Procedure B. A solution of the biacetyl–$(CH_3O)_2PC_6H_5$ adduct **18** (75 mmoles) in CH_2Cl_2 (40 ml) was placed in trap 3 of the apparatus described above. Carbon suboxide (74 mmoles) was allowed to evaporate, over a 20-hr period, from trap 2 (first at −35°, finally up to +10°) into trap 3 containing the phospholene solution at −78°. (The evaporation can be expedited under slight vacuum for 30 sec.) The solvent was removed and the residue was recrystallized from benzene. A mixture of two diastereomeric butenolide phosphinates **19** and **20** (60:40) was obtained in 65% of the theoretical yield.

A similar procedure was applied to the biacetyl–$CH_3OP(C_6H_5)_2$ adduct **22** and gave the butenolide phosphine oxide **23** in 65% of the theoretical yield. Very little suboxide polymer was observed.

Phostone Carboxylic Acids. The properties are given in Tables I and II. Five grams of the butenolide phosphonate **12** dissolved instantaneously in 1 ml of water. The solution was evaporated at 20° (0.2 mm). The residue was dissolved in 150 ml of ether; traces of insoluble orange oil were pipetted out. The solution was concentrated to 50 ml, cooled at 5°, and filtered, yielding 3.7 g of the **hemihydrate of 27 and 28** (about 50:50). Anhydrous **27** and **28** were obtained at 56° (0.1 mm).

A mixture containing 2 g of both diastereomeric butenolide phosphinates **19** and **20** (60:40 proportion), 5 ml of CH_2Cl_2, and 1 mole equiv of water was stirred 20 hr at 30°. The solvent was removed *in vacuo;* the residue was triturated with 75 ml of ether, and the first crop of acids **32** and **35** was filtered off. The filtrate was concentrated to give the second crop of **32** and **35,** total yield 70%.

Phostone Carboxylic Esters. The properties are given in Tables I and II. Diazomethane in ether was added to a solution containing both diastereomeric acids **27** and **28** (1.5 g), ether (50 ml), CH_2Cl_2 (2 ml), and methanol (0.5 ml). The solvent was evaporated *in vacuo;* the residue contained two diastereomeric esters **39** + **40,** according to ^1H and ^{31}P nmr spectra. This residue was stirred with ether (5 ml), and the crystals were filtered off. The ester **39** was obtained in *ca.* 40% yield and contained about 5% of diastereomer.

The same procedure gave the mixture of diastereomeric esters **41** and **42** from the mixture of diastereomeric acids **32** and **35.**

Preparation of Crotonic Acids from the Butenolide. The properties are given in Tables I and II. A mixture containing the butenolide phosphine oxide **23** (1 g), CH_2Cl_2 (5 ml), and water (5 mole equiv) was stirred 15 hr at 20°. The solvent was removed *in vacuo* and the residue was extracted with ether (100 ml). The filtered solution was kept 24 hr at 0° to give acids **36 and 37** (0.3 g, mp 104–105°). The spectral data of Table II were obtained on this sample. Another crystallization from ether gave the analytical sample of Table I (also a mixture of **36** and **37** as shown by the ^1H nmr spectra).

Condensations of 4-Methyl-4-dichloromethyl-2,5-cyclohexadienone

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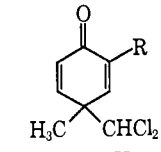
Abstract: The determination of the structure and stereochemistry of the products of base-induced condensations of 4-methyl-4-dichloromethyl-2,5-cyclohexadienone with dimethyl malonate and with methyl acetoacetate is presented. Facile syntheses of polyfunctional bicyclo[3.3.1]nonanes and *cis*-decalins are introduced.

The Reimer–Tiemann reaction, an interaction of phenols with chloroform and base, has been known for over half a century to lead to phenolic aldehydes and dichloromethylcyclohexadienones.[1] While it has been used to advantage for the preparation of aromatic aldehydes, only little attention has been paid to the cyclohexadienone products,[2,3] usually obtained in low yield. The presence of many, diverse functional groups encompassed in a small molecular framework in close proximity to each other make the cyclohexadienones interesting substances for general chemical study. Our previous utilization of a naphthalenone, prepared by the Reimer–Tiemann reaction of an α-naphthol derivative, in diterpene synthesis[4] and our discovery of an interesting rearrangement of another naphthalenone, derived from a β-naphthol derivative,[5] encouraged our further investigation of the chemistry of such compounds. The present communication illustrates the chemical behavior of cyclohexadienone **1a**[6] derived from *p*-cresol.

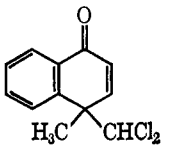


1a, R = H
b, R = Me

In analogy with the conversion of ketone **2** into tricyclic ketone **3**,[4a] whose first step involved a Michael condensation of acetoacetic ester with **2**, the transfor-

(1) H. Wynberg, *Chem. Rev.*, 60, 169 (1960).
(2) A. J. Waring, *Advan. Alicyclic Chem.*, 1, 129 (1966).
(3) These compounds have been described usually as *abnormal Reimer–Tiemann products* and reactions leading to them have been designated frequently as *abnormal Reimer–Tiemann reactions.* Since the term *abnormal* is only of historical significance, reflecting the concern of early workers about the unexpected formation of nonaromatic compounds [K. Auwers, *Ber.*, 17, 2976 (1884), and later papers], and since present-day mechanistic interpretation of the reaction and its products places them into the well-understood context of carbene chemistry [J. Hine and J. M. van der Veen, *J. Am. Chem. Soc.*, 81, 6446 (1959)], it is suggested that the Reimer–Tiemann reaction not be described henceforth in terms of *normal* or *abnormal* processes or products.
(4) (a) E. Wenkert and T. E. Stevens, *ibid.*, 78, 5627 (1956); (b) E. Wenkert, A. Afonso, J. B-son Bredenberg, C. Kaneko, and A. Tahara, *ibid.*, 86, 2038 (1964).
(5) R. M. Dodson, J. R. Lewis, W. P. Webb, E. Wenkert, and R. D. Youssefyeh, *ibid.*, 83, 938 (1961).
(6) K. Auwers and F. Winternitz, *Ber.*, 35, 465 (1902); K. Auwers and G. Keil, *ibid.*, 35, 4207 (1902).

mation of dienone **1a** into variously substituted bicyclic substances of interest in the field of organic natural products could be envisaged. Consequently a study of the Michael condensations of **1a** with malonic and acetoacetic esters was initiated.[7]



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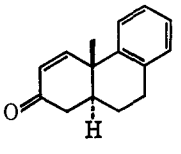
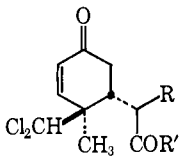
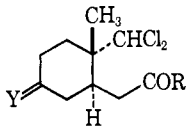


3

Condensation of dimethyl malonate with dienone **1a** under the influence of sodium methoxide in methanol produced a crystalline 1:1 adduct. Spectral analysis of the new compound revealed it to be a simple Michael condensation product (**4a**, stereochemistry undefined), no secondary structural changes having taken place. Acid hydrolysis of the product and decarboxylation yielded an acid (**4b**) whose hydrogenation, alongside that of its methyl ester (**4c**), produced a saturated keto acid (**5a**) and its derivative (**5b**), respectively. Although these experimental results were in accord with the formulation of the gross structure of the Michael adduct, they shed no light on its stereochemical environment. While the previous experience, acetoacetic ester interaction with **2** having produced an adduct whose new side chain was oriented *trans* to the dichloromethyl group,[4a] could not be ignored, its value as a model for the present case was hard to assess. Furthermore, any stereochemical analysis of the adduct based on the assumption of its being the product of kinetic control was cast into doubt, when the Michael reaction was shown to be reversible. Exposure of the adduct to sodium methoxide in methanol for a somewhat longer time than that of the initial condensation led to an *ca.* 7:1 mixture of dienone and adduct, respectively. Thus a rigorous determination of the stereochemistry of **4a** became necessary.

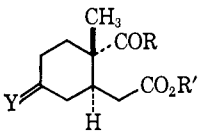


4a, R = CO_2Me; R′ = OMe
b, R = H; R′ = OH
c, R = H; R′ = OMe
d, R = H; R′ = Me
e, R = CO_2Me; R′ = Me

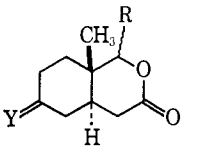


5a, R = OH; Y = O
b, R = OMe; Y = O
c, R = OH; Y = $(CH_2S)_2$
d, R = OMe; Y = $(CH_2O)_2$
e, R = OH; Y = $(CH_2O)_2$
f, R = Me; Y = O
g, R = Me; Y = $(CH_2S)_2$
h, R = Me; Y = $(CH_2O)_2$

Since an exact analysis of the configuration of **4a** was to be based on the spatial relationship of the acetic acid and dichloromethyl side chains with respect to each other, the nuclear keto group was superfluous and needed to be removed or, at least, to be masked. The latter process proved facile as the preparation of the ethylene thioketal **5c** (treatment of **5a** with 1,2-ethanedithiol and boron trifluoride) and the ethylene ketals **5d** and **5e** (treatment of **5b** with ethylene glycol and *p*-toluenesulfonic acid, followed by alkaline hydrolysis) indicated. In anticipation of the complete removal of the nuclear keto group the thioketal **5c** was used for further work. Hydrolysis thereof in aqueous alkali produced the aldehydo acid **6a** which was in ready equilibrium with the lactol **7a** and could be isolated in either form. Acetylation trapped the lactol as an acetate (**7b**). Silver oxide oxidation of **6a** and/or **7a** led to the diacid **6b**, which was characterized as the diester **6c**. Reduction of the latter with Raney nickel and alkaline hydrolysis of the product yielded a diacid whose melting point was identical with that reported for the compound with stereo structure **6d**.[8,9]

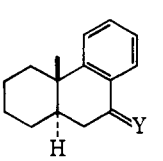


6a, R = R′ = H; Y = $(CH_2S)_2$
b, R = OH; R′ = H; Y = $(CH_2S)_2$
c, R = OMe; R′ = Me; Y = $(CH_2S)_2$
d, R = OH; R′ = H; Y = H_2

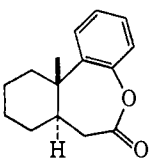


7a, R = OH; Y = $(CH_2S)_2$
b, R = OAc; Y = $(CH_2S)_2$
c, R = H; Y = H_2

A stereochemically unambiguous specimen of the diacid **6d** was prepared by the degradation of hydrophenanthrone **8b**.[10,11] Oxidation of the ketone with *m*-chloroperbenzoic acid gave a lactone (**9**), the ozonolysis (with oxidative work-up) of its hydrolysis product affording the diacid **6d**. The latter proved identical in all details with the acid derived from the Michael condensation product **4a**. Thus the addition of dimethyl malonate to the dienone **1a** had led exclusively to a cyclohexenone whose bulkiest substituents had a *trans* relationship to each other.



8a, Y = H_2
b, Y = O



9

Condensation of methyl acetoacetate with 4-methyl-4-dichloromethyl-2,5-cyclohexadienone (**1a**) in the presence of sodium methoxide in methanol produced a 1:1 adduct and a $C_{13}H_{15}O_4Cl$ compound. Spectral analysis of the former revealed it to be the product of consecutive Michael and intramolecular aldol condensations (**10a**, stereochemistry undefined),[12] a sequence of events observed also in the condensation of ethyl acetoacetate with the naphthalenone **2** (*cf.* **11**).[4a] Hydrogenation of **10a** yielded the dihydro derivative **12**.

(7) Two Michael condensations of **1a** are on record: (a) R. S. Corley, Ph.D. dissertation, Harvard University, 1950; (b) H. Stetter and J. Mayer, *Chem. Ber.*, **92**, 2664 (1959).

(8) (a) R. P. Linstead, A. F. Millidge, and A. L. Walpole, *J. Chem. Soc.*, 1140 (1937), and preceding references; (b) W. E. Bachmann and S. Kushner, *J. Am. Chem. Soc.*, **65**, 1963 (1943); (c) R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler, and W. M. McLamore, *ibid.*, 74, 4223 (1952).

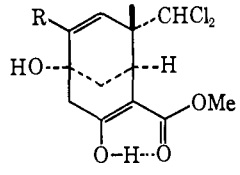
(9) Raney nickel desulfurization of the lactone ester **7b** yielded lactone 7c.

(10) E. Wenkert and J. W. Chamberlin, *J. Org. Chem.*, **25**, 2027 (1960).

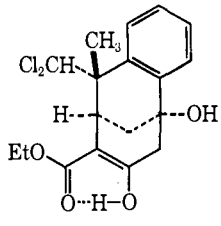
(11) The degradation paralleled the procedures of D. Arigoni, J. Kalvoda, H. Heusser, O. Jeger, and L. Ruzicka, *Helv. Chim. Acta*, **38**, 1857 (1955), and of E. Wenkert and D. P. Strike, *J. Am. Chem. Soc.*, **86**, 2044 (1964).

(12) The base-induced condensation of methyl acetoacetate with 2,4-dimethyl-4-dichloromethyl-2,5-cyclohexadienone (**1b**) produced the 1:1 adduct **10b** (undetermined stereochemistry) (see Experimental Section).

Aqueous acid hydrolysis and decarboxylation of the latter led to the ketol **13**. In contrast, similar treatment of the enol ester **10a** afforded diketone **14**,[7] a product of not only hydrolysis and decarboxylation but also retroaldol and intramolecular Michael reactions. While undoubtedly the last step, the irreversible transformation of **4d** into **14**, was the major cause for the dissimilar hydrolytic behavior of the bicyclic compounds **10a** and **12**, the result reflected in part the greater lability of the bicyclo[3.3.1]nonene system than that of its dihydro counterpart and, hence, the greater ease of establishment of equilibrium between **15** and **4d** than between **13** and **5f**. This effect also accounts well for two earlier experimental observations:[4a] (a) the formation of both **16** and **17a** on acid-catalyzed hydrolysis and decarboxylation of **11** (contrasted by the present change of **10a** to only **13**) and (b) the transformation of **16** into **17b** on hydrogenation in the presence of acid.



10a, R = H
b, R = Me



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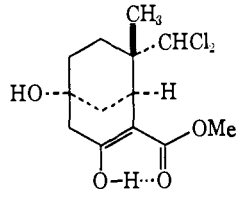

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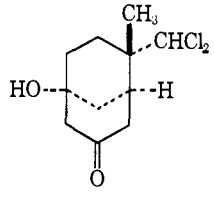

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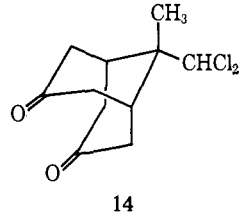

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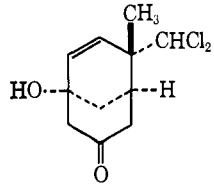

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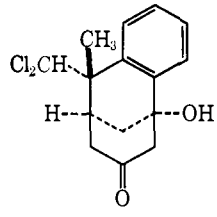

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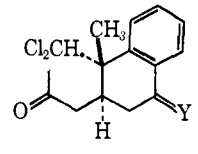
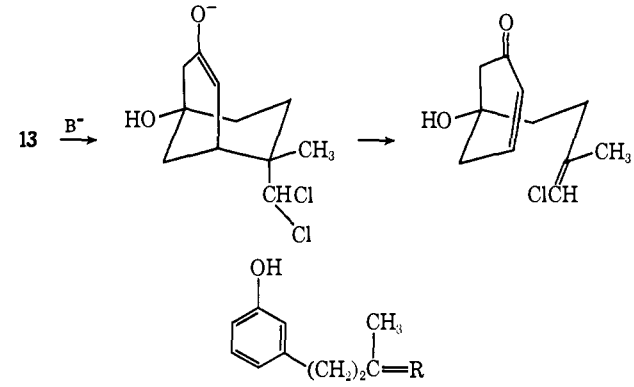


17a, Y = O
b, Y = H_2

A stereochemical analysis of the Michael adduct **10a** still had to be performed. For this purpose the unravelled, retroaldol form (**5f**) of ketol **13** was in demand, but in accord with expectation both acid and base treatments left the latter unphased. On the contrary, base treatment under forcing conditions (potassium *t*-butoxide in dimethyl sulfoxide) caused a deep-seated structural change. The ketol was converted thereby into the phenol **18a** whose structure was determined by spectral analysis and by the transformation of the product into *m*-isopentylphenol (**18b**) on hydrogenation. The **13** → **18a** change is interpreted most readily in terms of the following reaction scheme.[13]

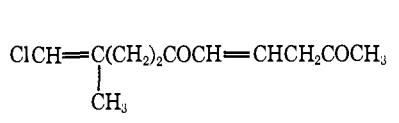


18a, R = CHCl
b, R = H, Me

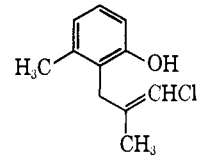
In view of the blockage of the stereo-controlled degradation of the ketol **13** its synthesis from compounds of known configuration was undertaken. In analogy with the conversion of the thioketal acid **5c** into the methyl ketone **5g** the ketal acid **5a** was transformed into its acyl chloride and the latter was exposed to dimethylcadmium. However, this led exclusively to the bicyclic compound **19** in place of the desired ketal ketone **5h**.[14]

Treatment of methyllithium with the acid chloride of **5e** gave the ketal ketone **5h** and the ketal carbinol **20**. Aqueous acid hydrolysis of the former yielded the diketone **5f**, whose mild base treatment led to ketol **13**. This completed the stereochemical relay and proved

(13) The fragmentation, a special example of a 1,3 elimination, constituted the first clue regarding the stereochemistry of **13** and, hence, of **10a** in view of the requirement of a *trans*-antiparallel arrangement of the diene-forming carbon atoms. While the over-all rearrangement could be visualized also to emanate from the retroaldol product **5f** (1,3 elimination, cyclization, and dehydration), this route was considered less likely in view of the ambiguity of the cyclization step, aldolization and dehydration of the intermediate dienedione i leading to **18a** and/or ii.

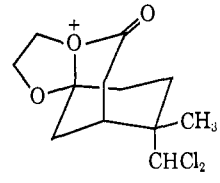


i



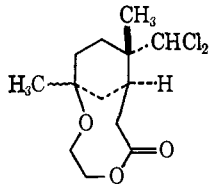
ii

(14) While an independent discovery, this unusual reaction represents one more example of the heretofore unknown, but recently investigated misbehavior of γ- or δ-ketal acid derivatives toward organocadmium reagents [R. A. LeMahieu, *J. Org. Chem.*, 32, 4149 (1967)]. On the assumption of the cadmium or magnesium salts of the solution acting as Lewis acids on the acyl chloride and the resultant acylium side chain intereacting with the proximate ketal moiety the oxonium salt iii can be envisaged as an important intermediate. Attack by the organometallic reagent on iii (perhaps after prior carbon–oxygen bond cleavage) leads to the nine-membered lactone (**19**). It is noteworthy



iii

that a novel method of synthesis of the basic ring skeleton of the macrolide antibiotics might be modeled after this reaction.



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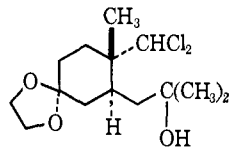
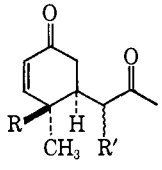


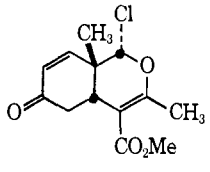
20

the stereochemistry of the Michael adduct of methyl acetoacetate and dienone **1a** to be that depicted in **10a**.

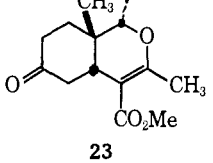
The second product of the Michael condensation, the $C_{13}H_{15}O_4Cl$ compound, represented a 1:1 adduct from which hydrogen chloride had been extruded. Since the loss of this moiety was most likely the consequence of intramolecular chloride displacement from the dichloromethyl group by the neighboring acetoactic ester unit (acting as a nucleophilic enolate) of the intermediate Michael adduct (**21a**, stereochemistry undefined) and since such displacement could involve carbon–carbon or carbon–oxygen bond formation, the product had to be bicyclic and either a β-keto ester or a β-alkoxyacrylic ester. Full spectral analyses of the compound and, more convincingly, of its dihydro derivative, the product of its hydrogenation, revealed these substances to possess structures **22** (stereochemistry undefined) and **23** (stereochemistry undefined), respectively. Aqueous acid hydrolyses and decarboxylations of these compounds led to the diketones **24** and **25a**, respectively. The interaction of water had liberated carboxaldehyde and acetone side chains, *e.g.*, **22** → **21b**, which had undergone intramolecular condensation and had been followed by acid-induced dehydration. Hydrogenation of **24** as well as of **25a** yielded the saturated diketone **26a**.



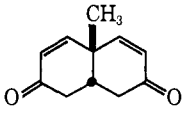
21a, R = $CHCl_2$; R′ = CO_2Me
b, R = CHO; R′ = H
c, R = $CHCl_2$; R′ = H



22

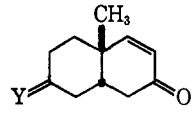


23

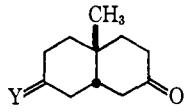


24

As proof of the relative configuration of the asymmetric centers of **22** correlation of the latter with a decalin derivative of known constitution was sought. As a consequence diketone **25a** was converted into its ethylene monothioketal (**25b**) which was treated with Raney nickel. Oxidation of the resultant saturated alcohol–ketone mixture with chromic acid yielded the *cis*-decalone **26b**.[15] To ensure the absence of isomerization of the bridgehead hydrogen during the nickel treatment, establishment of an alternate relay was thought desirable. Ketal **25c** was prepared by acid-induced ketalation of diketone **25a** with ethylene glycol or by similar ketalation of the saturated keto group of **23**, followed by aqueous, alkaline hydrolysis and decarboxylation of the resultant ketal. Hydrogenation of **25c**, Wolff–Kishner reduction of the dihydro derivative **26c** and aqueous acid hydrolysis of the product led once again to the *cis*-decalone **26b**.

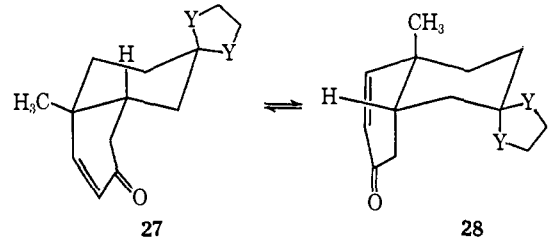


25a, Y = O
b, Y = $(CH_2S)_2$
c, Y = $(CH_2O)_2$



26a, Y = O
b, Y = H_2
c, Y = $(CH_2O)_2$

While the above results supported a *cis*-bridgehead relationship for **22** and its degradation products, they left the stereochemistry of the chlorine-bearing carbon unsettled. A high-resolution proton magnetic resonance (pmr) spectrum of **22** and a decoupling experiment revealed the chloromethine hydrogen weakly coupled (J = 0.8 cps) to the bridgehead hydrogen. Similar coupling (J = 1.3 cps) was noticeable in the spectrum of the ethylene ketal of **23**. Since such long-range coupling reflects a coplanar, W-form, five atom H–C_3–H relationship,[16] the hydrogens involved had to be oriented equatorially and *cis* with respect to each other. This fact led to the assignment of stereo structure **22** for the minor Michael condensation product. Long-range coupling (J = 2.0 and 1.6 cps, respectively) was strikingly apparent in the pmr spectra of the ketals **25b** and **25c** and revealed a 1,3 interaction between the bridgehead hydrogen and the β-hydrogen of the α,β-unsaturated ketone moiety.[16] Hence these substances possessed predominantly conformation **27** in solution, a conclusion in agreement with conformational analysis of the compounds (*inter alia*, strongly destabilizing, nonbonded interactions of the axial methyl and heteroatom substituents in the nonketonic ring of **28**).



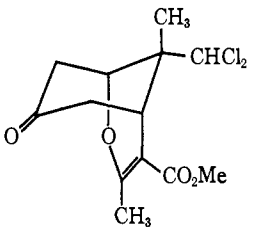
27 ⇌ 28

When the condensation of methyl acetoacetate with the dienone **1a** was executed in the presence of only 0.33 equiv of sodium methoxide, a third product accompanied **10a** and **22**. It proved to be the 1:1 adduct **29** on the basis of its spectral analysis. Aqueous acid hydrolysis and decarboxylation converted it into the diketone **14**. While its configuration was not determined by chemical means, comparison of the pmr spectra of **29** and **14** showed the Michael adduct to be a stereochemical kin of the other enol ether adduct (**22**). The methyl and dichloromethyl signals of **29** were upfield to those of **14**, but the difference of chemical shift of each group in the two substances was highly disparate, $\Delta\delta_{Me}$ 0.11 ppm and Δ_{CHCl_2} 1.22 ppm. The size of the latter value indicated that the dichloromethyl group of the Michael condensation product was within the shielding zone of the enol ether unit, in consonance with the

(15) M. Yanagita and K. Yamakowa, *J. Org. Chem.*, 22, 291 (1957).

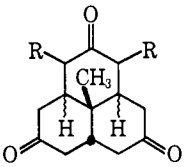
(16) *Cf.* (a) T. Nozoe, Y. S. Cheng, and T. Toda, *Tetrahedron Letters*, 3663 (1966); (b) A. G. Hortmann, D. S. Daniel, and J. Schaefer, *J. Org. Chem.*, 33, 3988 (1968).

stereochemistry depicted in **29**. Thus both **22** and **29** were derived from the primary Michael adduct **21a**, while **10a** had arisen from the alternate primary adduct **4e**. In the presence of sufficient base **21a** underwent chloride displacement and hence transformation into **22**, while in its absence **21a** merely experienced isomerization into **29**. The ratio of products resulting from the attack of methyl acetoacetate on the dienone **1a** from the latter's methyl side to that from the dichloromethyl side was 1.5–2:1.[17] In contrast, attack by acetoacetic ester on naphthalenone **2** had been shown to take place exclusively from the methyl side (*cf.* product **11**).[4a,18]



29

As illustrated above, a large variety of polyfunctional, bicyclic compounds are now readily available for organochemical synthesis. Perhaps the most interesting substance in this connection is the dienedione **24**. While prepared heretofore from **22** (*vide supra*), it could be obtained also by exhaustive dehydrohalogenation of the diketone **14** with potassium *t*-butoxide in dimethyl sulfoxide.[19] Although no general study of the diketone **24** has been undertaken, it has been exposed to base-catalyzed condensation with dimethyl acetonedicarboxylate. Acid hydrolysis and decarboxylation of the product **30a** has led to the topologically interesting triketone **30b**.[20]



30a, R = CO_2Me
b, R = H

Experimental Section

Melting points were determined on a Reichert micro hot stage and are uncorrected. Infrared spectra were obtained on Perkin-Elmer Model 137 and 137B spectrophotometers. Ultraviolet spectra were recorded on a Cary Model 14 spectrophotometer. Proton magnetic resonance spectra of deuteriochloroform solutions containing tetramethylsilane (δ = 0 ppm) as internal standard were taken on Varian Associates Model A-60 and HA-100 spectrometers. Neutral alumina of activity IV was used for chromatography.

4-Methyl-4-dichloromethyl-5-dicarbomethoxymethyl-2-cyclohexenone (4a). A solution of 945 mg of ketone **1a**, 660 mg of dimethyl malonate, and sodium methoxide (from 115 mg of sodium) in 15 ml of methanol was kept under nitrogen at room temperature for 2 hr. The yellow solution was evaporated under vacuum and ether was added. The resultant suspension was filtered and the precipitate was washed with ether. Evaporation of the combined filtrate and washings and crystallization of the solid residue yielded 350 mg of starting ketone **1a**. The precipitate was dissolved in a minimum amount of water, carbon dioxide was added, and the mixture was extracted with chloroform. The extract was dried over anhydrous sodium sulfate and evaporated. Crystallization of the solid residue, 540 mg, from ether gave keto ester **4a**: mp 108°; infrared (Nujol), C=O 5.69 (m), 5.78 (s), 5.93 (s) and C=C 6.10 (w) μ; ultraviolet (MeOH), λ_{max} 222 mμ (log ϵ 4.03); pmr, δ 1.38 (s, 3, C-Me), 3.75 and 3.80 (s, 3, methoxyls), 2.77 (q, 2, J = 2.0, 7.5 cps, α-keto-CH_2), 6.01 (s, 1, $CHCl_2$), 6.12 (d, 1, J = 10.0 cps, α-keto-CH), 6.94 (d, 1, J = 10.0 cps, β-keto-CH).[21]

Anal. Calcd for $C_{13}H_{16}O_5Cl_2$: C, 48.29; H, 4.99. Found: C, 48.16; H, 4.98.

A solution of 108 mg of **4a** and sodium methoxide (from 11 mg of sodium) in 3 ml of methanol was kept under nitrogen at room temperature for 4 hr. Work-up as above led to 40 mg of **1a** and 10 mg of starting material (**4a**).

4-Methyl-4-dichloromethyl-5-carboxymethyl-2-cyclohexenone (4b) and Its Ester (4c). A mixture of 100 mg of ester **4a** and 5 ml of 50% hydrochloric acid was refluxed for 4 hr. The cooled suspension was filtered, the filtrate was extracted with chloroform, and the extract was dried and evaporated. Crystallization of the combined residue and previous precipitate, a total of 65 mg, from ether yielded **4b**: mp 185–187°; infrared (Nujol), OH 3.0–3.3 (m), C=O 5.77 (s), 5.99 (s) μ; ultraviolet (MeOH), λ_{max} 221 mμ (log ϵ 4.04); pmr (deuterioacetone), δ 1.37 (s, 3, C-Me), 6.48 (s, 1, $CHCl_2$), 6.07 (d, 1, J = 10.0 cps, α-keto-CH), 7.07 (d, 1, J = 10.0 cps, β-keto-CH).

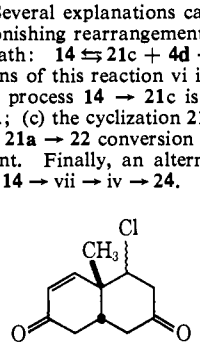
Anal. Calcd for $C_{10}H_{12}O_3Cl_2$: C, 47.81; H, 4.82. Found: C, 47.99; H, 4.86.

A solution of 200 mg of the acid **4b** in 50 ml of ether saturated with diazomethane was kept at room temperature for 2 hr. A few drops of acetic acid were added and the solution was washed

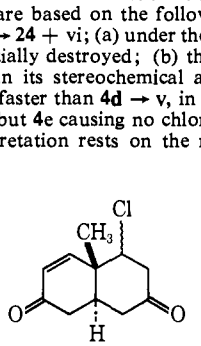
(17) The ratio is based on the assumption that much of the sensitive chloro compound **22** had undergone decomposition on work-up. While it could be obtained at best only in 8% yield, the combined yield of **22** and **29** under conditions of the latter's formation was 25% (although that of **22** alone was only 5%). The yield of **10a** (*ca.* 62%) proved invariant despite changes of reaction conditions.

(18) While qualitatively the same, the results represent a striking quantitative difference between the behavior of **1a** and **2** toward a bulky nucleophile. This effect appears to be the consequence of a nonbonded interaction of the dichloromethyl group with the neighboring *peri* aryl hydrogen in **2** absent in **1a**. If it is assumed that in the transition state of the Michael condensation the dichloromethyl group adopts such orientation as to minimize this energetically unfavorable interaction, it would be more axial in the case emanating from **2** than from **1a** and thus block entry of the nucleophile *cis* to itself more effectively in **2** than in **1a**.

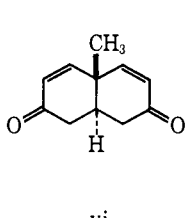
(19) Several explanations can be offered as mechanistic rationale of this astonishing rearrangement. Three are based on the following reaction path: **14** ⇆ **21c** + **4d** → iv + v → **24** + vi; (a) under the drastic conditions of this reaction vi is preferentially destroyed; (b) the retro-Michael process **14** → **21c** is faster than its stereochemical alternate **14** → **4d**; (c) the cyclization **21c** → iv is faster than **4d** → v, in analogy with the **21a** → **22** conversion occurring but **4e** causing no chloride displacement. Finally, an alternate interpretation rests on the reaction route: **14** → vii → iv → **24**.



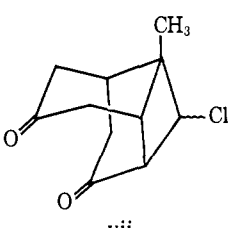
iv



v



vi



vii

(20) While the stereochemistry of this substance has not been elucidated, it can be assumed to be *cis,cis,trans* on the supposition of the initial Michael condensation having taken place from the top side of the roof-like starting material and the subsequent intramolecular carbon–carbon bond-forming reaction having taken a thermodynamic path.

(21) Deviation from these reaction conditions led to lower yields of **4a** and the appearance of a mixture of compounds of unknown constitution, *e. g.*, an acidic compound: mp 119°; infrared (Nujol) C=O 5.76 (s) 5.82 (s) 5.97 (s), C=C 6.17 (s) μ; ultraviolet (MeOH), λ_{max} 280 mμ, λ_{sh} 295 mμ; which gave a positive ferric chloride test and was converted to a carboxylic acid, mp 212–215°.

with water, dried, and evaporated. Crystallization of the residue, 200 mg, from hexane yielded the methyl ester **4c**: mp 89–90°; infrared (Nujol), C=O 5.75 (s), 5.94 (s) μ; pmr, δ 1.29 (s, 3, C-Me), 3.70 (s, 3, OMe), 5.89 (s, 1, $CHCl_3$), 6.08 (d, 1, J = 10.0 cps, α-keto-CH), 7.00 (d, 1, J = 10.0 cps, β-keto-CH).

Anal. Calcd for $C_{11}H_{14}O_3Cl_2$: C, 49.83; H, 5.32. Found: C, 50.01; H, 5.31.

Hydrogenations of 4b and 4c. A mixture of 100 mg of the acid **4b** and 10 mg of 10% palladium–charcoal in 15 ml of ethyl acetate was hydrogenated at room temperature and atmospheric pressure. The mixture was filtered and the filtrate was evaporated. Crystallization of the residue, 90 mg, from ether yielded the acid **5a**: mp 178–180°; infrared (Nujol), OH 3.0–3.3 (m), C=O 5.78 (s), 5.90 (s) μ; pmr (deuterioacetone), δ 1.31 (s, 3, C-Me), 6.52 (s, 1, $CHCl_2$).

Anal. Calcd for $C_{10}H_{14}O_3Cl_2$: C, 47.43; H, 5.54. Found: C, 47.73; H, 5.77.

Hydrogenation of a mixture of 500 mg of ester **4c** and 50 mg of 10% palladium–charcoal in 30 ml of ethyl acetate and work-up followed the above procedure. Crystallization of the product, 500 mg, from ether yielded **5b**; mp 90–91°; infrared (Nujol), C=O 5.76 (s), 5.83 (s) μ; pmr δ 1.24 (s, 3, C-Me), 3.68 (s, 3, OMe), 5.94 (s, 1, $CHCl_2$).

Anal. Calcd for $C_{11}H_{16}O_3Cl_2$: C, 49.45; H, 6.04. Found: C, 49.27; H, 6.04.

Thioketal 5c. A solution of 100 mg of acid **5a** and a few drops of boron trifluoride ethereate in 0.5 ml of ethanedithiol was kept at room temperature for 12 hr. Ice water was added and the mixture was extracted with ether. The extract was dried and evaporated under high vacuum. Crystallization of the solid residue, 93 mg, from ether gave acid **5c**; mp 171–172°; infrared (Nujol), OH 3.0–3.3 (m), C=O 5.76 (s), 5.88 (s) μ; pmr (deuterioacetone), δ 1.05 (s, 3, C-Me), 3.30 (s, 4, thiomethylenes), 6.25 (s, 1, $CHCl_2$).

Anal. Calcd for $C_{12}H_{18}O_2S_2Cl_2$: C, 43.76; H, 5.47. Found: C, 44.08; H, 5.64.

Ketals 5d and 5e. A solution of 240 mg of ester **5b**, 75 mg of ethylene glycol, and a few crystals of *p*-toluenesulfonic acid in 50 ml of benzene was refluxed under nitrogen in the presence of a water separator for 12 hr. A sodium bicarbonate solution and chloroform were added. The organic solution was separated, dried, and evaporated. Crystallization of the solid residue, 240 mg, from ether afforded ester **5d**: mp 97–98°; infrared (Nujol), C=O 5.76 (s) μ; pmr, δ 1.07 (s, 3, C-Me), 3.68 (s, 3, OMe), 3.94 (s, 4, oxymethylenes), 5.85 (s, 1, $CHCl_2$).

Anal. Calcd for $C_{13}H_{20}O_4Cl_2$: C, 50.17; H, 6.48. Found: C, 50.19; H, 6.23.

A solution of 150 mg of ester **5d** and 5 ml of 10% potassium hydroxide in 1:1 ethanol–water was kept at room temperature for 12 hr. It was acidified to pH 8 with 10% hydrochloric acid and extracted with chloroform. The extract was dried and evaporated. Crystallization of the oily residue, 130 mg, from ether led to the acid **5e**: mp 117–118°; infrared (Nujol), OH 3.0–3.3 (m), C=O 5.85 (s) μ; pmr, δ 1.07 (s, 3, C-Me), 3.96 (s, 4, oxymethylenes), 5.82 (s, 1, $CHCl_2$).

Anal. Calcd for $C_{12}H_{18}O_4Cl_2$: C, 48.48; H, 6.06. Found: C, 48.74; H, 6.29.

Lactol 7a and Its Acetate (7b). A solution of 100 mg of the acid **5c** and 150 mg of sodium hydroxide in 6 ml of water was refluxed for 12 hr. The solution was acidified and extracted with chloroform. The extract was dried and evaporated. Crystallization of the residual solid, 85 mg, from ether gave aldehydo acid **6a**: mp 136–137°; infrared (Nujol), OH 3.0–3.3 (m), C=O 5.78 (s), 5.88 (s) μ; pmr, δ 1.02 (s, 3, C-Me), 3.35 (s, 4, thiomethylenes), 9.33 (s, 1, CHO). Crystallization from chloroform gave **7a**: mp 125°; infrared (Nujol), OH 2.90 (m), C=O 5.77 (m), 5.85 (s) μ.

Anal. Calcd for $C_{12}H_{18}O_3S_2$: C, 52.55; H, 6.57. Found: C, 52.73; H, 6.46.

A solution of 60 mg of **6a–7a** and a few crystals of fused sodium acetate in 5 ml of acetic anhydride was refluxed for 1 hr. The excess anhydride was distilled under vacuum and the residue was treated with water and extracted with chloroform. The extract was dried and evaporated. Crystallization of the solid residue, 60 mg, from ether yielded **7b**: mp 180–185°; infrared (Nujol), C=O 5.66 (s) 5.73 (s) μ; pmr, δ 1.01 (s, 3, C-Me), 2.13 (s, 3, Ac), 3.32 (s, 4, thiomethylenes), 6.16 (s, 1, AcOCH). The broad melting point and extraneous pmr signals (methyls at 1.12 and 2.17 ppm) indicated the compound to be admixed with a minor amount of its anomeric acetate.

Anal. Calcd for $C_{14}H_{20}O_4S_2$: C, 53.16; H, 6.37. Found: C, 53.39; H, 6.59.

Diester 6c. A mixture of 100 mg of **6a–7a**, 50 mg of sodium hydroxide, and silver oxide (from 120 mg of silver nitrate and 60 mg of sodium hydroxide) in 7 ml of water was stirred at 0° for 12 hr. It was filtered and the filtrate was acidified and extracted with ethyl acetate. The extract was dried and evaporated. Crystallization of the solid residue, 95 mg, from ether yielded the diacid **6b**: mp 212–215°; infrared (Nujol), OH 3.0–3.3 (m), C=O 5.89 (s) μ. A solution of 50 mg of the acid and a few drops of methanol in 50 ml of ether saturated with diazomethane was kept at room temperature for 5 hr. Solvent removal gave a colorless oil, 50 mg, which was purified by sublimation. Crystallization from hexane afforded the diester **6c**: mp 78–79°; infrared (Nujol), C=O 5.78 (s) μ; pmr, δ 1.12 (s, 3, C-Me), 3.29 (s, 4, thiomethylenes), 3.66, 3.67 (s, 3, OMe).

Anal. Calcd for $C_{14}H_{22}O_4S_2$: C, 52.82; H, 6.97. Found: C, 52.95; H, 6.74.

2-Methyl-2-carboxycyclohexylacetic Acid (6d). A mixture of of 50 mg of diester **6c** and 2 g of Raney nickel in 15 ml of absolute ethanol was refluxed for 3 days. It was decanted and the residue was decomposed by the addition of 10 ml of 10% hydrochloric acid and stirring for 30 min. The nickel solution was extracted with ethyl acetate and the extract was dried. The combined ethanol and ethyl acetate solutions were evaporated. Distillation of the residual oil, 30 mg, gave the dimethyl ester of **6d** as a colorless oil: infrared (CCl_4) C=O 5.79 (s) μ; pmr, δ 1.12 (s, 3, C-Me), 3.68, 3.69 (s, 3, OMe). A solution of 30 mg of the ester and 5 ml of 10% sodium hydroxide in 1:1 ethanol–water was refluxed for 2 hr. It was acidified and extracted with ethyl acetate. The extract was dried and evaporated. Crystallization of the solid residue, 23 mg, from hexane yielded the diacid **6d**, mp 175–176° (lit. mp 175°,[8a] 175–177.8°,[8b] 177°[8c]), mmp 174–175° (with authentic sample, *vide infra*).

Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.00; H, 7.95.

Degradation of Hydrocarbon 8a. A solution of 480 mg of **8a** in 10 ml of acetic acid was added to 3 ml of a chromic acid solution, prepared from 2.5 g of chromium trioxide, 8 ml of acetic acid, and 2 ml of water, and the mixture was stirred at room temperature for 30 min. Ice water was added and the mixture was extracted with chloroform. The extract was washed with sodium bicarbonate solution, dried, and evaporated. Alumina chromatography of the residual oil, 470 mg, and elution with hexane led to recovery of 220 mg of starting material. Elution with 4:1 hexane–benzene gave 247 mg of oily ketone **8b** which was purified by distillation.[22]

A solution of 235 mg of ketone **8b** and 340 mg of *m*-chloroperbenzoic acid in 5 ml of chloroform was kept at 0° for 1 week. Ether, 100 ml, was added and the mixture was washed with aqueous solutions of potassium iodide, sodium sulfite, and sodium bicarbonate. The solution was dried and evaporated. Crystallization of the oily residue, 230 mg, from petroleum ether (bp 30–60°) yielded lactone **9**: mp 83–84°; infrared (Nujol), C=O 5.72 (s) μ; pmr, δ 1.33 (s, 3, C-Me).

Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.00; H, 7.95.

A mixture of 50 mg of the lactone and 10 ml of 10% potassium hydroxide in 1:1 ethanol–water was heated for 1 hr. It was acidified and extracted with ethyl acetate. The extract was dried and evaporated. Crystallization of the residue, 50 mg, from chloroform gave a hydroxy acid: mp 160–162°; infrared (Nujol), OH 2.98 (s), 3.0–3.3 (w), C=O 5.97 (s) μ; pmr (deuterioacetone), δ 1.31 (s, 3, C-Me). A solution of 200 mg of this acid in 20 ml of 9:1 chloroform-methanol was exposed to a stream of ozone at 0° for 5 hr. The two-layer mixture was kept at room temperature for 12 hr. A solution of 7 ml of formic acid and 7 ml of 30% hydrogen peroxide was added and the mixture was refluxed for 2 hr. It then was extracted with ethyl acetate and the extract was dried and evaporated. A solution of the oily residue, 180 mg, and 5 ml of methanol in 150 ml of ether saturated with diazomethane was kept at room temperature for 3 hr. Evaporation of the solvent, chromatography of the residue, 169 mg, on alumina, and elution with 9:1 hexane–benzene gave 20 mg of oily dimethyl ester of **6d**. A solution of this substance and 0.5 ml of 5% potassium hydroxide in 1:1 ethanol–water was kept at room temperature for 12 hr. It was concentrated under vacuum, acidified, and extracted with ethyl acetate. The extract was dried and evaporated. Crystallization of the solid residue, 15 mg, from ether gave the diacid

(22) This preparation of **8b** represents an improvement of the procedure described by E. Wenkert and J. W. Chamberlin, *J. Org. Chem.*, **25**, 2027 (1960).

6d: mp 174°; infrared spectrum identical with that of the synthetic sample (*vide supra*).

Condensations of Ketones 1a and 1b with Methyl Acetoacetate. A solution of 945 mg of ketone **1a**, 580 mg of methyl acetoacetate, and sodium methoxide (from 115 mg of sodium) in 15 ml of methanol was kept under nitrogen at room temperature for 48 hr. It was evaporated under vacuum and the residue was treated with 25 ml of water saturated with carbon dioxide. The mixture was extracted with chloroform. The extract was washed thoroughly with 10% sodium hydroxide solution, dried, and evaporated. Alumina chromatography of the residue, 300 mg, and elution with 7:3 hexane–benzene yielded 65 mg of starting ketone. Elution with 1:1 hexane–benzene and crystallization of the solid, 100 mg, from hexane yielded keto ester **22**: mp 119–121°; infrared (Nujol), C=O 5.83 (s), 5.96 (s), 6.02 (s), C=C 6.12 (s) μ; ultraviolet (MeOH), λ_{max} 223 mμ (log ϵ 4.23), λ_{sh} 240 mμ (log ϵ 4.00); pmr, δ 1.27 (s, 3, saturated Me), 2.30 (d, 3, J = 0.5 cps, olefinic Me), 3.78 (s, 3, OMe), 5.82 (d, 1, J = 0.8 cps, chloromethine), 6.10 (d, 1, J = 10.0 cps, α-keto-CH), 6.56 (d, 1, J = 10.0 cps, β-keto-CH).

Anal. Calcd for $C_{13}H_{15}O_4Cl$: C, 57.77; H, 5.55. Found: C, 57.91; H, 5.75.

The combined alkali washings were acidified and extracted with ethyl acetate. The extract was dried and evaporated. Crystallization of the solid residue, 860 mg, from ether–petroleum ether gave the ester **10a**: mp 125°; infrared (Nujol), OH 3.03 (m), C=O 6.06 (s), C=C 6.22 (s) μ; ultraviolet (MeOH), λ_{max} 255 mμ (log ϵ 4.86); pmr, δ 1.14 (s, 3, C-Me), 2.50 (s, 2, allylic CH_2), 3.79 (s, 3, OMe), 5.38 (q, 1, J = 1.3, 10.5 cps, olefinic CH), 5.74 (q, 1, J = 1.3, 10.5 cps, olefinic CH), 5.95 (s, 1, $CHCl_2$).

Anal. Calcd for $C_{13}H_{16}O_4Cl_2$: C, 50.83; H, 5.25. Found: C, 50.62; H, 5.05.

A solution of 717 mg of **10a** and sodium methoxide (from 92 mg of sodium) in 15 ml of methanol was kept under nitrogen at room temperature for 48 hr. Upon work-up as above there was obtained 700 mg of starting material.

A solution of 1.00 g of ketone **1a**, 648 mg of methyl acetoacetate and sodium methoxide (from 42 mg of sodium) in 15 ml of methanol was kept under nitrogen at room temperature for 5 days. Work-up as above gave 670 mg of neutral oil and 925 mg of acidic residue whose crystallization and spectra showed it to be **10a**. Alumina chromatography of the neutral material and elution with 7:3 hexane–benzene led to recovery of 70 mg of starting ketone (**1a**), while elution with 1:1 hexane–benzene gave 6 mg of keto ester **22**. Crystallization (from hexane–ether) of the solid, 275 mg, from the early 1:1 hexane–benzene eluates afforded keto ester **29**: mp 96°; infrared (Nujol), C=O 5.87 (s), C=C 6.24 (s) μ; ultraviolet (MeOH), λ_{max} 244 mμ (log ϵ 3.75); pmr, δ 1.57 (s, 3, saturated Me), 2.24 (s, 3, olefinic Me), 3.72 (s, 3, OMe), 4.72 (q, 1, J = 3.0, 7.0 cps, oxymethine), 5.97 (s, 1, $CHCl_2$).

Anal. Calcd for $C_{13}H_{16}O_4Cl_2$: C, 50.83; H, 5.25. Found: C, 51.07; H, 5.19.

A solution of 1.00 g of ketone **1b**,[23] 580 mg of methyl acetoacetate and sodium methoxide (from 40 mg of sodium) in 20 ml of methanol was kept under nitrogen at room temperature for 5 days. Work-up as above led to 430 mg of starting ketone **1b** and 198 mg of acidic material whose crystallization from ether–hexane gave colorless needles of **10b**; mp 126–128°; infrared ($CHCl_3$), C=O 6.06 (s), C=C 6.21 (s) μ; pmr, δ 1.10 (s, 3, saturated Me), 1.82 (d, 3, J = 1.5 cps, olefinic Me), 3.81 (s, 3, OMe), 5.06 (m, 1, olefinic H), 5.92 (s, 1, $CHCl_2$).

Anal. Calcd for $C_{14}H_{18}O_4Cl_2$: C, 52.35; H, 5.65. Found: C, 53.06; H, 5.69.

Hydroxy Ester 12. A mixture of 530 mg of **10a** and 50 mg of 10% palladium–charcoal in 20 ml of methanol was hydrogenated at room temperature and atmospheric pressure. The mixture was filtered and the filtrate was evaporated. Crystallization of the residual solid, 520 mg, from ether gave ester **12**: mp 158–160°; infrared (Nujol), OH 3.04 (m), C=O 6.07 (s), C=C 6.24 (s) μ; pmr, δ 0.94 (s, 3, C-Me), 2.54 (s, 2, allylic CH_2), 3.81 (s, 3, OMe), 6.34 (s, 1, $CHCl_2$).

Anal. Calcd for $C_{13}H_{18}O_4Cl_2$: C, 50.50; H, 5.87. Found: C, 50.83; H, 5.85.

(23) This ketone could be prepared in 13% yield by the published procedure.[6] Its physical characteristics were mp 53–55°; infrared ($CHCl_3$), C=O 6.00 (s), C=C 6.10 (s) μ; ultraviolet (95% EtOH), λ_{max} 234 mμ (log ϵ 4.13); pmr, δ 1.47 (s, 3, saturated Me), 2.05 (d, 3, J = 1.5 cps, olefinic Me), 5.96 (s, 1, $CHCl_2$), 6.19 (q, 1, J = 1.5, 2.0 cps, α-keto-CH next to Me), 6.42 (q, 1, J = 2.0, 10.0 cps, α-keto-CH), 7.13 (d 1, J = 10.0 cps, β-keto-CH).

Ketol 13. A solution of 200 mg of ester **12** and 10 ml of 50% hydrochloric acid in 1:1 methanol–water was refluxed for 4 hr and then extracted with chloroform. The extract was dried and evaporated. Crystallization of the solid residue, 140 mg, from ether yielded ketol **13**: mp 98–100°; infrared (Nujol), OH 2.90 (m), 3.03 (m), C=O 5.85 (s), 5.92 (s) μ; pmr, δ 1.11 (s, 3, Me), 6.34 (s, 1, $CHCl_2$).

Anal. Calcd for $C_{11}H_{16}O_2Cl_2$: C, 52.60; H, 6.42. Found: C, 52.85; H, 6.60.

A solution of 100 mg of ketol **13** and 2 ml of 10% sodium hydroxide in 3 ml of dioxane was kept at room temperature under nitrogen for 12 hr. Usual work-up led to quantitative recovery of starting material. When the reaction was executed with refluxing, starting material was decomposed and a mixture of sensitive products resulted.

Diketone 14. A solution of 300 mg of **10a** in 20 ml of 50% hydrochloric acid solution was refluxed for 4 hr and then extracted with chloroform. The extract was dried and evaporated. Crystallization of the residual solid, 220 mg, from benzene gave diketone **14**: mp 207° (lit.[7b] mp 201°); infrared (Nujol), C=O 5.87 (s) μ; pmr, δ 1.67 (s, 3, Me), 7.20 (s, 1, $CHCl_2$).

Anal. Calcd for $C_{11}H_{14}O_2Cl_2$: C, 53.03; H, 5.66. Found: C, 53.02; H, 5.64.

A similar treatment of 1.00 g of **29** gave 602 mg of **14**.

Phenols 18. A solution of 502 mg of ketol **13** and potassium *t*-butoxide (from 155 mg of potassium) in 25 ml of dimethyl sulfoxide was stirred at room temperature for 24 hr. The brown mixture was poured into 200 ml of water, acidified, and extracted with chloroform. The extract was washed with sodium bicarbonate solution and with water, dried, and evaporated. Chromatography on silica gel and elution with benzene gave an oil whose distillation at 0.2 mm (bath temperature 150°) yielded 210 mg of liquid phenol **18a**: infrared (neat), OH 2.8–3.2 (m), C=C 6.09 (w), 6.19 (m), 6.26 (m) μ; ultraviolet (EtOH), λ_{max} 274 mμ (log ϵ 3.24), 282 mμ (log ϵ 3.19); pmr, δ 1.80 (d, 3, J = 1.5 cps, Me), 5.78 (broad s, 1, chloromethine).

Anal. Calcd for $C_{11}H_{13}OCl$: C, 67.17; H, 6.66; Cl, 18.03. Found: C, 67.36; H, 6.43; Cl, 17.75.

A mixture of 90 mg of **18a** and 30 mg of palladium–charcoal in 5 ml of 95% ethanol was hydrogenated at room temperature and atmospheric pressure. It then was filtered and evaporated. Distillation of the residue at 0.1 mm (bath temperature 85°) gave 45 mg of *m*-isopentylphenol (**18b**): infrared (neat), OH 2.8–3.2 (m), C=C 6.19 (m), 6.26 (m) μ; ultraviolet (EtOH), λ_{max} 274 mμ (log ϵ 3.21), 280 mμ (log ϵ 3.17); pmr, δ 0.90 (d, 6, J = 6.5 cps, Me_2).

Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.83. Found: C, 80.54; H, 9.94.

1-Methyl-1-dichloromethyl-3-acetonyl-4,4-ethylenedithiocyclohexane (5g). A mixture of 1.5 g of acid **5c** and 1.5 ml of oxalyl chloride in 50 ml of 1:1 petroleum ether–benzene was stirred at room temperature for 12 hr. The solvent and excess reagent were removed under vacuum. Crystallization of the residual solid, 1.3 g, from petroleum ether–ether gave an acid chloride: mp 90–92°; infrared (Nujol), C=O 5.58 (s) μ; pmr, δ 1.07 (s, 3, Me), 3.30 (s, 4, thiomethylenes), 5.74 (s, 1, $CHCl_2$).

A mixture of 100 mg of magnesium in 8 ml of dry ether was saturated with dry methyl bromide at 0° until all magnesium had dissolved. Cadmium chloride, 500 mg, was added and the mixture was refluxed for 30 min. The solvent was evaporated and replaced by 3 ml of dry benzene. A solution of 200 mg of the acid chloride of **5c** in 2 ml of benzene was added and the mixture refluxed for 1 hr. Aqueous ammonium chloride solution was added and the mixture was extracted with chloroform. The extract was washed with sodium bicarbonate solution, dried, and evaporated. Chromatography of the residue, 180 mg, on alumina and elution with 4:1 hexane–benzene gave 20 mg of a solid whose crystallization from hexane yielded thioketal **5g**: mp 112–114°; infrared (Nujol), C=O 5.82 (s) μ; pmr, δ 1.05 (s, 3, Me), 2.17 (s, 3, Ac), 3.30 (s, 4, thiomethylenes), 5.80 (s, 1, $CHCl_2$).

Anal. Calcd for $C_{13}H_{20}OS_2Cl_2$: C, 47.70; H, 6.11. Found: C, 47.55; H, 6.32.

Lactone 19. The above procedure of acid chloride formation was applied to 130 mg of acid **5e** (0.3 ml of oxalyl chloride and 20 ml of petroleum ether). Crystallization of the solid residue, 130 mg derived from work-up, from ether yielded an acid chloride: mp 80–82°; infrared (Nujol), C=O 5.56 (s) μ; pmr, δ 1.08 (s, 3, Me), 3.95 (s, 4, oxymethylenes), 5.81 (s, 1, $CHCl_2$).

The above procedure was followed for the preparation of the organocadmium reagent (100 mg of magnesium, 500 mg of cadmium chloride finally in 3 ml of benzene) and for its interaction with

the acid chloride (200 mg in 2 ml of benzene) of **5e**. Normal work-up led to an oily residue whose crystallization from ether gave lactone **19**: mp 168–169°; infrared (Nujol), C=O 5.83 (s) μ; pmr, δ 1.15 (s, 3, Me), 1.18 (s, 3, Me), 3.6–3.8 (m, 2, oxymethylene), 4.1–4.2, 4.4–4.9 (m, 1 each, acyloxymethylene), 6.14 (s, 1, $CHCl_2$).

Anal. Calcd for $C_{13}H_{20}O_3Cl_2$: C, 52.88; H, 6.77. Found: C, 52.77; H, 6.93.

Ketals 5h and 20. A solution of 0.15 *N* methyllithium in 6.3 ml of ether was added dropwise over 30 min to a solution of 300 mg of the acid chloride of **5e** in 10 ml of ether at −75° under nitrogen The mixture was stirred at this temperature for 2 hr. Aqueous ammonium chloride solution was added and the mixture was extracted with ether. The extract was dried and evaporated. Alumina chromatography of the residue, 280 mg, and elution with 1:1 hexane–benzene gave 30 mg of a solid whose crystallization from hexane yielded the ketone **5h**: mp 95–97°; infrared (Nujol), C=O 5.82 (s) μ; pmr, δ 1.08 (s, 3, Me), 2.18 (s, 3, Ac), 3.97 (s, 4, oxymethylenes), 5.88 (s, 1, $CHCl_2$).

Anal. Calcd for $C_{13}H_{20}O_3Cl_2$: C, 52.89; H, 6.83. Found: C, 53.05; H, 6.73.

Further elution with benzene gave 100 mg of a solid whose crystallization from hexane yielded carbinol **20**: mp 96–97°; infrared (Nujol), OH 2.85 (m) μ; pmr, δ 1.03 (s, 3, Me), 1.25 (s, 6, isopropyl), 3.92 (s, 4, oxymethylenes), 5.87 (s, 1, $CHCl_2$).

Anal. Calcd for $C_{14}H_{24}O_3Cl_2$: C, 54.01; H, 7.71. Found: C, 54.19; H, 7.65.

3-Acetonyl-4-methyl-4-dichloromethylcyclohexanone (5f). A mixture of 35 mg of ketone **5h** in 5 ml of 10% sulfuric acid in 1:1 dioxane–water was stirred at room temperature for 3 hr. Sodium bicarbonate was added and the mixture was extracted with chloroform. The extract was dried and evaporated. Crystallization of the residue, 30 mg, from hexane–ether yielded diketone **5f**; mp 112–113°; infrared (Nujol), C=O 5.85 (s) μ; pmr, δ 1.24 (s, 3, Me), 2.17 (s, 3, Ac), 5.97 (s, 1, $CHCl_2$).

Anal. Calcd for $C_{11}H_{16}O_2Cl_2$: C, 52.59; H, 6.37. Found: C, 52.68; H, 6.46.

A solution of 30 mg of diketone **5f** and four drops of 50% aqueous potassium hydroxide in 3 ml of methanol was kept under nitrogen at room temperature for 30 hr. It was acidified with 10% hydrochloric acid and extracted with chloroform. The extract was dried and evaporated. Crystallization of the residue, 28 mg, from ether gave ketol **13**, mp 99°, mmp 98–100°, infrared spectrum (Nujol) identical with that of the above sample.

Keto Ester 23. A mixture of 50 mg of ester **22** and 10 mg of 10% palladium–charcoal in 10 ml of ethyl acetate was hydrogenated at room temperature and atmospheric pressure. After the uptake of 1 mole of hydrogen the mixture was filtered and the filtrate was evaporated. Crystallization of the residue, 45 mg, from hexane afforded keto ester **23**: mp 118–119°; infrared (Nujol), C=O 5.82 (s), C=C 6.08 (s) μ; pmr, δ 1.20 (s, 3, saturated Me), 2.23 (d, 3, J = 1.0 cps, olefinic Me), 3.77 (s, 3, OMe), 5.85 (s, 1, chloromethine).

Anal. Calcd for $C_{13}H_{17}O_4Cl$: C, 57.46; H, 6.30. Found: C, 57.65; H, 6.34.

Hydrolyses of Esters 22 and 23. A mixture of 100 mg of keto ester **22** and 5 ml of 10% sulfuric acid in 1:1 dioxane–water was refluxed for 5 hr. Sodium bicarbonate was added and the mixture was extracted with chloroform. The extract was dried and evaporated. Crystallization of the oily residue, 65 mg, from ether–hexane yielded diketone **24**: mp 76–78°; infrared (Nujol), C=O 5.90 (s), 5.99 (s) μ; ultraviolet (MeOH), λ_{max} 217 mμ (log ϵ 4.22), λ_{sh} 228 mμ (log ϵ 4.19); pmr, δ 1.51 (s, 3, Me), 6.05 (d, 2, J = 10.0 cps, olefinic α-ketomethines), 6.65 (d, 2, J = 10.0 cps, olefinic β-ketomethines).

Anal. Calcd for $C_{11}H_{12}O_2$: C, 74.97; H, 6.86. Found: C, 74.94; H, 6.55.

A mixture of 200 mg of keto ester **23** and 10 ml of 10% sulfuric acid in 1:1 dioxane–water was refluxed for 5 hr. Work-up as above led to 132 mg of oily residue. Alumina chromatography and elution with benzene gave a solid, 48 mg, whose crystallization from hexane yielded diketone **25a**: mp 67–68°; infrared (Nujol), C=O 5.85 (s), 5.99 (s) μ; pmr, δ 1.41 (s, 3, Me), 6.01 (d, 1, J = 10.0 cps, α-keto-CH), 6.78 (broad d, 1, J = 10.0 cps, β-keto-CH).

Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 78.28; H, 7.97.

***cis*-10-Methyldecalin-2,7-dione (26a).** A mixture of 40 mg of diketone **24** and 10 mg of 10% palladium–charcoal in 10 ml of ethyl acetate was hydrogenated at room temperature and atmospheric pressure. After completion of hydrogen uptake the mixture was filtered and the filtrate was evaporated. Crystallization of the residual solid, 35 mg, gave the diketone **26a**, mp 91°; infrared (Nujol), C=O 5.84 (s), 5.90 (s) μ; pmr, δ 1.37 (s, 3, Me).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.00; H, 8.70.

Hydrogenation of 50 mg of diketone **25a** under the above conditions and crystallization of the crude product, 45 mg, gave **26a**, mp and mmp 90–91°, infrared spectrum identical with that of the above sample.

Thioketal 25b. A solution of 98 mg of diketone **25a**, 51 mg of ethanedithiol, and a few drops of boron trifluoride etherate in 1.8 ml of acetic acid was kept at room temperature for 12 hr. Water was added and the mixture was extracted with ethyl acetate. The extract was dried and concentrated. Alumina chromatography of the residual oil, 110 mg, and elution with 1:1 hexane–benzene gave a solid whose crystallization from ether–hexane yielded thioketal **25b**: mp 106–107°; infrared (Nujol), C=O 6.01 (s) μ; pmr, δ 1.25 (s, 3, Me), 3.28 (s, 4, thiomethylenes), 5.90 (q, 1, J = 10.5, 0.9 cps, α-keto-CH), 6.54 (q, 1, J = 10.5, 2.0 cps, β-keto-CH).

Anal. Calcd for $C_{13}H_{18}OS_2$: C, 61.38; H, 7.13. Found: C, 61.08; H, 7.34.

Ketal 25c. A solution of 100 mg of diketone **25a**, 35 mg of ethylene glycol, and a few crystals of *p*-toluenesulfonic acid in 30 ml of benzene was refluxed for 5 hr and water was removed azeotropically. An aqueous sodium bicarbonate solution was added and the mixture was extracted with chloroform. The extract was dried and concentrated. Alumina chromatography of the residual oil, 110 mg, and elution with 1:1 hexane–benzene yielded 60 mg of a solid whose crystallization from hexane produced ketal ketone **25c**: mp 71–72°; infrared (Nujol), C=O 6.01 (s) μ; pmr, δ 1.22 (s, 3, Me), 3.92 (s, 4, oxymethylenes), 5.93 (d, 1, J = 10.0 cps, α-keto-CH), 6.59 (q, 1, J = 10.0, 1.6 cps, β-keto-CH).

Anal. Calcd for $C_{13}H_{18}O_3$: C, 47.70; H, 6.11. Found: C, 47.55; H, 6.32.

Ester **23**, 200 mg, was added to a previously dried solution of 60 mg of ethylene glycol and a few crystals of *p*-toluenesulfonic acid in 30 ml of benzene and the mixture refluxed for 1 hr under azeotropic removal of water. An aqueous sodium bicarbonate solution was added and the mixture was extracted with chloroform. The extract was dried and concentrated yielding oily ethylene ketal of **23**: 210 mg; infrared (CCl_4), C=O 5.85 (s), C=C 6.12 (m) μ; ultraviolet (MeOH), λ_{max} 240 mμ; pmr, δ 1.06 (s, 3, Me), 3.76 (s, 3, OMe), 3.95 (s, 4, oxymethylenes), 5.68 (d, 1, J = 1.3 cps, chloromethine). A mixture of 100 mg of the ketal and 10 ml of 10% potassium hydroxide in 1:1 ethanol–water was refluxed for 4 hr and then extracted with chloroform. The extract was dried and concentrated. Crystallization of the residue, 50 mg, from hexane gave ketal **25c**, mp 70–72°, mmp 71°, infrared spectrum identical with that of the above specimen.

***cis*-10-Methyl-2-decalone (26b).** A mixture of 100 mg of thioketal **25b** and *ca.* 1 g of Raney nickel in 20 ml of absolute ethanol was refluxed under nitrogen for 18 hr. It then was decanted and the solution was evaporated. The residual oil, 45 mg, showed hydroxyl and carbonyl absorption in the infrared spectrum. It was dissolved in 3 ml of acetone and treated with 0.3 ml of Jones reagent. Sodium bicarbonate was added and the mixture was extracted with chloroform. The extract was dried and evaporated. Distillation of the remaining oil, 34 mg, at 0.25 mm (bath temperature 100°) gave ketone **26b**; infrared (CCl_4), C=O 5.83 (s) μ; pmr, δ 1.18 (s, 3, Me); 2,4-dinitrophenylhydrazone, mp 170–172°, mmp 169–170°; infrared spectrum identical with that of an authentic sample.[15]

A mixture of 70 mg of ketoketal **25c** and 10 mg of 10% palladium–charcoal in 10 ml of ethyl acetate was hydrogenated at room temperature and atmospheric pressure. After completion of hydrogen uptake the mixture was filtered and the filtrate was evaporated. Crystallization of the remaining oil, 66 mg, from hexane gave ketoketal **26c**; mp 80–82°; infrared (Nujol), C=O 5.84 (s) μ; pmr, δ 1.25 (s, 3, Me), 3.92 (s, 4, oxymethylenes). A mixture of 85 mg of **26c**, 250 mg of hydrazine, and 200 mg of potassium hydroxide in 5 ml of ethylene glycol was treated according to the Huang-Minlon conditions of the Wolff–Kishner reduction. Filtration of a hexane solution of the residue through a short alumina column and evaporation yielded 50 mg of the ethylene ketal of **26b**; pmr, δ 1.00 (s, 3, Me). A solution of this oil and 5 ml of 10% hydrochloric acid in acetone was heated on a steam bath for 20 min. Aqueous sodium bicarbonate solution was added and the mixture was extracted with ether. The extract was dried and evaporated. Distillation of the residue, 40 mg, at 0.25 mm (bath temperature 100°) gave ketone **26b**: spectra same as above; 2,4-dinitrophenylhydrazone, mp

170–172°, mmp 170–171°; infrared spectrum identical with that of an authentic specimen.

Diketone 24. A solution of 300 mg of diketone **14** and 160 mg of dry potassium *t*-butoxide in 5 ml of dimethyl sulfoxide was kept at room temperature under nitrogen for 1.5 hr. Water was added and the mixture was extracted with chloroform. The extract was dried and evaporated. Alumina chromatography of the residue, 300 mg, and elution with benzene gave 70 mg of a solid whose crystallization from hexane and vacuum sublimation yielded **24**, mp and mmp 76–78°, infrared spectrum identical with that of the above sample. Elution with chloroform led to the recovery of 60 mg of starting ketone **14**.

Triketones 30. A solution of 100 mg of diketone **24**, 100 mg of dimethyl acetonedicarboxylate, and sodium methoxide (from 10 mg of sodium) in 0.5 ml of methanol was refluxed for 8 hr. The cooled mixture was acidified with 10% sulfuric acid and filtered. The precipitate was washed with water, dried, and crystallized from methanol–ether yielding 156 mg of colorless needles of triketo diester **30a**: mp 197°; infrared ($CHCl_3$), C=O and C=C 5.76 (s), 5.82 (s), 6.02 (s), 6.16 (m) μ; ultraviolet (EtOH), λ_{max} 253 mμ (log ϵ 3.96); pmr, δ 1.38 (s, 3, Me), 3.89, 3.91 (s, 3, OMe).

Anal. Calcd for $C_{16}H_{22}O_7$: C, 61.70; H, 6.33. Found: C, 61.65; H, 6.66.

A mixture of 100 mg of **30a** and 2 ml of 10 *N* hydrochloric acid in 2 ml of methanol was heated on a water bath for 9 hr. Water was added and the mixture was extracted with chloroform. The extract was washed with saturated sodium bicarbonate solution and with water, dried, and evaporated. Sublimation (190°) of the residual solid, 60 mg, yielded white plates of triketone **30b**; mp 217–218°; infrared (Nujol), C=O 5.85 (s) μ; pmr, δ 1.57 (s, 3, Me).

Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.77. Found: C, 72.00; H, 8.11.

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Solvolytic Studies of Bicyclooctenyl Derivatives. The Epimeric Bicyclo[3.2.1]oct-6-en-3-yl Tosylates[1]

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Abstract: The synthesis and characterization of *exo*(equatorial)-bicyclo[3.2.1]oct-6-en-3-ol, *endo*(axial)-bicyclo[3.2.1]oct-6-en-3-ol, and derivatives thereof are reported. Analysis of the kinetic data from the acetolyses of these compounds and their β-tetradeuterated analogs suggests that the rates are "normal" for these constrained cyclohexyl tosylates; no anchimeric assistance seems to be provided by the double bond for the *exo* isomer, or by the axial β-hydrogen for the *endo* isomer. Preparative solvolyses show that the reaction mixtures contain products of elimination, substitution without skeletal rearrangement, as well as rearranged products. The rearranged acetates arise from the tricyclo[3.2.1.$0^{2,7}$]octan-6-yl cation, and this intermediate is generated by way of a stereospecific hydride-shift pathway. A hydrogen-bridged intermediate cation, intervening after the first-formed ion pair, nicely accommodates the data. Secondary acetolysis products are encountered as well, and mechanisms for their formation are proposed.

The unique variety of structural types available in bicyclooctene carbon skeletons provides opportunity for assessment of the relative importance of σ *vs.* β-π-(homoallylic) participation in solvolytic reactions. Often the latter type of assistance has been accompanied by the direct generation of cationic intermediates which maintain their structural integrity (show little tendency to "leak" into other systems) as evidenced by high product selectivity. The bicyclo[2.2.2]oct-2-en-5-yl tosylates are exemplary cases. The *endo* epimer **1** undergoes accelerated acetolysis directly to the bicyclo[3.2.1]oct-2-en-3-yl cation (**2**), and solvent capture gives nearly exclusively *exo*-bicyclo[3.2.1]oct-2-en-3-yl acetate (**3**).[2] On the other hand, acetolysis of *exo*-bicyclo[2.2.2]oct-2-en-5-yl tosylate (**4**) is also accelerated, and the products are *exo*-tricyclo[3.2.1.$0^{2,7}$]-octan-6-yl acetate (**6**) (90%), *exo*-bicyclo[2.2.2]oct-2-en-5-yl acetate (**7**) (~7%), and *exo*-bicyclo[3.2.1]oct-6-en-2-yl acetate (**8**) (~3%). The intermediate cation involved in the acetolysis of **4** is probably best described as an unsymmetrical cyclopropylcarbinyl cation (**5**), rather than the homoallylic designation previously used,[3] because very little of the epimer of **6** could be detected. In **5**, the *endo* lobe of the p orbital at C_6 overlaps to a significantly greater extent with the bent bond of C_2–C_7 than does the *exo* lobe with the C_1–C_7 bond, and stereoelectronic control of solvent capture would lead preferentially to **6** as the tricyclic product. No crossover between the two cationic systems **2** and **5** was noted. That **5** possesses unique stability is evidenced by its generation from the σ-route precursor **6**-OTs,[3] and by ring expansions of *anti*-2-norbornene-7-carbinyl precursors.[4,5]

The recent availability of bicyclo[3.2.1]oct-6-en-3-one (**9**)[6] prompted an extension of our studies to include the bis homoallylic *exo*- and *endo*-bicyclo[3.2.1]oct-6-en-3-yl tosylates (**10a** and **11a**), respectively). Although it was anticipated that some participation in the solvolysis of the *exo* epimer **10a** might be provided by the two-carbon-removed, but symmetrically and

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