{2,8}]tetradeca-3,5,10,12-tetraen-7-ylpotassium (3) in Ammonia-d_3 at $-55°$

Proton(s)[a]	Chemical shift (ppm)[b]	Proton(s)[a]	Chemical shift (ppm)[b]
H_1, H_9	2.25	H_{10}, H_{13}	~6.2
H_2, H_8	3.17	H_{11}, H_{12}	~5.8
H_3, H_7	3.75	H_{14a}	0.80
H_4, H_6	5.77	H_{14b}	3.03
H_5	3.18		

[a] $J_{1,13} \approx J_{1,14b} \approx 6.9$; $J_{23} = J_{78} = 4.0$; $J_{34} = J_{67} = 10.5$; $J_{45} = J_{56} = 8.0$; $J_{35} = J_{57} = 1.2$; $J_{12} \approx J_{89} \approx 0$ Hz; $J_{14a,14b} \approx 12$ Hz. [b] Trimethylamine ($\delta_{TMS}^{NH_3} = 2.135$) was used as an internal standard.

bicyclo[4.2.1]nona-2,4-diene,[5] bicyclo[4.2.1]nona-2,4,7-

(1) (a) R. Breslow and H. W. Chang, *J. Amer. Chem. Soc.*, 84, 1484 (1962); 87, 2200 (1965); (b) L. C. Snyder, *J. Phys. Chem.*, 66, 2299 (1962); (c) M. J. S. Dewar and N. Trinajstić, *Tetrahedron*, 26, 4269 (1970).

(2) For studies of anion 1, see (a) H. J, Dauben, Jr., and M. R. Rifi, *J. Amer. Chem. Soc.*, 85, 3041 (1963); (b) W. von E. Doering and P. P. Gaspar, *ibid.*, 85, 3043 (1963); (c) R. Breslow and W. Chu, *ibid.*, 95, 411 (1973).

(3) For studies of derivatives of 1, see ref 1a and (a) S. W. Staley and A. W. Orvedal, *J. Amer. Chem. Soc.*, 95, 3382 (1973); (b) K. Takahashi, H. Yamamoto, and T. Nozoe, *Bull. Chem. Soc. Jap.*, 43, 200 (1970).

(4) I. Melczynski, *Angew. Chem.*, 74, 32 (1962). We thank Dr. John Morrison for assistance with the preparation of ammonia-d_3.

(5) C. W. Jefford and F. Delay, *J. Amer. Chem. Soc.*, 94, 4794 1972) C. W. Jefford, U. Barger, and F. Delay, *Helv. Chim. Acta*, 56, 1083 (1973). We thank Professor Jefford and Dr. Delay for a copy of the nmr spectrum of this compound.

triene[6] and its 7,8-benzo derivative,[7] and for various cycloheptatrienyl anions.[8] Analysis was also aided by the elucidation (by 220-MHz nmr spectroscopy) of the structures of dimers **4** and **5**.[9] The fact that $J_{12} = J_{89} \approx 0$ Hz indicates that the stereochemistry of **3** at the ring fusion is cis, exo.

The observation of the above cycloaddition raises two interesting questions; *viz.*, is the cycloheptatrienyl anion (**1**) an intermediate in the reaction and, if so, is the cycloaddition process concerted or nonconcerted? The answer to the first question is by no means clear in view of the recognized facility of addition of strong bases to the cycloheptatriene ring.[10] The mechanism shown in Scheme I, for example, finds close analogy for
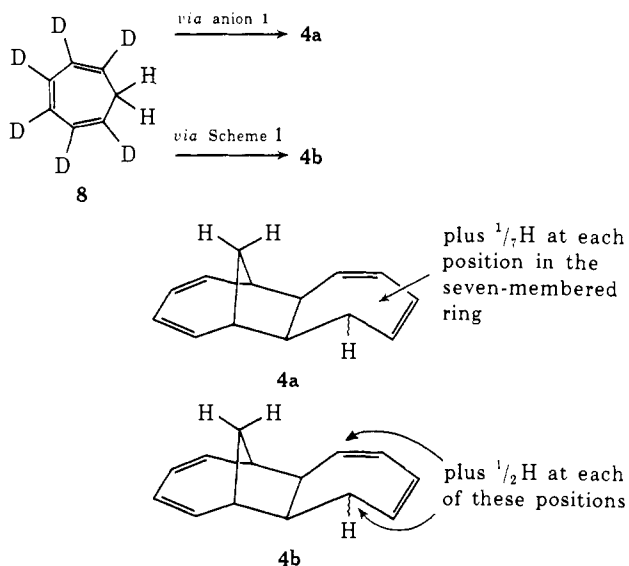
Scheme I
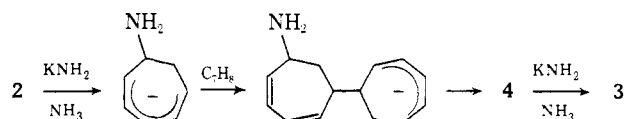
the initial step in the attack by amide on 7,7-dimethyl-cycloheptatriene (**6**)[8d] at 25° to afford anion **7**.[10c]
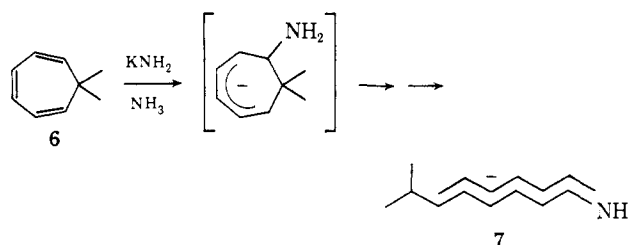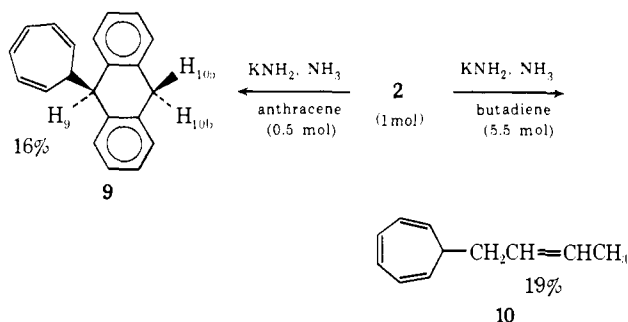
In order to establish the intermediacy of **1**, 1,3,5-cyclo-heptatriene-*1,2,3,4,5,6-d₆* (**8**) was prepared[11] and treated with potassium amide in liquid ammonia at −33° for 10 min followed by proton quenching (water). In the absence of rapid proton exchange or scrambling in **8**, the following *proton* distributions in dimer **4** would be

plus $^1/_7$H at each position in the seven-membered ring

4a

plus $^1/_2$H at each of these positions

4b

expected for anion **1** and Scheme I mechanisms. Nmr spectra of dimer **4** obtained from **8** were *completely consistent* (within the limits of integration error ($\pm 5\%$)) with the proton distribution shown in **4a**[12] and we therefore conclude that this reaction proceeds *via* a highly efficient addition of anion **1** to cycloheptatriene.

We have also observed that cycloheptatriene adds to anthracene and to 1,3-butadiene in potassium amide–ammonia at −33° to afford **9**[13] and **10**,[14] respectively, in addition to cycloheptatriene dimers. Note that the formation of the thermodynamically least stable 7-substituted derivatives of cycloheptatriene[15] (**9** and **10**) also implicates anion **1** in these reactions.[16]

The foregoing results lead to the second mechanistic question; is the cyclodimerization reaction a concerted ($_6\pi_s + {}_8\pi_s$) or a nonconcerted process (Scheme II)?

Scheme II
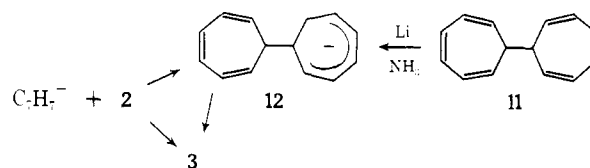
High stereoselectivity in cycloaddition reactions has often led to the proposal of concerted mechanisms. However, the formation of adducts **9** and **10** clearly

Pays-Bas, **88**, 1084, 1471 (1969); (b) H. Kloosterziel and E. Zwanen-burg, *ibid.*, **88**, 1373 (1969); (c) R. B. Bates, W. H. Deines, D. A. Mc-Combs, and D. E. Potter, *J. Amer. Chem. Soc.*, **91**, 4608 (1969); (d) F. L. Wiseman, Jr., Ph.D. Thesis, University of Maryland, 1970; (e) S. W. Staley, N. J. Pearl, and A. S. Heyn, unpublished results.

(9) S. W. Staley and A, W. Orvedal, manuscript submitted for publication.

(10) (a) K. Hafner and W. Rellensmann, *Chem. Ber.*, **95**, 2567 (1962); (b) R. B. Bates, S. Brenner, and B. I. Mayall, *J. Amer. Chem. Soc.*, **94**, 4765 (1972); (c) S. W. Staley and N. J. Pearl, unpublished results.

(11) Prepared by the cuprous chloride-catalyzed decomposition of diazomethane (W. v. E. Doering and W. R. Roth, *Tetrahedron*, **19**, 715 (1963)) in the presence of benzene-*d₆*.

(12) For a previous use of deuterium scrambling to detect the presence of anion **1**, see ref 2b.

(13) Compound **9** (mp 112–113.5°) had an nmr spectrum (CCl₄) which was assigned by analogy with that for 9-phenyl-9,10-dihydro-anthracene (A. W. Brinkmann, M. Gordon, R. G. Harvey, P. W. Rabi-deau, J. B. Stothers, and A. L. Ternay, Jr., *J. Amer. Chem. Soc.*, **92**, 5912 (1970): cycloheptatriene protons at δ 6.54 (m, H₃ and H₄), 6.07 (m, H₂ and H₅), 5.24 (m, H₁ and H₆), and 2.03 (d of t, H₇, $J_{17} = J_{67} = 6.5$, $J_{79} = 10.0$ Hz) and dihydroanthryl protons at δ 7.12 (apparent s, 8, aromatic), 4.04 (d, H₁₀ₐ, $J_{10a,10b} = 17.5$ Hz), 3.89 (d, H₉), and 3.67 (d, H₁₀ᵦ).

(14) Nmr (of a cis–trans mixture) (CCl₄): two-proton multiplets at δ 6.57 (H₃ and H₄), 6.10 (H₂ and H₅), and 2.40 (side chain meth-ylene) and a four-proton multiplet at 1.67 (H₇ and methyl); catalytic hydrogenation afforded *n*-butylcycloheptane.

(15) For equilibrium studies of methylcycloheptatrienes, see (a) K. Conrow, *J. Amer. Chem. Soc.*, **83**, 2343 (1961); (b) A. P. ter Borg, E. Razenberg, and H. Kloosterziel, *Recl. Trav. Chim. Pays-Bas*, **84**, 1230 (1965); (c) K. W. Egger, *J. Amer. Chem. Soc.*, **90**, 1 (1968).

(16) The behavior of **2** in potassium amide–liquid ammonia con-trasts with that of cyclopropene in this medium. The latter com-pound suffers loss of an olefinic proton prior to dimerization: A. J. Schipperijn, *Recl. Trav. Chim. Pays-Bas*, **90**, 1110 (1971).

(6) (a) L. G. Cannell, *Tetrahedron Lett.*, 5967 (1966); (b) W. Grimme, *Chem. Ber.*, **100**, 113 (1967). We thank Professor S. S. Olin for the nmr spectrum of this compound.

(7) R. C. Hahn and R. P. Johnson, *Tetrahedron, Lett.*, 2149 (1973). We thank Professor R. C. Hahn for providing us with a copy of the nmr spectrum of this compound.

(8) (a) H. Kloosterziel and J. A. A. van Drunen, *Recl. Trav. Chim.*

indicates that reactions similar to the first step of the stepwise process in Scheme II compete effectively with the cyclodimerization process (which is occurring simultaneously).

In order to test the viability of the second step of the two-step mechanism in Scheme II, ditropyl (11)[17] was subjected to lithium–ammonia reduction at $-33°$ which, by analogy with the similar reduction of cycloheptatriene,[18] is expected to produce the proposed intermediate 12 (Scheme II). In fact, partial reduction of 11 for 5 min at $-33°$ gave a product mixture consisting of ca. 40% dimer 4,[19] ca. 50% unchanged 11, and ca. 10% 5.

In summary, we suggest that the available data are best accommodated by a rapid stepwise cycloaddition of the cycloheptatrienyl anion (1) and cycloheptatriene (2) (Scheme II) and that the high stereoselectivity of this reaction is best explained on the basis of steric effects in the second step of this process. The latter point is supported by an examination of molecular models. Furthermore, since this is the first time in which the feasibility of the second step of a possible two-step ionic cycloaddition has been tested, our results provide a caveat regarding the common conclusion that stereoselectivity in ionic cycloadditions implies concertedness.

Acknowledgment. We thank the National Science Foundation for support of this work.

(17) W. von E. Doering and L. H. Knox, *J. Amer. Chem. Soc.*, **79**, 352 (1957).
(18) A. P. ter Borg and A. F. Bickel, *Recl. Trav. Chim. Pays-Bas*, **80**, 1229 (1961).
(19) This conversion could, in principle, occur *via* an initial cleavage of 12 to 1 and 2, but this is expected to be highly unfavorable on thermodynamic grounds.
(20) Gillette Research Foundation Fellow, 1972–1973.
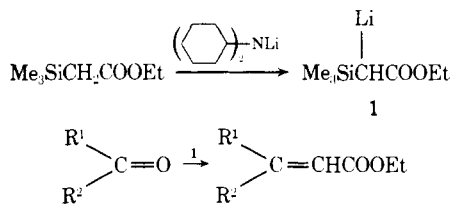
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A New Synthesis of α,β-Unsaturated Carboxylic Esters

Sir:

This communication describes a new synthetic method which allows the conversion of carbonyl compounds to α,β-unsaturated carboxylic esters in high yields. The method was designed on the assumption that the well-known affinity of the suitably substituted silyl group to an alkoxide ion[1] should result in transformation of ethyl lithiotrimethylsilylacetate (1) as shown below.

$$Me_3SiCH_2COOEt \xrightarrow{\text{NLi}} Me_3Si\overset{Li}{\underset{|}{C}}HCOOEt$$
$$1$$

$$\overset{R^1}{\underset{R^2}{>}}C{=}O \xrightarrow{1} \overset{R^1}{\underset{R^2}{>}}C{=}CHCOOEt$$

(1) (a) D. J. Peterson, *J. Org. Chem.*, **33**, 780 (1968); (b) T. H. Chan, E. Chang, and E. Vinokur, *Tetrahedron Lett.*, 1137 (1970); (c) F. A. Carey and A. S. Court, *J. Org. Chem.*, **37**, 939, 1926 (1972); (d) D. Seebach, B-Th. Gröbel, A. K. Beck, M. Braun, and K.-H. Geiss, *Angew. Chem. Int. Ed. Engl.*, **11**, 443 (1972); (e) C. Trindle, J-T. Hwang, and F. A. Carey, *J. Org. Chem.*, **38**, 2664 (1973); (f) F. A. Carey and O. Hernandez, *ibid.*, **38**, 2670 (1973); (g) H. Sakurai, K. Nishiwaki, and M. Kira, *Tetrahedron Lett.*, 4193 (1973); (h) see, also, D. J. Peterson, *Organometal. Chem. Rev., Sect. A*, **7**, 295 (1972).

Ethyl trimethylsilylacetate was known to be condensed with aromatic aldehydes under rather drastic conditions in the presence of basic catalyst to yield β-trimethylsiloxycarboxylates.[2] The mechanism proposed earlier[2] to involve ethyl sodiotrimethylsilylacetate was questioned and the intermediacy of ethyl sodioacetate was shown to be more probable (Me_3SiCH_2CO-$OEt + B^- \rightarrow {}^-CH_2COOEt + Me_3SiB$).[3] The formation of the lithium enolate 1 was realized by treatment of ethyl trimethylsilylacetate[4] with lithium dicyclohexylamide[5,6] in dry tetrahydrofuran at $-78°$ for 10 min. Quenching with water followed by analysis by glpc revealed >95% recovery of the starting ester. The formation of the anion 1 was further verified by reaction with carbonyl compounds to yield the bis-homologated carboxylic esters in the yields indicated: benzaldehyde $\rightarrow$ ethyl cinnamate (84%, $E/Z = 3:1$); nonanal $\rightarrow$ ethyl 2-undecenoate (81%, $E/Z = 1:1$); cyclohexanone $\rightarrow$ ethyl cyclohexylideneacetate (95%); cyclododecanone $\rightarrow$ ethyl cyclododecylideneacetate (94%); cyclopentanone $\rightarrow$ ethyl cyclopentylideneacetate (81%); chalcone $\rightarrow$ ethyl 2,4-diphenylbutadiene-1-carboxylate (86%, $E/Z = 7:3$).

The best current method for the above transformations involves a direct analog of the Emmons–Wadsworth–Horner method,[7] which generally works fairly well. Although often an excellent procedure, the aforementioned results revealed several situations where our new, milder method would be preferred. Readily enolizable ketone may be inert to the phosphonate carbanion.[8] Proton transfer reactions may occur faster than carbonyl addition with the risk of enolate condensation reactions. Such behavior is especially characteristic of cyclopentanone in the Wittig-type reaction,[8a,c] whereas we obtain exclusively ethyl cyclopentylideneacetate in good yield.[9] Chalcone is known to react with the phosphonate anion to give either/both a Michael or a Wittig–Horner product in low yields,[7f] whereas the lithium enolate 1 gave only the 1,2-addition product.

The reaction of cyclododecanone to ethyl cyclododecylideneacetate is typical. A solution of dicyclohexylamine (3.65 g, 20 mmol) in dry tetrahydrofuran (100 ml) was treated with n-butyllithium (13.5 ml of a

(2) L. Birkofer and A. Ritter, *Chem. Ber.*, **95**, 971 (1962).
(3) C. Eaborn and R. W. Bott in "Organometallic Compounds of the Group IV Elements," Vol. 1, A. G. MacDiarmid, Ed., Marcel Dekker, New York, N. Y., 1968, p 1; L. Birkofer and A. Ritter, *Angew. Chem.*, **77**, 414 (1965).
(4) This colorless liquid was easily prepared on a 0.1–0.3 M scale from ethyl bromoacetate by the method of Fessenden [*J. Org. Chem.*, **32**, 3535 (1967)] in 70–80% yield after distillation, bp 85° (68 mm).
(5) R. A. Olofson and C. M. Dougherty, *J. Amer. Chem. Soc.*, **95**, 582 (1973).
(6) Preparation and reactions of ethyl lithioacetate: M. W. Rathke, *J. Amer. Chem. Soc.*, **92**, 3222 (1970); M. W. Rathke and A. Lindert, *ibid.*, **93**, 2318 (1971); M. W. Rathke and J. Deitch, *Tetrahedron Lett.*, 2953 (1971).
(7) (a) W. S. Wadsworth, Jr., and W. D. Emmons, *J. Amer. Chem. Soc.*, **83**, 1733 (1961); (b) H. Takahashi, K. Fujiwara, and M. Ohta, *Bull. Chem. Soc. Jap.*, **35**, 1498 (1962); (c) A. K. Bose and R. T. Dahill, Jr., *Tetrahedron Lett.*, 959 (1963); *J. Org. Chem.*, **30**, 505 (1965); (d) J. Wolinsky and K. L. Erickson, *ibid.*, **30**, 2208 (1965); (e) W. S. Wadsworth, Jr., and W. D. Emmons, *Org. Syn.*, **45**, 441 (1965); (f) E. D. Bergmann and A. Solomonovici, *Tetrahedron*, **27**, 2675 (1971).
(8) (a) E. J. Corey and J. I. Shulman, *J. Org. Chem.*, **35**, 777 (1970); (b) R. L. Sowerby and R. M. Coates, *J. Amer. Chem. Soc.*, **94**, 4758 (1972), and references cited therein; (c) see, also, D. R. Coulson, *Tetrahedron Lett.*, 3323 (1964).
(9) The reaction should be quenched at $-25°$ in this case; the usual reaction conditions gave a mixture of α,β- and β,γ-unsaturated ester in 9:1 ratio (by nmr assay).