from methylene chloride-petroleum ether (b.p. 32-36°) to give the products listed in Table I.

Reaction of I and 1,2-epoxides without pyridine present. These reactions were carried out exactly as described, above, but no pyridine was added. After standing at least 12 hours, at room temperature, cyclohexene (1.0 ml.) was added and the mixture was allowed to stand for several hours. Chromatographing, as above, gave the known adduct of I and cyclohexene, m.p. 117-118°, in the yields shown in Table I.

Reaction of I and chlorohydrins in the presence of pyridine. These reactions were carried out in exactly the same way as were the epoxide reactions. The yields, melting points, and analytical figures are reported in Table I.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF SOUTHERN CALIFORNIA
LOS ANGELES 7, CALIFORNIA

5-(1',2',3'-Trimethoxyphenyl)-4,6-dicarbethoxycyclohexanedione-1,3

PHILIPPOS E. PAPADAKIS AND ROBERT MATHIESEN

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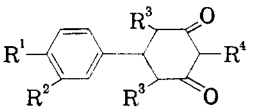
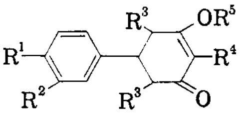
Compounds of the types (I) and (II) below with different substituents for R^1, R^2, R^3, R^4 and R^5 have been synthesized in the Department of Therapeutics of New York University and in this laboratory by Papadakis and co-workers. Some of these derivatives have been reported previously.[1-5]

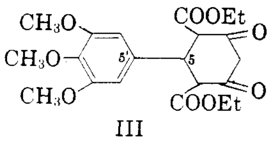


I



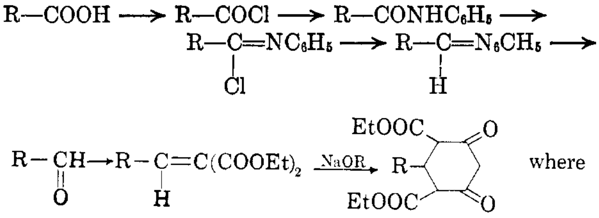
II

The present report is an extension of previous work and deals with the preparation of 5-(1',2',3'-trimethoxyphenyl)-4,6-dicarbethoxycyclohexanedione-1,3 (III). The purpose of this investigation is the preparation of III as an intermediate for the synthesis of compounds having structural relation to known anticancer agents or to other substances of physiological importance.

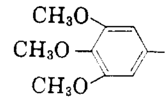


III

The sequence of synthesis is as follows:



where R is



EXPERIMENTAL

The preparation of *trimethoxybenzaldehyde* from trimethoxybenzoyl chloride is described by A. Sonn and E. Muller[6] and by J. W. Cook and co-workers.[7] The trimethoxybenzaldehyde was distilled at 163-166° and 10 mm. pressure. The distillate crystallized and gave a melting point of 75-76°. (Melting points are uncorrected.) The over-all yield from trimethoxybenzoylanilide to trimethoxybenzaldehyde was 59%.

Ethyl trimethoxybenzylidenemalonate. A mixture of 6.2 g. of 3,4,5-trimethoxybenzaldehyde, 5.1 g. of diethyl malonate, and 0.3 ml. of piperidine was refluxed for five hours at 150°. The product was dissolved in a small amount of alcohol and was reprecipitated with distilled water, m.p. 71-71.5°. The mixture m.p. of the product with trimethoxybenzaldehyde was 58-60°. The yield of pure product was 5.6 g.

Anal. Calc'd for $C_{17}H_{22}O_7$: C, 60.34; H, 6.55. Found: C, 60.08; H, 6.45.

5-(1',2',3'-Trimethoxyphenyl)-4,6-dicarbethoxycyclohexanedione-1,3. To a solution of 0.4 g. of sodium in absolute ethanol 2.2 g. of ethyl acetoacetate was added and the mixture was refluxed for an hour. To this, 5.6 g. of ethyl-3,4,5-trimethoxybenzylidenemalonate was added and the mixture was further refluxed for five hours at 110-115°. After cooling to 0°, cold dilute acetic acid was added. The yellowish crystals which formed were recrystallized from ethyl alcohol and were washed with dioxane; yield 3.6 g. of white needles, m.p. 191-192°.

Anal. Calc'd for $C_{21}H_{26}O_9\cdot{}^1/_2\,H_2O$: C, 58.45; H, 6.07. Found: C, 58.31; H, 6.04. *Anal.* Dried at 100° in a vacuum, Calc'd for $C_{21}H_{26}O_9$: C, 59.71; H, 6.16. Found: C, 59.60; H, 5.84. *Anal.* Calc'd for $3(-OCH_3)$ and $2(-OC_2H_5)$: % alkoxy, 43.36. Found: 43.35, 43.10.

CHEMISTRY DEPARTMENT
CREIGHTON UNIVERSITY
OMAHA 2, NEBRASKA

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Meta Amination as a 1,3-Addition Process

AVERY A. MORTON

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The "benzyne" intermediate[1,2] for *meta* amination is a product of a theory that many reactions be-

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