CHEMISTRY LETTERS, pp. 337-340, 1982. © The Chemical Society of Japan 1982

FORMATION OF CYCLOPROPANE DERIVATIVES IN THE BLAISE REARRANGEMENT

Yukio ABE and Tadashi SUEHIRO

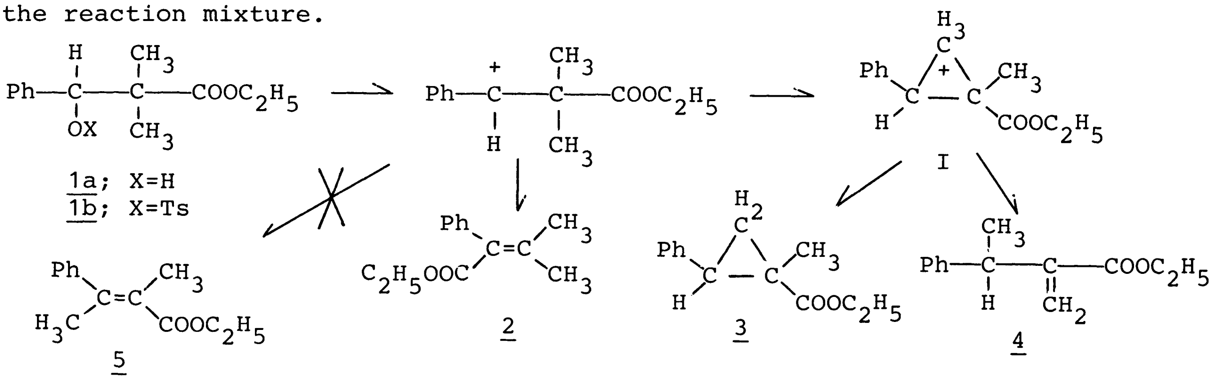
Chemistry Department, Faculty of Sciences, Gakushuin University
Mejiro, Toshimaku, Tokyo 171

On heating tosylates of ethyl 2-alkyl-2-methyl-3-hydroxy-3-phenylpropanoate (R=Me, 1b; R=Et, 6) in o-dichlorobenzene at 170 °C, ethyl 1-methyl-2-phenyl- and 1,2-dimethyl-3-phenylcyclopropanecarboxylates, 3, and 8, were formed in both 5% yield, respectively, whereas the alkyl migration products, ethyl 3-alkyl-2-methyl-3-phenylpropenoates, were not produced. The mode of the reaction of the methyl group with the cationic carbon was described.

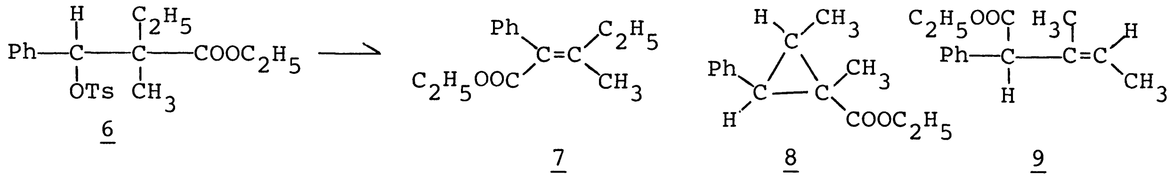
In the Blaise rearrangement ethyl 2,2-dimethyl-3-hydroxy-3-phenylpropanoate (1a, X=H) was transformed into ethyl 3-methyl-2-phenyl-2-butenoate (2) via the rearrangement of the ethoxycarbonyl group, when it was heated in benzene at 80 °C in the presence of phosphor pentoxide.[1)] Because in this rearrangement the migration of the electron-withdrawing ethoxycarbonyl group to the cationic carbon proceeded in preference to the migration of the electron-releasing methyl group, much attentions were paied on the migration aptitude of the ethoxycarbonyl group and recently the ring opening reaction of glycidic esters in the presence of Lewis acid were reported comfirming the facile movement of the ester group.[2)]

To make clear the nature of the nucleophilic migration of substituent groups, we took the Blaise rearrangement in homogenous conditions using the tosylate of 1a, (1b, X=Ts), and we made again certain of the migration of the ethoxycarbonyl group to the cationic center, and furthermore we found that the methyl group reacted with cationic carbon to yield a cyclopropane compound, whereas the reaction of the methyl group leading to a cinnamate derivative was completely suppressed.

On heating in o-dichlorobenzene at 170 °C, 1b afforded 2 as the main product (58%) together with ethyl 1-methyl-2-phenylcyclopropanecarboxylate (3) and ethyl 2-methylene-3-phenylbutanoate (4), in 5 and 4% yields, respectively. Ethyl 2-methyl-3-phenyl-2-butenoate (5), however, was not found in the reaction mixture.



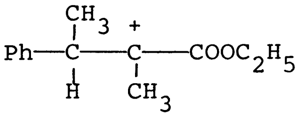
The formation of the cyclopropane compound seems to be general in the Blaise rearrangement of esters because ethyl 2-ethyl-2-methyl-3-phenyl-3-p-toluenesulfonyloxypropanoate (6) gave ethyl 1,2-dimethyl-3-phenylcyclopropanecarboxylate (8) in a 5% yield under the same reaction conditions as for 1b. The ethyl group is more reactive than the methyl group in the formation of a cyclopropane ring. The main products derived from 6 were 7 and 9 (in 30 and 21% yields) which were formed by the migration of the ethoxycarbonyl group to the cationic carbon, followed by deprotonation.[3)] The alkyl migration products such as ethyl 2-methyl-3-phenyl-2-pentenoate and ethyl 2-ethyl-3-phenyl-2-butenoate, however, were not found in the reaction mixture.



All the products were isolated from the reaction mixtures using gas chromatography and high speed liquid chromatography, analyzed by i.r., n.m.r., and mass spectrometry, and identified by comparison with the authentic samples prepared by the standard methods.[4)]

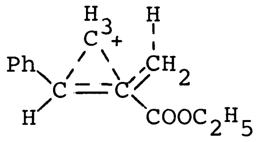
The formation of 3 and 8 proves without doubt the intermediacy of cyclopropane acidium cation (I) during the displacement of the methyl group in the Blaise rearrangement. Although the cyclopropane structures were often proposed as the intermediate in the rearrangement reactions, the isolation of the cyclopropane derivatives from the reaction mixture was rare.

The methylene compound 4 was formed very likely also from the intermediate I. If 1,2-dimethyl-1-ethoxycarbonyl-2-phenylethyl cation II were the intermediate leading to 4, then the methyl migration product 5 could also be produced in an appreciable amount from 1b in the Blaise rearrangement, because the compound 4 was accompanied by 5 in a mole ratio 4:5 = 1:1 in the standard preparation of 4 over ethyl 2,3-dimethyl-2-hydroxy-3-phenylpropanoate4c) and because 5 did not change to 4 and remained almost unaltered on heating with toluenesulfonic acid.4g) A proton was eliminated only from the methyl group beta to the ethoxycarbonyl group and not from the methyne group alpha to the phenyl group during the reaction of the methyl with the carbocation. This implies that the reaction should proceed in a way other than that via the route over II. It is adequate to the reaction to suppose the intermediate I, to which a canonical structure, olefin - methyl cation pi-complex, III, contributes.



$Ph-\underset{H}{\overset{CH_3}{C}}-\underset{CH_3}{\overset{+}{C}}-COOC_2H_5$

II



III

The formation of 3 and 4 but not of 5 is the characteristic feature of the manner of the reaction of the methyl group with the cationic carbon in the Blaise rearrangement of 1b.

The authers are very grateful to Prof. M. Goto and Dr. K. Sugiura of Gakushuin University for mass spectrometric measurements.

References

1) E. E. Blaise and A. Courtot, Compt. rend., 141, 724 (1905); Y. Yokoyama and Y. Yukawa, Nippon Kagaku Zasshi, 82, 259 (1961).

2) J. Kagan, D. A. Agdeppa, Jr., S. P. Singh, D. A. Mayers, C. Boyajian, C. Poorker, and B. E. Firth, J. Am. Chem. Soc., 98, 4581 (1976); R. D. Bach and J. M. Domagala, Tetrahedron Lett., 1976, 4025.

3) When 7 was heated in dichlorobenzene in the presence of toluenesulfonic acid, 7 was isomerized to 9 until an equibrium with a mole ratio 7:9 = 7:2 was attained. More 9 was formed in the reaction of 6.

4) a) 2: The parent peak M^+/e was 204. The compound was obtained by the Wittig reaction between ethyl benzoylformate and isopropyltriphenylphosphonium iodide with butyllithium; bp 114-122 °C/8 Torr.

b) 3: N.m.r. of the compound 3 indicated a cyclopropane ring structure; δ 7.23 (s, 5H), 4.17 (q, 2H, J=7 Hz), 2.75 (m, 1H), 1.63 (m, 2H), 1.28 (t, 3H, J=7 Hz), 0.97 (s, 3H). Based on the chemical shift of the methyl proton of cis- and trans-1-methyl-2-phenylcyclopropanecarboxylic acid, 3 has probably the cis configuration: C. H. DePuy, F. W. Breitbeil, and K. R. DeBruin, J. Am. Chem. Soc., 88, 3347 (1966). The synthetic route of 3, heating an ether solution of diazomethane and ethyl E-2-methyl-3-phenylpropenoate followed by the separation from a by-product 5, support this conclusion.

c) 4: N.m.r. of 4 suggested an oxo methylene structure; δ 7.22 (s, 5H), 6.26 (s, 1H), 5.57 (s, 1H), 4.10 (q, 2H, J=7 Hz), 4.02 (q, 1H, J=7 Hz), 1.18 (t, 3H, J=7 Hz). The authentic compound of 4 was prepared by the reaction between ethyl pyruvate and a Grignard reagent from α-bromoethylbenzene, followed by dehydration and by purification to be free from by-product 5.

d) 7: The parent peak M^+/e was 218. 7 was a 1:1 mixture of E- and Z-isomers. The authentic compound was obtained as a mixture, E:Z =1:1, by the reaction between ethyl benzoylformate and sec-butyltriphenylphosphonium iodide with butyllithium; bp 135 °C/7 Torr.

e) 8: N.m.r. δ 7.24 (s, 5H), 4.18 (q, 2H, J=7 Hz), 2.75 (d, 3H, J=6 Hz), 1.88 (m, 1H), 1.28 (t, 3H, J=7 Hz), 1.07 (s, 3H), 1.05 (d, 3H, J=6 Hz). The authentic compound was obtained as the minor product of the two isomeric cyclopropane derivatives by heating a mixture of diazoethane and ethyl E-2-methyl-3-phenylpropenoate.

f) 9: The parent peak M^+/e was 218. The compound was prepared by the Reformatsky reaction between ethyl chlorophenylacetate and ethyl methyl ketone in a poor yield; n.m.r. δ 7.27 (s, 5H), 5.38 (m, 1H), 4.30 (s, 1H), 4.18 (q, 2H, J=7 Hz), 1.64 (d, 3H), 1.62 (d, 3H), 1.24 (t, 3H, J=7 Hz).

g) On heating Z-5 in dichlorobenzene in the presence of toluenesulfonic acid, Z-5 decomposed slowly into 2,3-dimethylindenone; L. M. Jackman and J. W. Lown, J. Chem. Soc., 1962, 3776. E-5 was stable under these conditions.

(Received October 28, 1981)