See Editorial, *J. Org. Chem.*, **37**, No. 13, 4A (1972).

A Synthesis of Rosenonolactone from Podocarpic Acid

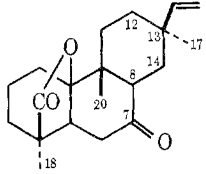
Summary: The 10 → 9 methyl group shift, with concomitant lactonization, effected by Lewis acid treatment of 12,12-ethylenedioxy-8α,9α-epoxypodocarpan-16-oic acid (**3**), provides the basis for a new synthesis of rosenonolactone (**1**).

Sir: The greater thermodynamic stability of rosane compounds over that of pimarane derivatives[1] has been exploited in a biogenetically modeled synthesis[2] of rosenonolactone (**1**) from isocupressic acid. We report a similar synthesis which, in contrast, however, is completely stereoselective and introduces the lactone function directly during the isomerization step. The brevity of the following sequence, which begins with abundantly available podocarpic acid, offers a particularly attractive route to rosane compounds.

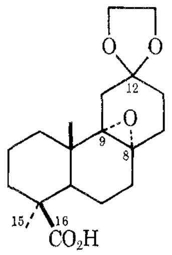
The Δ^8-ethylene acetal[3] derived from 12-oxopodocarp-9(11)-en-16-oic acid[4] was oxidized in quantitative yield by *m*-chloroperoxybenzoic acid to the α-epoxide **3**. When a dilute solution of the epoxide in nitromethane[5] was treated with 2 molar equiv of boron trifluoride etherate for 0.5 hr, the hydroxy lactone **4** (55% yield) was the only neutral product isolated. With 12 equiv of reagent a 2:2:1 mixture (59% yield) of the 8(14)-en-12-one **5**, the Δ^7 isomer **6**, and hydroxy ketone **4** was obtained.[6] Olefin **5** was rapidly isomerized by ethanolic HCl to the α,β-unsaturated lactone **7**,[7] whereas olefin **6** was recovered unchanged.

The elaboration of a rosadiene derivative from ketone **6** was completed simply by C-methylation of its 13-ethylidene derivative,[8] affording a single stereoisomer (**8**, 65% overall yield) in which the vinyl group could be assigned the β configuration from Eu(dpm)$_3$-induced shifts in the nmr spectra of the derived (NaBH$_4$) 12α and 12β alcohols. A correlation of these compounds with rosenonolactone (**1**) to confirm the stereochemical assignments was thwarted by complications arising from the labile vinyl group and an alternative sequence was therefore initiated.

Methoxycarbonylation (NaH, $CH_3OCO_2CH_3$) of ketone **6** followed by *in situ* methylation (MeI) gave a single stereoisomer (**9**, 80% yield) which was converted to its ethylene dithioacetal derivative (33% yield) under carefully controlled conditions (rigorously dried reagents, brief reaction times with recycling of recovered ketone).[9] Desulfurization (W2 Raney nickel) was accompanied by partial double-bond migration (3:2 mixture of Δ^7 and $\Delta^{8(14)}$ olefins) but the triol **10** could be obtained cleanly (40% yield) from hydroboration of the mixture. Ketoaldehyde **11** from oxidation by excess Collins' reagent[10] reacted selectively with methylenetriphenylphosphorane to give isorosenonolactone (**2**, 80% yield)[11] which, on equilibration in HCl–CCl$_4$, gave a 1:1 mixture with rosenonolactone (**1**). Synthetic **1** was indistinguishable (melting point, mixture melting point, and tlc, ir, and nmr spectra)



1, 8α H
2, 8β H



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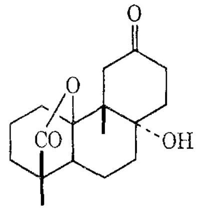

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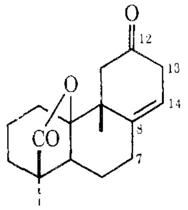

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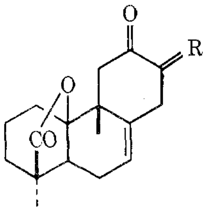
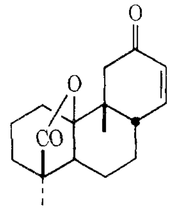


6, R = H$_2$
8, R = β CH=CH$_2$, α CH$_3$
9, R = β CO$_2$CH$_3$, α CH$_3$



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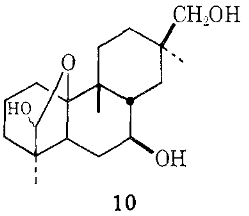

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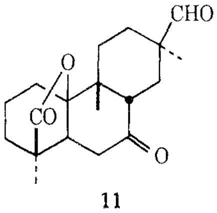

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(1) T. McCreadie and K. H. Overton, *J. Chem. Soc. C*, 312 (1971).

(2) T. McCreadie, K. H. Overton, and A. J. Allison, *J. Chem. Soc. C.*, 317 (1971).

(3) See paragraph at end of paper regarding supplementary material.

(4) R. H. Bible and R. B. Burtner, *J. Org. Chem.*, **26**, 1174 (1961).

(5) Reduced yields of lactonic products were obtained in benzene, acetonitrile, or ether; the acetal function survived in the last solvent.

(6) Several analogous epoxy acids were treated similarly with equivalent results.

(7) Resonances in the nmr spectrum of **7** at δ 5.87 (H-13, d, $J_{13,14}$ = 10 Hz) and 6.93 ppm (H-14, dd, $J_{13,14}$ = 10 Hz, $J_{8,14}$ = 6 Hz) clearly indicated that the C-8 hydrogen substituent was quasiequatorial with respect to ring C. Therefore **7** possesses the trans,syn,cis configuration as assigned, since the cis,syn,cis isomer merits no consideration and trans,syn,trans or cis,-syn,trans backbones would confer a quasiaxial conformation (in both rings) on C-8 substituents.

(8) R. E. Ireland and P. W. Schiess, *J. Org. Chem.*, **28**, 6 (1963).

(9) The lactone function was degraded to the $\Delta^{5(10)}$ olefinic acid at a rate marginally slower than that of thioacetal formation. *Cf.* N. Kiriyama, Y. Yamamoto, and Y. Tsuda, *Chem. Commun.*, 37 (1971).

(10) J. C. Collins, W. W. Hess, and F. J. Frank, *Tetrahedron Lett.*, 3363 (1968).

(11) A. Harris, A. Robertson, and W. B. Whalley, *J. Chem. Soc.*, 1799 (1958).

from an authentic sample.[12] The surprisingly efficient lactonization–migration step[13] is an intriguing aspect of this synthesis and is the subject of current investigation. The utility of this approach in preparing further analogs of rosenonolactone, *e.g.*, the 11β-hydroxy derivative, Rosein III,[9] is also under examination.

Supplementary Material Available.—Complete experimental details on all compounds described in this communication will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 20 × reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D. C. 20036. Remit check or money order for \$3.00 for photocopy or \$2.00 for microfiche, referring to code number JOC-73-4090.

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(12) We are grateful to Professor R. W. Rickards, Australian National University, for this compound.

(13) *Cf.* W. Herz and H. J. Wahlborg, *J. Org. Chem.*, **30**, 1881 (1965).

DEPARTMENT OF ORGANIC CHEMISTRY,
UNIVERSITY OF ADELAIDE,
ADELAIDE, SOUTH AUSTRALIA,
AUSTRALIA, 5001

W. S. HANCOCK
L. N. MANDER*
R. A. MASSY-WESTROPP

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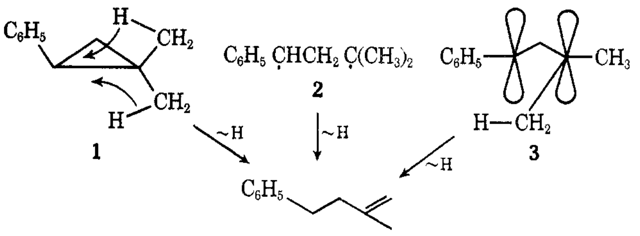
The Photoisomerizations of 2-Methylphenylcyclopropanes. Isotope Effects and Stereochemistry

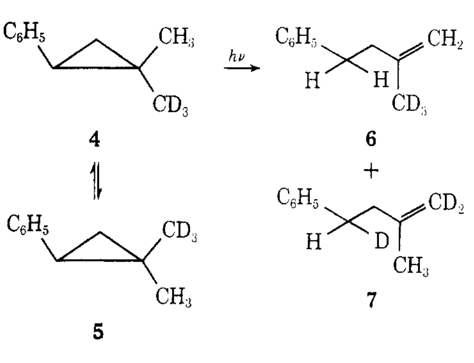
Summary: A deuterium-labeling study on 2,2-dimethylphenylcyclopropane has resulted in the determination of secondary and rather small primary isotope effects for the photochemical reaction and has shown that hydrogen migration in this system takes place preferentially from the methyl group trans to the benzene ring.

Sir: The photochemistry of phenylcyclopropanes has been the subject of intensive investigation recently.[1–6] In particular the isomerizations of 2-alkylphenylcyclopropanes to 4-phenyl-1-butenes[7–11] are of interest since they could represent an example of the allowed $[{}_{\sigma}2_s + {}_{\sigma}2_s]$ concerted[12] photochemical cycloaddition. Alternatively the reaction could proceed *via* preliminary opening to a classical diradical (**2**) or a π cyclopropane-like[13] intermediate (**3**) resulting from disrotatory or conrotatory opening of **1** with subsequent hydrogen migration affording the observed product. *A priori* one expects equivalent migration from *cis*- and *trans*-methyl groups *via* the ${}_{\sigma}2 + {}_{\sigma}2$ route with steric factors possibly causing a slight preponderance of migration from the *trans*-methyl group, whereas, if **2** is the intermediate, stereochemical information on the initial locus of the migrating hydrogen must be lost. Preferred disrotatory opening to **3** for electronic or steric reasons requires migration from the *trans*-methyl group, whereas migration from the *cis*-methyl group would result from conrotatory opening. Stereochemical information is thus of value in elucidating the mechanism of this rearrangement.



In principle the problem could be solved by examining the relative rates of rearrangement of *cis*- and *trans*-2-methylphenylcyclopropane; however, this system is complicated by the fact that the ground-state conformations and energies of the isomers differ significantly[14] and photochemical cis → trans isomerization[4] is so fast that it completely dominates terminal olefin formation.

The problem can be solved by examining the products from photolysis of labeled materials such as **4**. The cis to trans migration ratio is simply the **6**:**7** ratio obtained on photolysis of **4**,[15] and this ratio is amenable to mass spectroscopic analysis; *i.e.*, whereas **6** affords a normal tropylium ion at *m/e* 91, the tropylium ion from **7** (C_7H_6D) appears at *m/e* 92. The **6**:**7** ratio is obtained from the suitably corrected[16] *m/e* 91/92 peak intensity ratio (H/D). As expected geometrical isomerization (*i.e.*, **4** → **5**) is slower in this system than in the 2-methylphenylcyclopropanes and the experimental **6**:**7** ratios from **4** were obtained by determining



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(1) W. von E. Doering and M. Jones, *Tetrahedron Lett.*, 791 (1963).

(2) G. S. Hammond and R. S. Cole, *J. Amer. Chem. Soc.*, **87**, 3256 (1965).

(3) E. W. Valyocsik and P. Sigal, *J. Org. Chem.*, **36**, 66 (1971).

(4) K. Salisbury, *J. Amer. Chem. Soc.*, **94**, 3707 (1972).

(5) G. W. Griffin, *Angew. Chem., Int. Ed. Engl.*, **10**, 537 (1971).

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(10) J. Meinwald and D. A. Seely, *Tetrahedron Lett.*, 3739 (1970).

(11) L. Ulrich, H. J. Hansen, and H. Schmid, *Helv. Chem. Acta*, **53**, 1323 (1970).

(12) R. B. Woodward and R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, **8**, 781 (1969).

(13) R. Hoffmann, *J. Amer. Chem. Soc.*, **90**, 1475 (1968). Hoffmann's calculations suggest that there is no distinct energy minimum in the singlet or triplet excited states of the trimethylene diradical.

(14) J. J. Rocchio, Ph.D. Thesis, University of Maryland, 1970.

(15) Details of the synthesis of the labeled compounds used will be presented elsewhere.

(16) An empirical correction factor was calculated from *m/e* 91/92 ratios obtained from synthetic mixtures of 2-methyl-4-phenyl-1-butene and 2-methyl-4-phenyl-4-d_1-1-butene. Scrambling of deuterium from the methyl and vinyl positions to the benzylic position in the mass spectrum was also considered. Examination of the mass spectra of suitable model compounds showed that this was not a major process. The error limits reflect our estimation of the magnitude of this process.