Tetrahedron Letters No. 19, pp 1683 - 1686, 1973. Pergamon Press. Printed in Great Britain.

MECHANISM, STEREOSELECTIVITY AND GENERALITY OF A NOVEL CYCLOPROPANE FORMATION[1]

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(Received in UK 20 March 1973; accepted for publication 28 March 1973)

In our previous communication[2], we just mentioned that the epoxide (1) on interaction with sodium diethyl methylmalonate (2) under refluxing benzene (30 hr.) furnishes the cyclopropane derivative (3). We now wish to report the generality, mechanism and stereoselectivity of this novel reaction.

The simpler epoxide (4)[3] also afforded under the above condition the lactone (20)[4] (7%) and a cyclopropane ester characterised as the crystalline acid+(5) (47%), m.p. 131-132°; the methyl ester (6) had b.p. 130°/2 mm. Sodium-liquid ammonia reductive cleavage of the conjugated cyclopropane bond in (5) provided the acid (7) as a mixture of diastereomers from which a pure isomer[5] m.p. 116-117° could be isolated.

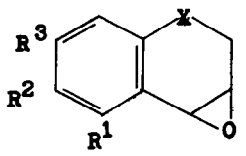
The epoxide (8)‡ prepared from 8-bromo-7-methoxy-6-methyl-1-tetralone[6], on similar treatment with (2) furnished an ester which on hydrolysis gave the crystalline cyclopropane derivative (9) (37%), m.p. 182-184°. Na-NH_3 reduction of (9) afforded a diastereomeric mixture of (10); repeated crystallisations finally gave a pure isomer, m.p. 125-126°.

+ All new compounds gave satisfactory microanalytical and spectral data.

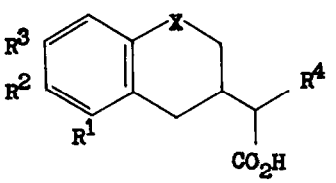
‡ The preparation of this epoxide will be reported in the full paper.

Similar treatment of the epoxide (11)[7] with (2) gave in 64% yield the cyclopropyl ester (12), b.p. 110-115° (bath)/0.3 mm ; and this on hydrolysis furnished the crystalline acid (13), m.p. 125-126°; methyl ester (14) had m.p. 47-50°. Metal-ammonia reduction of (13) afforded (15) as a mixture; a pure isomer had m.p. 153-154°.

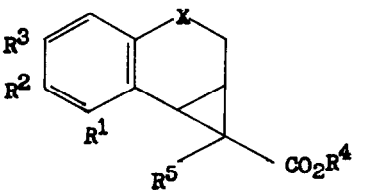
The interaction of (4) with the more sterically hindered carbanion derived from diethyl isopropylmalonate provided a liquid ester ; and this on hydrolysis furnished the crystalline acid (16) (26%), m.p. 158-159°, methyl ester (17) had m.p. 68-70°. Sodium-liquid ammonia reduction of (16) gave (18) initially as a mixture ; a pure isomer had m.p. 104-105°. Under the same reaction condition, the epoxide (4) was practically recovered unchanged when treated with the anion of diethyl phenylmalonate.



	X	R^1	R^2	R^3
(1)	CH_2	Me	OMe	H
(4)	CH_2	H	H	H
(8)	CH_2	Br	OMe	Me
(11)	O	H	H	H

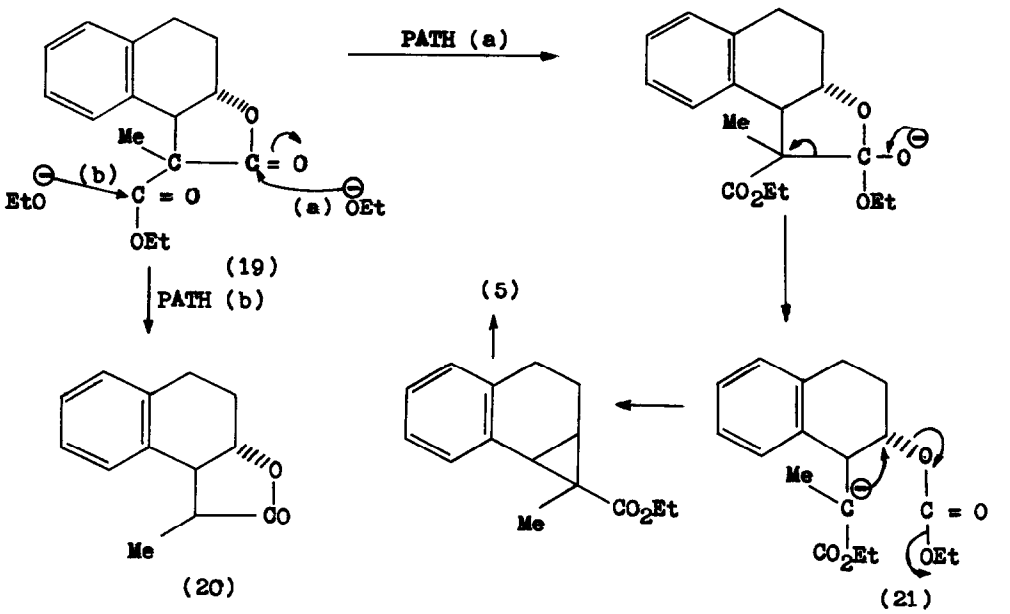


	X	R^1	R^2	R^3	R^4
(7)	CH_2	H	H	H	Me
(10)	CH_2	Br	OMe	Me	Me
(15)	O	H	H	H	Me
(18)	CH_2	H	H	H	$CH(Me)_2$



	X	R^1	R^2	R^3	R^4	R^5
(3)	CH_2	Me	OMe	H	Et	Me
(5)	CH_2	H	H	H	H	Me
(6)	CH_2	H	H	H	Me	Me
(9)	CH_2	Br	OMe	Me	H	Me
(12)	O	H	H	H	Et	Me
(13)	O	H	H	H	H	Me
(14)	O	H	H	H	Me	Me
(16)	CH_2	H	H	H	H	$CH(Me)_2$
(17)	CH_2	H	H	H	Me	$CH(Me)_2$

Lactonic ester (19) was considered to be the possible intermediate for the novel cyclopropane formation described above. trans-2-Bromo-1,2,3,4-tetrahydronaphthalene-1-ol[3] on treatment with two equivalents of (2) under refluxing benzene (30 hr.) gave a separable mixture of the lactone (20)[4](40%) and the above lactonic ester (19) (38%) as an oil. This ester was proved by n.m.r. to be an epimeric mixture at the asymmetric centre carrying the methyl and carbethoxylic groups. The lactonic ester (mixture) thus obtained on refluxing (27 hr.) under benzene with dry sodium ethoxide afforded the lactone (20) (16%) and a liquid ester (31%) b.p. 140-145°(bath)/1 mm. This ester on alkaline hydrolysis furnished the same cyclopropane acid (5) mentioned above. The above experiments lend support to the following mechanism proposed for the novel cyclopropane formation.



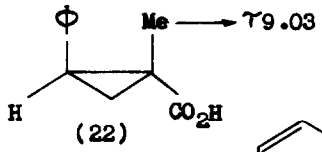
It is significant to note that in all the cases mentioned above, one single cyclopropyl carboxylic acid could be isolated. The n.m.r. signals for the methyl groups attached to the cyclopropane ring carbon are informative (Table 1). Comparing the methyl signals with those of the known cyclopropane derivatives[8] (22) and (23), it is reasonable to predict that the methyl groups are shielded

by the phenyl ring as shown in the stereostructure (24). The steric requirement of the carbanion (21) in the transition state is possibly the reason for the stereoselective formation of the cyclopropyl compounds described above.

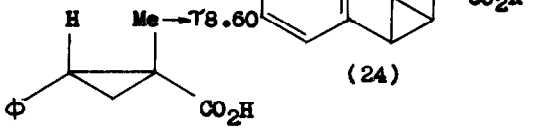
TABLE 1

N.m.r. signal for Cyclopropyl methyl

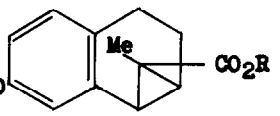
Compound	$\tau(CDCl_3)$
(3)	9.21
(5)	9.05
(6)	9.12
(9)	9.12



(22)



(23)



(24)

In contrast to the epoxide stated above, cyclohexene oxide and 3,4-epoxy-1,2-benzocyclohept-1-ene[9] failed to provide any cyclopropane derivative.

As far as we know the formation of the cyclopropane compounds by nucleophilic opening-up of epoxides in nonpolar aprotic solvent has not been reported earlier in the literature.

We thank C.S.I.R., New Delhi, for Research Fellowships (to R.M. and B.B.), and Dr. M.M.Dhar for n.m.r. spectra.

1. Presented in part at the 8th International Symposium on the Chemistry of Natural Products, New Delhi, India, Feb. 6-12, 1972.

2. A. Chatterjee and D. Banerjee, Tetrahedron Letters, 1969, 4559.

3. Straus and Rohrbacher, Ber, 1921, 54, 40.

4. E.E.van Tamelen, G. Van Zyl and G.D.Zuidema, J.Amer.Chem.Soc., 1950, 72, 488.

5. A. Chatterjee, S. Banerjee, A. K. Sarkar and B. G. Hazra, J. Chem. Soc. (C), 1971, 661.

6. A. Chatterjee and D. Banerjee, J.Chem.Soc. (C), 1971, 1859.

7. W. D. Cotterill, J. Cottam and R. Livingstone, J. Chem. Soc. (C), 1970, 1006.

8. C.H.DePuy, F.W. Breitheil and K.R. DeBruin, J.Amer. Chem. Soc., 1966, 88, 3347.

9. T. A. Crabb and K. Schofield, J. Chem. Soc., 1958, 4280.