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SELECTIVE CLEAVAGE OF BRIDGED-RING CYCLOPROPYL KETONES

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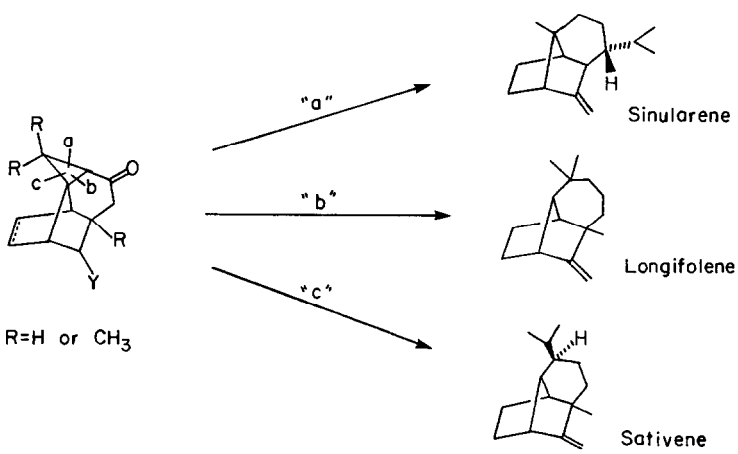
Summary: Reductive ring opening of the tetracyclic cyclopropyl ketones 1 to 3 is described and affords selective entry to the tricyclo[4.4.$0^{1,6}0^{5,9}$]decane (sinularene) and to the tricyclo[5.4.$0^{1,7}.0^{6,10}$]undecene (longifolene) skeletons.

Controlled cleavage of cyclopropane intermediates provides a useful method for the total synthesis of multicyclic natural products and has been successfully employed in the stereo-controlled synthesis of (±)hinesol, (±)epihinesol,[1] (-)-acorenone B and (±)-α-chamigrene.[2] We are developing a general, intramolecular Diels-Alder approach to the tricyclic skeletons represented in nature by sinularene, longifolene and sativene.[3] As illustrated, this strategy requires, after construction of the appropriate tetracyclic precursor, selective cyclopropane bond cleavage (a, b, or c) to afford the desired tricylic ring systems. Reductive opening of the conjugated cyclopropyl ketones 1 to 3 with controlled rupture of bonds "a" or "b" is described.



TABLE

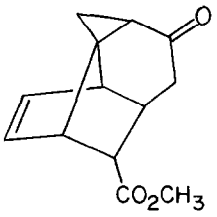
Ketone	Reagent	Products "Sinularene Type"	Products "Longifolene Type"
1	H_2, 10% Pd/C MeOH, 1 atm	4 (95%)	-
1	Li/NH_3, tBuOH (H_2,Pd/C)	7 (70%)	8 (25%)
2	$Zn/ZnCl_2$ MeOH, 23°	5 (25%)	6 (75%)
3	$CrSO_4$ DMF:H_2O (2:1)	9 (20%)	10 (79%)
2	$CrSO_4$ DMF:H_2O (2:1)	-	6 (84%)

It is well established that upon hydrogenolysis cyclopropanes afford as the predominant product, compounds which result from preferential cleavage of the least substituted bond.[4] In accord with this precedent, hydrogenolysis of the cyclopropyl ketone 1[5] occurred under very mild conditions (23°, CH_3OH, 10% Pd/C) to give the tricyclo[4.4.$0^{1,6}$.$0^{5,9}$]decane (sinularene-type) ketone 4 exclusively in 95% isolated yield.

Dissolving metal reductions of unsymmetrical, conjugated cyclopropyl ketones are subject to a variety of influences.[6] Studies by Norin[7] and Dauben[8] with lithium in ammonia have revealed that in general cyclopropane bond rupture occurs preferentially at the bond which overlaps most efficiently with the π orbital of the carbonyl group. Molecular models imply that the least substituted bond "a" should cleave most readily although a mixture of products is likely. Consistent with this, lithium:ammonia reduction of 1 afforded 70% of the sinularene and 25% of the longifolene-type products, 7 and 8. To facilitate the analysis the reduction was carried to completion and the resulting diols hydrogenated and separated.

Solvent and counter ions often influence the course of cyclopropyl ketone reductions.[6] Treatment of 2[9] with zinc/zinc chloride in methanol[10] at room temperature afforded 75% of the bridged cycloheptanone 6 and 25% of 5. The dominance of the longifolene product suggests that an intermediate salt of type 11 (bonding and charges not specified), in which the double bond plays an influence, may be involved.

Solutions containing chromium(II) salts reduce conjugated enones under certain conditions[11] but the reactions of cyclopropyl ketones under these conditions do not appear to have been investigated. Treatment of 3[9] with $CrSO_4$ in DMF:H_2O (2:1) gave a mixture of 9 and 10 in 20% and 79% yield respectively, however exposure of ketone 2 to these conditions afforded the longifolene-type ketone 6 selectively. Clearly the double bond exerts a beneficial influence directing cleavage to the most substituted bond "b". Cyclopropyl methyl ketone reacted very



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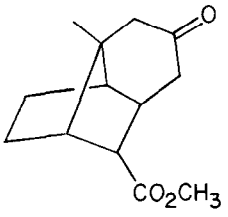

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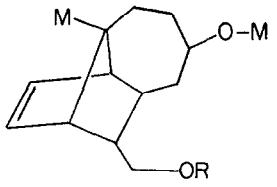

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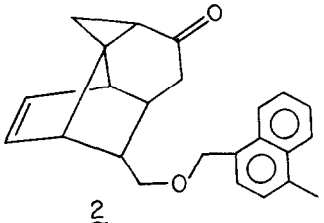

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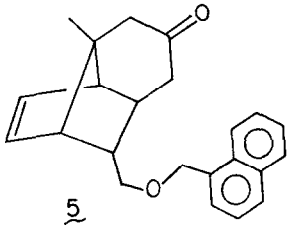

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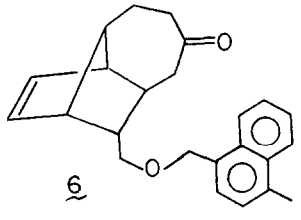

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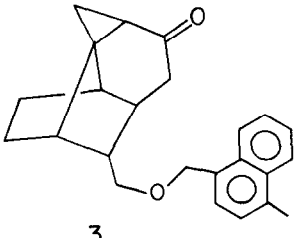

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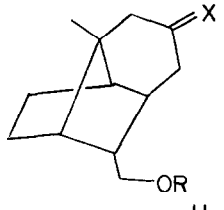
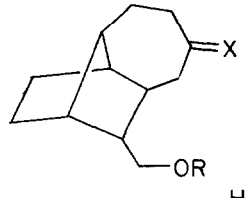


7 R=H, X= 

9 R= 

, X=O



8 R=H, X= 

10 R= 

, X=O

sluggishly, further establishing the importance of the double bond, and a more active form of Cr(II) (possibly as a diamine complex) is required for chromium to be generally useful for cyclopropane cleavage. In keeping with mechanistic studies by House and Kinlock[11] an intermediate species such as 11, in which the solvated chromium at the bridgehead is favourably disposed for interaction with the π system of the olefin, accounts for our results. In a related case, recent calculations[12] have indicated that the lithium in 7-lithionorbornadiene is strongly coordinated to the neighbouring π bond.

As summarized in the Table these results allow controlled cyclopropane ring cleavage to either the tricyclo[4.4.0^{1,6}.0^{5,9}]decane (sinularene) skeleton or the tricyclo[5.4.0^{1,7}.0^{6,10}]-undecene (longifolene) ring system. These principles are currently being extended to an asymmetric synthesis of longifolene from ascorbic acid and the total synthesis of sinularene and 12-acetoxysinularene.

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REFERENCES AND NOTES

1. J. Lafontaine, M. Mongrain, M. Sergent-Guay, L. Ruest, and P. Deslongchamps, Can. J. Chem. 58, 2460 (1980).
2. J.D. White, J.F. Ruppert, M.A. Avery, S. Torii, and J. Nokami, J. Am. Chem. Soc., 103, 1813 (1981).
3. S.K. Attah-Poku, G. Gallacher, A.S. Ng, L.E.B. Taylor, S.J. Alward, and A.G. Fallis, Tetrahedron Lett., 24, 0000 (1983) preceeding communication.
4. C.W. Woodworth, V. Buss, and P.V.R. Schleyer, Chem. Commun., 569 (1968).
5. Ketone 1 was prepared by Jones oxidation (88%) of the corresponding alcohol.[3]
6. S.W. Staley in Selective Organic Transformations, Ed. B.S. Thyagarajan, Vol. 2, Wiley-Interscience New York, 1972, p 309.
7. T. Norin, Acta Chem. Scand., 19, 1289 (1965).
8. W.G. Dauben and E.J. Deviny, J. Org. Chem., 31, 3794 (1966); W.G. Dauben, and R.W. Wolf, J. Org. Chem., 35, 374 (1970).
9. Ketone 2 was synthesized from the diol obtained by $LiAlH_4$ reduction of the hydroxy-ester adduct[3] followed by selective protection of the primary alcohol function (NaH,  , THF, 23°) and oxidation.
   Ketone 3 was prepared from the same hydroxy-ether intermediate by hydrogenation and Jones oxidation.
10. Cf., J. Dekker, F.J.C. Martins, and J.A. Kruger, Tetrahedron Lett., 2489 (1975); W.S. Murphy and S. Wattanasin, Tetrahedron Lett., 22, 695 (1981).
11. H.O. House and E.F. Kinlock, J. Org. Chem., 39, 1173 (1974).
12. S. Nagase and K.N. Houk, Tetrahedron Lett., 23, 19 (1982).

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