Synthesis of Methyl Sterculate

ERICH R. ALTENBURGER, JAMES W. BERRY and ARCHIE J. DEUTSCHMAN, JR.,
Department of Agricultural Biochemistry, University of Arizona, Tucson, Arizona 85721

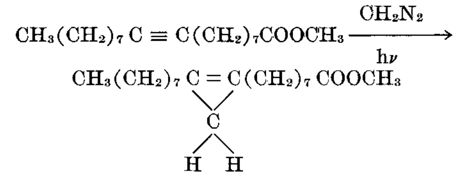
Abstract

Methyl sterculate was isolated from an irradiation mixture obtained by photolysis of diazomethane in presence of methyl stearolate by column chromatography on silicic acid. The separable amount of the photoproduct was 9.5%. The presence of the cyclopropene structure was proved by spectroscopy and chemical methods.

Introduction

The unusual ring structure of cyclopropene compounds is not only of theoretical and synthetic interest (1) but might also be responsible for the unique biological effects caused by fatty acids and their derivatives such as sterculic acid (2). Our interest is based on this fact and led us to studies of a synthesis of ^{14}C-3 labeled methyl sterculate.

One of the synthetic pathways to cyclopropene compounds is the addition of a divalent carbon species (carbene) to a triple bond. In this one-step synthesis the attacking carbene can be generated by photolytic decomposition of diazo compounds as reported by Doering and Mole (3) and Lind and Deutschman (4). Recently our studies showed (5) that, in a photoinduced reaction of diazomethane with methyl stearolate, addition of the formed carbene to the triple bond yielded 10–11% methyl sterculate as determined by Halphen Test (6). When the reaction mixture was used in poultry tests, the physiological effects confirmed the presence of the cyclopropene structure (7).



$$CH_3(CH_2)_7C\equiv C(CH_2)_7COOCH_3 \xrightarrow[h\nu]{CH_2N_2}$$

Since the rather unstable methyl sterculate was obtained only in small amounts from the irradiation and had almost the same R_f value on TLC as the starting material, separation of the complex mixture proved to be difficult. Now we wish to report that it was achieved by column chromatography on silicic acid. Recently a multi-step synthesis of methyl sterculate has been reported by Gensler et al. (8).

Experimental Procedures

Column chromatography was carried out on silicic acid (Mallinckrodt, 100 mesh, activated for 6 hr at 120 C), ratio adsorbent-substrate (100:1).

Thin layer chromatography was carried out on glass plates (20 × 20 cm) spread with a 0.25 mm layer of Silica Gel G (Merck). Developing solvent: hexane-ether (9:1); visualization with iodine at room temperature.

Elemental analysis was carried out by Schwarzkopf Microanalytical Laboratory, Woodside, N.Y.

Infrared spectra were determined by a Perkin Elmer Infracord Model 137 B.

Nuclear magnetic resonance (NMR) spectra were recorded on a Varian HA-100 instrument.

Preparation of the Starting Materials

Stearolic acid was prepared by the method of Butterfield and Dutton (9) and converted into the methyl ester as described by Schlosser et al. (5).

Diazomethane was prepared as reported by Moore and Reed (10) using bis-(N-methyl-N-nitroso)-terephthalamide as precursor.

Preparation of Methyl Sterculate

The irradiation system consisted of a mercury lamp (GE bulb A 85/UV 4; mounting designed and built in this laboratory) surrounded by a water cooled (20–25 C) transparent Pyrex jacket. A Pyrex test tube attached to the jacket served as a reaction flask. This reaction unit was immersed in an ice water bath which maintained the temperature at 5–10 C. A nitrogen stream was passed slowly through the etheral diazomethane solution (dried over potassium hydroxide pellets and cooled to 5–10 C) and the diazomethane was thereby introduced into the reaction tube containing 10 g (0.034 mole) of purified methyl stearolate. Gas introduction and irradiation time were maintained for 7–8 hr. Consumption of diazomethane was checked as described in (5). The crude irradiation mixture was chromatographed on 1 kg silicic acid and the progressing elution was determined by TLC. Petroleum ether containing 20% benzene eluted consecutively methyl sterculate, mixtures of methyl sterculate and methyl stearolate and finally methyl stearolate.

Results and Discussion

Using a 10 g batch of irradiation product for chromatography the petroleum ether benzene (4:1) mixture eluted 700 mg of slightly impure (TLC) methyl sterculate followed by mixed fractions and rather pure starting material (TLC). Subsequent chromatography of the mixed fractions gave an additional 250 mg methyl sterculate thereby giving a conversion of 9.5%. Final purification was effected by quick filtration of the combined cyclopropene samples through alumina (Merck, activity I; elution with Skelly F). An analytical sample had mp 12 C (Lit.-11.3 C) (11) and gave the following results in elemental analysis: Analysis Calculated for $C_{20}H_{36}O_2$: C, 77.82; H, 11.76; Found: C, 77.82; H, 11.84.

The IR spectrum (liquid film) showed absorption at 1865 (cyclopropenyl C = C stretch), 1740 and 1007 cm^{-1}. The NMR spectrum (in $CHCl_3$) showed the following pattern: δ 0.77 (s, 2 H, cyclopropenyl CH_2), 0.91 (t, 3 H, terminal CH_3), 1.31 (m, 22 H), 2.20–2.40 (m, 6 H, α to cyclopropenyl and $-COOCH_3$), 3.62 (s, 3 H, CH_3COO-). Natural methyl sterculate prepared from Sterculia foetida (12,13) and synthetic material showed the same features in their IR and NMR spectra and had the same R_f values on TLC.

For further proof of its structure, methyl sterculate was converted to dihydrosterculic acid by hydrogenation and subsequent saponification as reported by Nunn (17). The obtained product melted at 38 C (Lit. 39.7–40.5 C) (14). The mixed melting point with a sample prepared from natural sterculic acid gave no depression and the IR spectra were identical. Conversion to the amide gave a crystalline product, mp 85 C (Lit. 86.4 C) (15).

Prolongation of the reaction time after 8 hr did not improve the yield of methyl sterculate. It is not known if photolytically formed methyl sterculate undergoes further reactions during irradiation.

An etheral diazomethane solution was used since its synthesis is more convenient in this solvent than in any other. By passing the dried nitrogen stream slowly and carefully through the cooled diazomethane container no measurable amount of ether could be noticed in the reaction tube.

Diazomethane concentration and consumption was determined by titration with benzoic acid as reported by Schlosser et al. (5).

It is well known that carbene generated from diazomethane not only adds to the triple bond but also undergoes insertion reactions (3,4). For an example of insertion reaction of carbene, see Kirmse (16). TLC showed the presence of several by-products in the reaction mixture, but no attempts were made to isolate and identify such insertion products in this work. Starting material was estimated at about 55–60%.

The silicic acid for column chromatography was used in the neutral and in the acidic form. The two types of absorbent showed no difference in their efficiency of separation. No significant loss of cyclopropene compound seemed to occur even when the substrate was kept on the column for more than 24 hr.

Investigations to synthesize and separate ^{14}C-3 labeled methyl sterculate by the described method and to study the biological effects are in progress.

ACKNOWLEDGMENT

This work was supported by Public Health Research Grant ES 00262–07 from the Division of Environmental Engineering and Food Protection.

REFERENCES

1. Closs, G. L., in "Advances in Alicyclic Chemistry," Academic Press, New York, 1966, p. 53.
2. Phelps, R. A., F. S. Shenstone, A. R. Kemmerer and R. J. Evans, Poultry Sci. *44,* 358 (1965).
3. Doering, W. von E., and T. Mole, Tetrahedron *10,* 65 (1960).
4. Lind, H., and A. J. Deutschman, Jr., J. Org. Chem. *32,* 326 (1967).
5. Schlosser, M. M., A. J. Longo, J. W. Berry and A. J. Deutschman, Jr., JAOCS *46,* 171 (1969).
6. Deutschman, A. J., Jr., and I. S. Klaus, Anal. Chem. *32,* 1809 (1960).
7. Schlosser, M. M., J. W. Berry, B. L. Reid and A. J. Deutschman, Jr., Poultry Sci. *47,* 1383 (1968).
8. Gensler, W. J., M. Brawner Floyd, R. Yanase and K. Pober, J. Am. Chem. Soc. *91,* 2397 (1969).
9. Butterfield, R. O., and H. J. Dutton, JAOCS *45,* 635 (1968).
10. Moore, A., and D. E. Reed, Org. Syn. *41,* 16 (1961).
11. Feuge, R. O., Zigrida Zarins, J. L. White and R. L. Holmes, JAOCS *46,* 185 (1968).
12. Nordby, H. E., B. E. Heywang, H. W. Kircher and A. R. Kemmerer, Ibid. *39,* 183 (1962).
13. Kircher, H. W., Ibid. *41,* 4 (1964).
14. Hofmann, K., O. Jucker, W. R. Miller, A. C. Young, Jr. and F. Tausig, J. Am. Chem. Soc. *76,* 1799 (1954).
15. Hofmann, K., S. F. Orchena and C. W. Yoho, Ibid. *79,* 3608 (1957).
16. Kirmse, W., "Carbene Chemistry," Academic Press, New York, 1964, p. 21 ff.
17. Nunn, J. R., J. Chem. Soc. *1952,* 313.

[Received September 4, 1969]