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A SYNTHON FOR SESQUITERPENES RELATED TO TRICYCLENE

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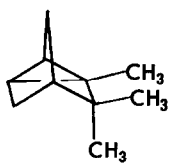
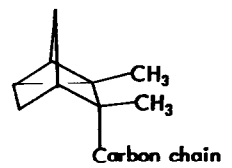
A number of terpenes contain cyclopropane rings.[1,2] That several of these compounds have a common structural feature becomes evident when their structural formulas are drawn from a certain perspective. Thus elements of the tricyclene molecule, I, are clearly present in the terpene skeleta II, III and IV.[3,4,5] But whereas the tricyclene molecule is symmetrical (point group C_s), these terpenes are not. Their structures incorporate five to eight asymmetric carbon atoms, and this presents quite a challenge for total synthesis.



I



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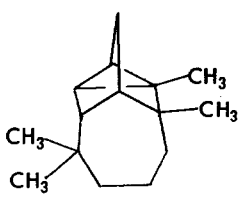

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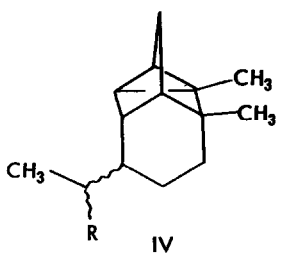

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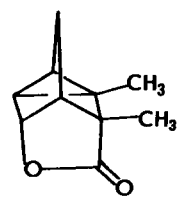
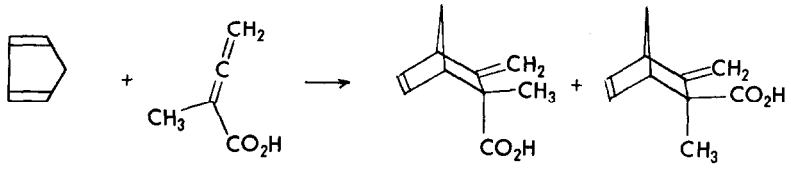


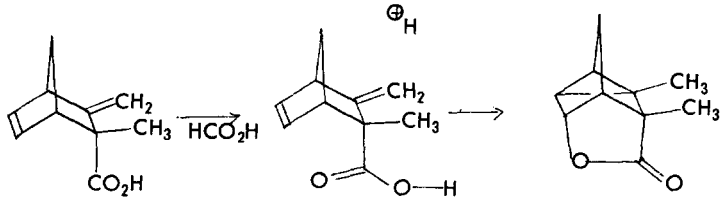
V

In terms of molecular architecture, an intriguing feature of these strained skeleta is the location of most of the asymmetry in the regions related to tricyclene. This suggested an approach to the synthesis of such systems might be directed through a common intermediate, itself related to tricyclene. Other recent synthetic work[6,7,8,9,10,11,12,13,14] in this area is notable for the diversity of approaches leading to some of these systems. We have been working on routes designed to synthesize a common synthetic intermediate which could lead to any of the sesquiterpenes related to tricyclene. We now report the construction of a synthon having such potential. The lactone, V, is an intermediate having all five of the required asymmetric centers present in natural products of the type II. Furthermore, this lactone contains functionality for building an additional ring as required for III and IV.

The attractiveness of lactone V as a general synthon is greatly enhanced because it can be produced in just two steps from available materials having no dissymmetry whatsoever. In the first step, the Diels-Alder reaction of cyclopentadiene and allenic acid VI[17] produces a mixture of bicyclic acids, VII and VIII. In the second step, VII undergoes a novel acid-catalyzed[15] lactonization affording tetracyclic lactone V.



VI VII VIII

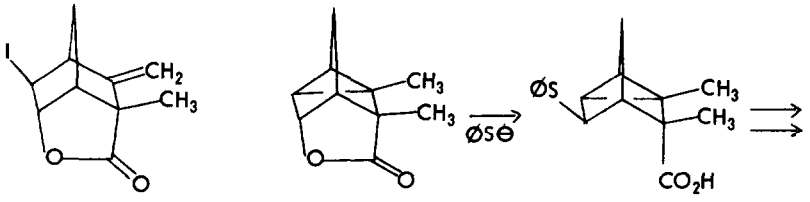


VII V

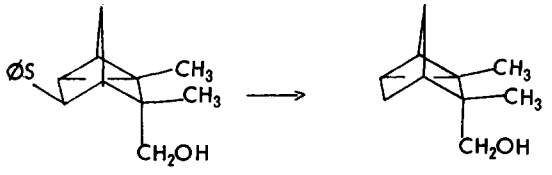
Lactone V is produced in good yield by treating the pure endo acid, VII, with 97% formic acid at 90°. Using the standard iodolactone method,[16] pure endo acid could be separated from the endo-exo mixture of VII and VIII. The NMR spectrum of the endo-exo mixture contained all of the peaks of the pure endo acid showing that no rearrangement had taken place during iodolactonization or zinc regeneration of VII from the iodolactone. The NMR spectrum of the iodolactone was consistent with structure IX, having only one singlet methyl group at high field (δ = 1.22) and only two methylene protons in the vinyl hydrogen region (mult., δ = 5.06). In contrast the lactone V showed two singlet methyl groups at high field (δ = 1.06, 1.16). It was obvious from characteristic IR bands that V and IX were γ-lactones and alternative γ-lactone structures seemed to be ruled out on the basis of the NMR spectra.

The structure and utility of lactone V were confirmed by using it for a total synthesis of teresantalol. Sodium thiophenoxide reacted with lactone V to give, after acidification, the acid X. Esterification by diazomethane, reduction with lithium aluminum hydride to XI, and Raney Nickel desulfurization produced synthetic teresantalol, XII, in racemic form.

We are continuing to study other aspects of the novel lactonization and lactone ring-opening reactions as well as the general utility of V for synthesizing tetracarbocyclic sesquiterpenes of the type III and IV.



IX V X



XI XII

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References

1. R. Soman, J. Sci. Ind. Res. (India) 26, 508 (1967); a review of cyclopropane containing terpenes.
2. J. Simonsen and D. H. R. Barton, "The Terpenes," Vol. III, Cambridge University Press (1952) p. 98, and p. 188.
3. U. R. Nayak and S. Dev, Tetrahedron 24, 4099 (1968).
4. L. Smedman and E. Zavarin, Tetrahedron Letters, 3833 (1968).
5. F. Kido, R. Sakuma, A. Uda, and A. Yoshikoshi, Tetrahedron Letters, 3169 (1969).
6. E. J. Corey and M. F. Semmelhack, J. Am. Chem. Soc. 89, 2755 (1967).
7. E. J. Corey, S. W. Chow, and R. A. Scherrer, J. Am. Chem. Soc. 79, 5773 (1957).
8. S. Y. Kamat, K. K. Chakravarti, and S. C. Bhattacharyya, Tetrahedron 23, 4487 (1967).
9. R. G. Lewis, D. H. Gustafson, and W. F. Erman, Tetrahedron Letters, 401 (1967).
10. J. Colonge, G. Descotes, Y. Bahurel, and A. Menet, Bull. Soc. Chim. France, 374 (1966).
11. J. Simonsen and L. N. Owen, "The Terpenes," Vol. II, Cambridge University Press (1957) p. 382.
12. P. Rani Bai, S. Y. Kamat, B. B. Ghatge, K. K. Chakravarti, and S. C. Bhattacharyya, Tetrahedron 21, 629 (1965).
13. J. E. McMurry, Tetrahedron Letters, 55 (1969).
14. J. E. McMurry, J. Am. Chem. Soc. 90, 6821 (1968).
15. P. von R Schleyer and R. E. O'Connor, 134th Meeting, ACS, Sept. 1958, Abstracts, p. 39P.
16. H. O. House, "Modern Synthetic Reactions," Benjamin, New York (1965) p. 144.
17. H. J. Bestmann and H. Hartung, Chem. Ber. 99, 1198 (1966).