Tetrahedron Letters No.46, pp. 5685-5689, 1966. Pergamon Press Ltd.
Printed in Great Britain.

SYNTHESIS OF 4-CHLOROBICYCLO[2.2.0]HEXANE-1-CARBOXYLIC ACID

Kirby V. Scherer, Jr.
Department of Chemistry, University of California,
Berkeley, California 94720

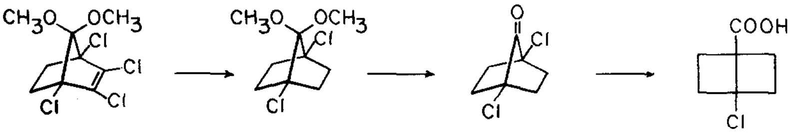
(Received 29 August 1966)

Most previous syntheses of the bicyclo[2.2.0]hexane system have been photochemical, and have not made available derivatives of the parent molecule bearing only functional substituents at the bridgehead positions (1). We (2) and others (3) have recently used the Favorskii rearrangement to make bicyclo[2.2.0]hexane-1-carboxylates fused within more complex structures, and so its extension to the parent system seemed feasible. We report here a convenient preparation of the title compound; studies of its further transformations, as well as extension of this synthetic approach to related molecules, are in progress.

The Diels-Alder adduct, II (4) of ethylene and 5,5-dimethoxytetrachlorocyclopentadiene, I (5), was hydrogenated in a Parr apparatus over 5% palladium-charcoal in ethanol containing excess triethylamine; three (or slightly more*) moles of hydrogen were consumed, and after work-up and recrystallization from methanol at -10°, 1,4-dichloro-7,7-dimethoxybicyclo[2.2.1]heptane, III, was obtained in

---

*Usually a little more than three moles of hydrogen was consumed, probably by close-boiling impurities present in II.



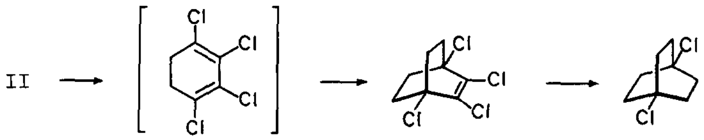
II III IV V

93% yield. The nmr spectrum of III in CCl_4 displayed a sharp singlet at 6.40 τ (6H, $-OCH_3$) and a centro-symmetric multiplet at 7.5-8.4 τ (8H). A sample prepared for analysis melted at 95.0-95.6° (calc. for $C_9H_{14}Cl_2O_2$: C 48.02, H 6.27, Cl 31.50; found: C 47.85, H 6.24, Cl 31.52). We infer that II is adsorbed on the catalyst surface from the *endo* side, since the (presumably *endo*) adduct of I and vinyl acetate is not reduced under these conditions. The observation of Wilcox and Zajacek (6) that reduction of 1,2,3,4-tetrachlorobicyclo[2.2.1]heptene is blocked by a 7-*syn* chlorine is striking, since its *endo* face is as accessible as that of II, and somewhat less hindered than the readily reduced 1,2,3,4-tetrachlorobicyclo[2.2.2]octene (7).

Ketal III was hydrolyzed at room temperature in dichloromethane solution by stirring with 96% sulfuric acid; the product, 1,4-dichlorobicyclo[2.2.1]heptan-7-one, IV, ν_{CO} 1815 cm^{-1} (CS_2), crystallized as the separated organic phase was distilled to dryness on the steam bath and was used without purification in the next step. Favorskii rearrangement was effected by dissolving the crude IV in tetrahydrofuran and adding rapidly a 100% excess of powdered sodium hydroxide while stirring at 0-5° (ice bath). After five hours excess concentrated hydrochloric acid was added and the mixture was worked up at room temperature or below. Acidification of the bicarbonate washings and extraction with ether gave 92.6% (from III) of crude colorless 4-chlorobicyclo[2.2.0]hexane-1-carboxylic acid, V, m.p. 110-137°, whose infrared spectrum differed only slightly from that of the analytical sample, m.p. 143.0-143.9° [calc. for $C_7H_9ClO_2$ (160.60): C 52.35, H 5.65. Cl 22.07; found: C 52.21, H 5.61, Cl 22.28, equiv. wt. 160]. Acid V may be purified by recrystallization from ether or carbon tetrachloride, with only fair recovery per step, and by sublimation at 60° in high vacuum. The infrared spectra of V and its methyl ester (V-Me) are consistent with the assigned structure, and in particular show no evidence of unsaturation. The nmr spectrum in benzene of V-Me displays a sharp singlet at 6.52 τ (3H) and a complex pattern of at least 21 lines at 6.9-8.6 τ (8H).

When V-Me in benzene solution was heated to 100°, it was smoothly isomerized, with a half-life of about 1.5 hours, to methyl 5-chlorohexa-1,5-diene-2-carboxylate, with nmr absorption at 3.90 (1H, d, 1.4 cps), 4.76 (1H, m), 4.97 (1H, d, 1.2 cps), 5.18 (1H, m), 6.62 (3H, s) and 7.57 τ (4H, broad singlet). The structure of the product was assigned on the basis of its nmr spectrum and by analogy (8); since methyl cyclobutanecarboxylate opens more easily than cyclobutane (9), it was to be expected that V-Me would be more labile than bicyclo[2.2.0]hexane itself. It appears that V and particularly its anion are even less stable, so that gentle work-up conditions are essential if the acid is to be isolated in pure condition.

In some preparations of V, a bicarbonate-insoluble substance, m.p. 234-236°, was isolated also; it was found to have remarkably simple infrared and nmr spectra, and analyzed for $C_8H_{12}Cl_2$. These data suggested that the by-product was 1,4-dichlorobicyclo[2.2.2]octane, VII (7), and this identification was confirmed by comparison with an authentic sample. The presence of VII may be rationalized by supposing that under the conditions of its formation, adduct II may lose the elements of dimethoxycarbene (10) to give 1,2,3,4-tetrachlorocyclohexadiene, which then adds to ethylene to form 1,2,3,4-tetrachlorobicyclo[2.2.2]octene, VI, in turn reduced in the next step to VII. Although VII was usually present only in traces, in one preparation it was isolated in 6% yield.



VI VII

Acknowledgement: I am indebted to Mr. Roger Birnbaum and Miss Elaine Holstein for preparative assistance, and to Dr. J. C. Kauer of the DuPont Company for a sample of VII. Grateful acknowledgement is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the Public Health Service for grants, PRF #2191-A1,4 and GM-12731-02, in support of this work.

REFERENCES

1. A recent review: D. Seebach, *Angew. Chem. Intern. Ed. Engl.* **4**, 121 (1965).
2. K. V. Scherer, Jr., R. S. Lunt, III, and G. A. Ungefug, *Tetrahedron Letters*, 1199 (1965).
3. P. E. Eaton and T. W. Cole, Jr., *J. Am. Chem. Soc.*, **86**, 962 (1964); J. C. Barborak, L. Watts and R. Pettit, *ibid.*, **88**, 1328 (1966); R. J. Stedman, L. S. Miller and J. R. E. Hoover, *Tetrahedron Letters*, 2721 (1966); G. L. Dunn, V. J. DiPasquo and J. R. E. Hoover, *ibid.*, 3737 (1966).
4. (a) P. E. Hoch, *J. Org. Chem.*, **26**, 2066 (1961).
   (b) P. G. Gassman and P. G. Pape, *ibid.*, **29**, 160 (1964).
5. E. T. McBee, D. L. Crain, R. D. Crain, L. R. Belohlav and H. P. Braendlin, *J. Am. Chem. Soc.*, **84**, 3557 (1962).
6. C. F. Wilcox, Jr. and J. G. Zajacek, *J. Org. Chem.*, **29**, 2209 (1964).
7. J. C. Kauer, French Pat. 1,345,138 (1963); *Chem. Abstr.*, **60**, 14407 (1964); cf. *ibid.*, **62**, 14529 (1965).
8. C. Steel, R. Zand, P. Hurwitz and S. G. Cohen, *J. Am. Chem. Soc.*, **86**, 679 (1964).
9. M. Zupan and W. D. Walters, *ibid.*, **86**, 173 (1964).
10. R. W. Hoffmann and H. Häuser, *Tetrahedron*, **21**, 891 (1965).