Tetrahedron Letters No. 10, pp 779 - 782, 1976. Pergamon Press. Printed in Great Britain.

SYNTHESIS OF AN OPTICALLY ACTIVE CYCLIC ALLENONE[1]

Jean-Claude Damiano, Jean-Louis Luche and Pierre Crabbé*

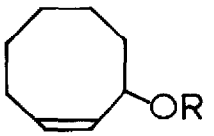
C.E.R.M.O., Université Scientifique et Médicale

38041 Grenoble, France

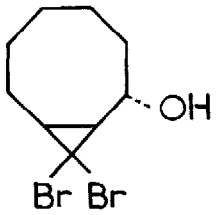
(Received in UK 12 January 1975; accepted for publication 29 January 1976)

Little information is available on the synthesis and properties of chiral allenic ketones in general, in particular cyclic allenones[2,3]. To our knowledge no optically active cyclic allenone has been described, in which the chirality is given by the sole allene unit. In this letter we wish to mention the preparation of the allenone (6) in the optically active form and discuss some of its properties.

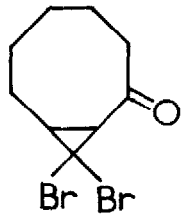
Base hydrolysis of the allylic acetate (1a)[4], obtained by mercuric acetate oxidation of cis-cyclooctene, gave the corresponding alcohol (1b). Dibromocarbene addition[5] afforded the crystalline trans-dibromocyclopropyl alcohol (2) [m.p. 87° ; ν 3450 cm^{-1} (hydroxyl) ; δ 3.6 p.p.m. (base H of hydroxyl) ; m/e 300 (M^+)][6] in 63% yield. Brown oxidation[7] of the alcohol (2) furnished quantitatively the ketone (3), which provided the corresponding cycloethyleneketal (4a) by treatment with ethyleneglycol in the presence of p-toluenesulphonic acid (PTS) in refluxing dichloromethane. Reaction of the dibromocyclopropane derivative (4a) with 1 equiv. of methyllithium, in ether solution at -45°, produced the allenyl ketal (5a) in 70% yield. The reaction conditions are critical, since all experiments performed at higher temperatures gave substitution of a bromide in compound (4a) by a methyl group.



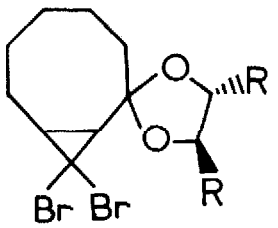
1 a, R = Ac
b, R = H



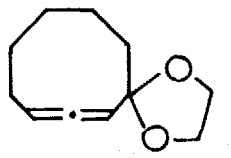
2



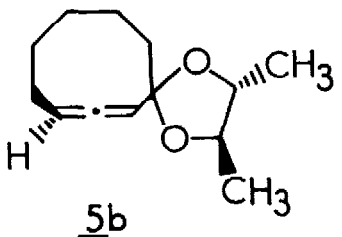
3



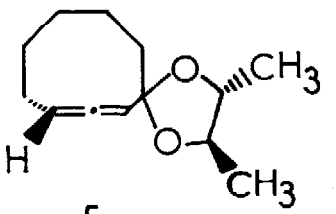
4 a, R = H
b, R = CH_3



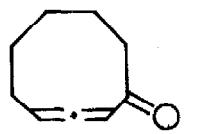
5a



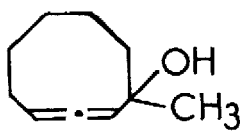
5b



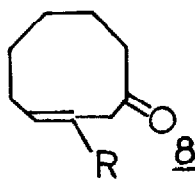
5c



6



7



8a, R = CH_3
b, R = nC_4H_9

While hydrolysis of the ketal group of the intermediate (5a) could be performed under mild conditions, the usual reagents (e.g. oxalic acid, acetic acid, PTS, magnesium sulphate, etc.) did not give satisfactory results, due to the apparent degradation of the allenone upon formation. However, hydrolysis of ketal (5a) with a trace of methanesulphonic acid in acetone solution at room temperature for 15 min. did afford the cyclic allenone (6) [oil ; ν 1940 (allene), 1680 cm^{-1} (carbonyl) ; λ_{max}^{EtOH} 229,298 nm (ε : 2350, 242) ; δ 5,6 p.p.m. (m, 2 vinylic H) ; m/e 136 (M^+)], purified by thin layer chromatography (ca. 40%).

On the one hand, reaction of the ketone (6) with methyllithium in ether at -10°, furnished a mixture of tertiary alcohols (7) in 34% yield by 1,2-addition to the carbonyl. On the other hand, treatment of the allenone (6) with 1,2 equiv. of lithium dimethylcopper at -5°, in ether solution, provided the 1,4-addition compound (8a) in 85% yield. Similarly, addition of lithium dibutylcopper gave compound (8b) in 56%.

The optically active allenone (6) was prepared as follows. Treatment of ketone (3) with (-)-2,3-butanediol in benzene solution in the presence of PTS as a catalyst afforded the corresponding ketal (4b). This was treated with methyllithium in ether solution at -90° to provide the allenic ketals (5b) and (5c) in 75% yield. GLC analysis[8] indicated a 54-46% diastereomeric mixture, which could not be resolved by the usual techniques (preparative T.L.C. or G.L.C.). Acid hydrolysis afforded the optically active allenone (6) [oil ; $[\alpha]_D$ + 1,25° (dioxane) ; C.D. $\Delta\varepsilon_{255}$ + 5,45 ; $[\theta]_{255}$ + 18.000 ; $\Delta\varepsilon_{297}$ + 0,550 ; $[\theta]_{297}$ + 1.900] (optical purity ca. 8%), which rapidly lost optical activity in dioxane solution at room temperature.

Work is in progress aimed at the generalization of the above observations and their implications in organic synthesis.

References

1. Contribution N°9 from the Laboratoire de Chimie Organique, CERMO. For N°8, see : P. Crabbé, "Prostaglandin Research", Academic Press, New York, in press.
2. Th. F. Rutledge, "Acetylenes and Allenes", Reinhold Publ., New York, N.Y. (1969).
3. Inter alia : a. S.W. Russell and B.C.L. Weedon, Chem. Comm., 85 (1969) ; b. R. Gouffignal and M. Gaudemar, Bull. Soc. Chim. France, 3218 (1969) ; c. P. Crabbé and E. Velarde, Chem. Comm., 241 (1972) ; d. P.J. Garratt, K.C. Nicolaou and F. Sondheimer, J. Org. Chem., 15, 2715 (1973) ; e. M. Santelli and M. Bertrand, Bull. Soc. Chim. France, 2326 (1973) ; f. R.G. Carlson, D.E. Henton and W.W. Cox, First Chemical Congress of the North American Continent, Abstract n°136, Organic Section, Mexico-City, December 1975.
4. A.C. Cope, M.R. Kinter and R.T. Teller, J. Amer. Chem. Soc., 76, 2757 (1954)
5. M. Makosza and M. Wawryniewicz, Tetrahedron Letters, 4659 (1969).
6. All new compounds gave satisfactory analyses and/or mass spectra. I.R. and N.M.R. properties are consistent with their formulation.
7. H.C. Brown, C.P. Garg, J. Amer. Chem. Soc., 83, 2952 (1961).
8. GLC, Carlo Erba Fractovap 2100, Carbowax Column 20 M 10%, 130° ; 12 ml N_2 per minute.