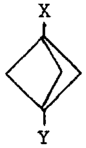
Tetrahedron Letters No. 39, pp 3411 - 3412, 1977. Pergamon Press. Printed in Great Britain.

SYNTHESIS OF 1,3-DISUBSTITUTED BICYCLO[1.1.1]PENTANES

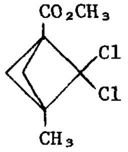
Douglas E. Applequist* and James W. Wheeler
Department of Chemistry, University of Illinois, Urbana, Illinois 61801

(Received in USA 29 July 1977; received in UK for publication 9 August 1977)

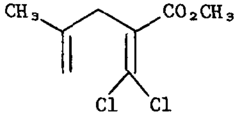
For the purpose of physical studies, a variety of 1,3-disubstituted bicyclo[1.1.1]pentanes (1) were required. Although there are now numerous reports of the formation of bicyclo[1.1.1]pentanes (1), few of these provide useful yields, and there appears to be no satisfactory entry to the 1,3-disubstituted system. The 1,3-dichloro compound (1, X = Y = Cl) can be made in very low yield from the parent hydrocarbon, which is itself still not obtainable in quantity (2).



1



2

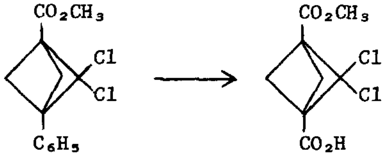


3

We wish to report that certain 1,3-disubstituted bicyclobutanes add dichlorocarbene to give synthetically useful yields of 1,3-disubstituted bicyclo[1.1.1]pentanes. Previous attempts by others had not been promising: Wiberg (3) reported only acyclic products from addition of dichlorocarbene to methyl bicyclobutane-1-carboxylate. Hall (4) reported only a three percent yield of bicyclopentane 2 from methyl 3-methylbicyclobutane-1-carboxylate. We repeated the latter reaction with a different dichlorocarbene source (5) and obtained the same product (from spectral identity) in 19 percent yield, but concluded from a 100 MHz nmr spectrum that the compound was actually 3 rather than 2. A two proton signal at δ 4.73 in the 60 MHz spectrum (4), attributable previously to two of the ring hydrogens, split at 100 MHz into two distinct multiplets at δ 4.69 and 4.76 (attributed now to the vinyl hydrogens in 3). The compound also showed unsaturation in the Raman spectrum at 1620 and 1670 cm^{-1}; rapidly decolorized bromine in carbon tetrachloride; and had uv absorptions at 276 nm (log ε 3.65) and 310.5 nm (log ε 1.64). However, from the reaction mixture containing 3 was isolated in 27 percent yield an isomer of 3 to which we assign structure 2. The nmr spectrum showed singlets at δ 1.30 and 3.75 for the two methyl groups and broad two-proton singlets at δ 2.05 and 2.60 for the ring methylenes. There were no olefinic peaks in the Raman spectrum and the compound did not decolorize bromine.

Reduction of 2 with tri-n-butyltin hydride and azoisobutyronitrile at 130° followed by an aqueous workup gave 70 percent of 3-methylbicyclo[1.1.1]pentanecarboxylic acid (1, X = CO_2H, Y = CH_3), mp 122-122.5°; nmr ($CDCl_3$) δ 1.17, s, 3H; 1.93, s, 6H; 10.30, s, 1H.

Even more useful was the addition of dichlorocarbene under the same conditions (5) to methyl 3-phenylbicyclobutane-1-carboxylate, which gave the corresponding bicyclopentane 4 in 46 percent yield, mp 80-82°, nmr ($CDCl_3$) δ 2.4, s, 2H; 3.1, s, 2H; 3.8, s, 3H; and 7.4, s, 5H.



4 5

Oxidation of 4 with ruthenium dioxide and sodium hypochlorite in water-carbon tetrachloride (6) gave the carboxylic acid 5 in 80 percent yield, mp 104-5°, nmr (CDCl) δ 2.25, d, J = 1, 2H; 3.1, d, J = 1, 2H; 3.83, s, 3H; and 8.9, broad, 1H. Reduction of 5 with tri-*n*-butyltin hydride led to a 47 percent yield of bicyclo[1.1.1]pentane-1,3-dicarboxylic acid (1, X = Y = CO_2H), mp 250°dec, nmr (acetone $-d_6$) δ 2.28, s, 6H; 8.18, s, 2H. A sublimed analytical sample sublimed without melting at 260-295°.

Dichlorocarbene was also successfully added to 1-cyano-3-phenylbicyclobutane (15 percent yield), but could not, in our hands, be added to dimethyl bicyclobutane-1,3-dicarboxylate or 1,3-dicyanobicyclobutane.

References

(1) (a) K. B. Wiberg, D. S. Connor, and G. M. Lampman, *Tetrahedron Lett.*, 531 (1964); (b) K. B. Wiberg and D. S. Connor, *J. Am. Chem. Soc.*, *88*, 4437 (1966); (c) S. Masamune, *Tetrahedron Lett.*, 945 (1965); (d) R. Srinivasan and K. H. Carlough, *J. Am. Chem. Soc.*, *89*, 4932 (1967); (e) J. Meinwald, W. Szkrybalo, and D. R. Dimmel, *Tetrahedron Lett.*, 731 (1967); (f) T. W. Gibson and W. F. Erman, *J. Org. Chem.*, *37*, 1148 (1972); (g) T. W. Gibson, *J. Org. Chem.*, *39*, 845 (1974); (h) A. Padwa and E. Alexander, *J. Am. Chem. Soc.*, *89*, 6376 (1967); (i) F. T. Bond, Abstracts of Papers, 159th National Meeting of the American Chemical Society, Division of Petroleum Chemistry, Feb. 23-27, 1970, Houston, Texas, Paper 13; (j) E. C. Alexander and J. A. Uliana, *J. Am. Chem. Soc.*, *96*, 5644 (1974); (k) F. T. Bond and C.-Y. Ho, *J. Org. Chem.*, *41*, 1421 (1976).

(2) K. B. Wiberg and V. Z. Williams, Jr., *J. Org. Chem.*, *35*, 369 (1970).

(3) K. B. Wiberg, G. M. Lampman, R. P. Ciula, D. S. Connor, P. Schertler, and J. Lavanish, *Tetrahedron*, *21*, 2749 (1965).

(4) H. K. Hall, Jr., C. D. Smith, E. P. Blanchard, Jr., S. C. Cherkofsky, and J. B. Sieja, *J. Am. Chem. Soc.*, *93*, 121 (1971).

(5) L. F. Fieser and D. H. Sachs, *J. Org. Chem.*, *29*, 1113 (1964).

(6) D. G. Lee and M. van den Engh, in "Oxidation in Organic Chemistry, Part B," edited by W. S. Trahanovsky, Academic Press, New York, N.Y., 1973, pp. 177-228.