in the capillary withdrawal tube on the absorption flask was not included. This factor was included in Howland's calculations since the capillary withdrawal tube contained some hydrogen bromide gas which was pushed over with the sample into the sample flask. It can, however, be justifiably omitted from our calculations since the first few milliliters of sample and any hydrogen bromide gas in the tube were collected in a trap and did not enter the sample flask.

$$K_s = \frac{N_{HBr}}{P_{HBr}}$$

$$N_{HBr} = \frac{\frac{ml \times N}{1000}}{\frac{\text{wt of sample} - b}{\text{mol wt of solvent}} + \frac{ml \times N}{1000}}$$

$$P_{HBr} = P_{total} - P_{solvent}(1 - N_{HBr})$$

where N_{HBr} = mole fraction of HBr in each sample, P_{HBr} = partial pressure of HBr in the gas phase, K_s = solubility constant, ml = milliliters of NaOH solution used for titration, N = normality of NaOH, b = weight in grams of gas in sample, P_{total} = total pressure in millimeters, $P_{solvent}$ = vapor pressure of pure solvent in millimeters.

Registry No.—Hydrogen bromide, 10035-10-6; deuterium bromide, 13536-59-9.

Direct Synthesis of 1,1,4,4-Tetraethylpiperazinium Dichloride

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The formation of 1,1,4,4-tetraethylpiperazinium dichloride has been reported[2-6] on a number of occasions where the hydrochloride of β-chloroethyldiethylamine was treated in alkaline media. The unstable chloroamine cyclodimerizes to the title product through the aziridine intermediate.[5] Cope[7] has reported formation of the tetraalkylpiperazinium salts under acidic conditions. We wish to report a facile single-step process which gives practically quantitative yields of the tetraalkylpiperazinium dichloride when β-chloroethyldiethylamine hydrochloride is added to an epoxide, which acts as an acid scavenger and is converted into the chlorohydrin.

Experimental Section

To 17.0 g (0.099 mole) of β-chloroethyldiethylamine hydrochloride, reagent grade recrystallized from absolute ethanol, in 50 ml of absolute ethanol was added 10 g (0.108 mole) of 1,2-epoxy-3-chloropropane (epichlorohydrin). The mixture became homogeneous when heated to approximately 60°. Crystals of the product formed within 30 min; the reaction mixture was maintained at 60° for an additional 1.5 hr and then cooled to −10° to give 13.3 g (97%) of white crystalline product (dec. 270°). The presence of 1,3-dichloropropanol in the alcoholic mother liquor was shown by glpc. The DTA curve showed an initial rapid endotherm at 270° which continued to 342°. The infrared spectrum contained no peaks due to unsaturation or NH^+.

Anal. Calcd for $C_6H_{14}NCl$: C, 53.14; N, 10.33; H, 10.33; total Cl, 26.20; ionic Cl, 26.20. Found: C, 53.13; N, 10.33; H, 10.32; total Cl, 26.25; ionic Cl, 25.91.

The reaction can be run neat, using epichlorohydrin as the solvent and the acid scavenger, to give a 95% yield. Epoxides other than epichlorohydrin can be used. For example, 1,2-epoxybutane at a 1:1 mole ratio in absolute ethanol gave a 95% yield of the piperazinium dichloride product.

Registry No.—1,1,4,4-Tetraethylpiperazinium dichloride, 5449-19-4.

(1) One of the laboratories of the Southern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture.

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(3) R. R. Burtner, *J. Am. Chem. Soc.*, **71**, 2578 (1949).

(4) J. Cadogan, *J. Chem. Soc.*, 2971 (1955); 4154 (1957).

(5) P. D. Bartlett, S. D. Ross, and C. G. Swain, *J. Am. Chem. Soc.*, **71**, 1415 (1949).

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Preparation of 2-Carbethoxycyclopentane-1,3-dione

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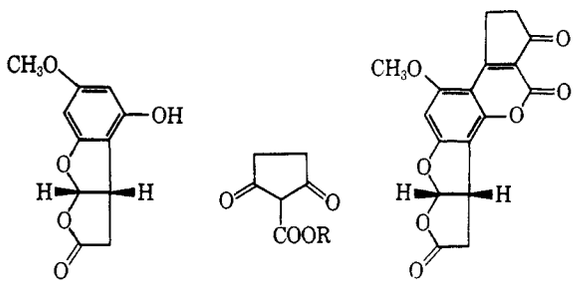
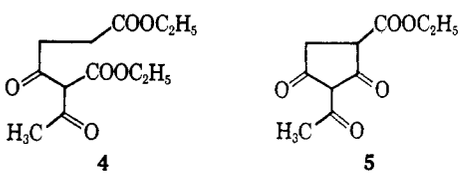
Received July 25, 1967

Condensation of phenol **1** with a 2-carbalkoxycyclopentane-1,3-dione (**2**) appeared to be an expeditious method for the preparation of the pentacyclic coumarin **3** which is an intermediate in the synthesis of aflatoxin B_1.[2] Syntheses of 2-carbethoxycyclopentane-1,3-dione (**12**) have been claimed in the literature but none could be verified.[3] The most direct approach



1 2 3

involving a Dieckmann cyclization of methyl ethyl β-ketoadipate could never be reduced to practice[3] but the successful cyclization of 1,4-dicarbethoxyhexane-3,5-dione (**4**) to 2-acetyl-4-carbethoxycyclopentane-1,3-dione (**5**)[4] led us to investigate the cyclization of



4 5

the corresponding malonic ester **6**. This intermediate has now been synthesized as follows.

The mixed anhydride prepared from ethyl chloroformate and *t*-butyl hydrogen succinate in the presence of triethylamine was condensed with diethyl ethoxymagnesiomalonate to give diethyl 3-carbo-*t*-butoxy-

(1) National Institutes of Health Postdoctoral Fellow 1964-1965.

(2) G. Büchi, D. M. Foulkes, M. Kurono, and G. F. Mitchell, *J. Am. Chem. Soc.*, **88**, 4534 (1966).

(3) J. H. Boothe, R. G. Wilkinson, S. Kushner, and J. H. Williams, *ibid.*, **75**, 1732 (1953).

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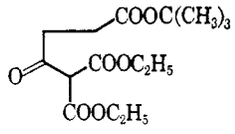
propionylmalonate (6). Cyclization by the agency of potassium *t*-butoxide in hot benzene furnished crystalline 2-carbethoxy-4-carbo-*t*-butoxycyclopentane-1,3-dione (7). This substance must be virtually completely enolic for the following reasons. (a) The ketone



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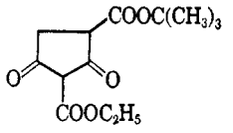

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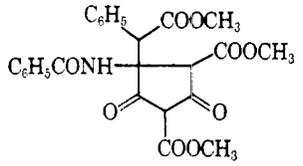
function in 2-carbethoxycyclopentanone gives rise to a carbonyl stretching vibration at 1753 cm^{-1} ($CHCl_3$).[5] No such band is present in the spectrum ($CHCl_3$) of the ester 7 which exhibits a pair of intense absorptions at 1660 and 1610 cm^{-1} typical of enolized β-keto esters.[5] An unsymmetrical and intense band situated between 1730 and 1710 cm^{-1} is attributed to the superposition of ester and cyclopentenone stretching modes. (b) The ultraviolet spectrum in neutral or acidic ethanol displays a maximum at 248 mμ (ε 21,000) while the enol tautomer of 2-carbethoxycylopentanone[6] and the enol of cyclopentane-1,3-dione[6] absorb at 255 and 242 mμ, respectively. Changing to 0.1 *N* sodium hydroxide–ethanol had little effect on the position of the maximum in the spectrum of the diketo diester 7 but did cause an increase in intensity (250 mμ, ε 27,000). As anticipated the maxima of both 2-carbethoxycyclopentanone and of cyclopentane-1,3-dione (13) were bathochromically shifted to 287[7] and 257[6] mμ, respectively. This observation suggests that the undissociated enol and the corresponding anion of the β-tricarbonyl compound 7 both absorb at approximately the same wavelength. An entirely analogous situation has recently been encountered with a more highly substituted 2,5-dicarbomethoxycyclopentane-1,3-dione 8: λ_{max} (EtOH) 254 mμ (ε 21,900); λ_{max} (0.01 *N* NaOH–EtOH) 254 mμ (ε 25,300).[8] (c) The nuclear magnetic resonance spectrum of 7 is fully in accord with either



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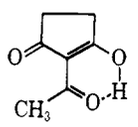

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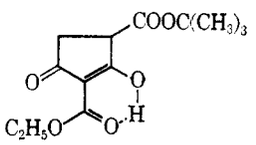

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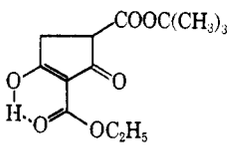
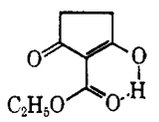


11

of the two external tautomers[9] 10 or 11 and exhibits the following resonances: 11.67 (1 H, broad), 4.53 (2 H, quartet), 3.7 (1 H, four lines corresponding to X portion of ABX pattern), 3.04 (2 H, multiplet), 1.53 (9 H, singlet), and 1.43 (3 H, triplet).

It remained to remove the carbo-*t*-butoxy group and this was accomplished by exposure of the diester 7 to *p*-toluenesulfonic acid in hot benzene. The resulting 2-carbethoxycyclopentane-1,3-dione (12), mp 104°, again is completely enolized as judged by intense infrared absorptions at 1714, 1656, and 1609 cm^{-1} and ultraviolet maxima at 243 mμ (ε 22,200) in 0.1 *N* HCl–EtOH and at 252 mμ (ε 29,800) in 0.1 *N* NaOH–EtOH. The proton spectrum (in $CDCl_3$) is extremely simple; somewhat unexpectedly the four cyclopentane protons proved to be equivalent appearing as a singlet at δ 2.65. In contrast, interconversion of the two external tautomers ($CDCl_3$) in 2-acetylcyclopentane-1,3-dione (9) is slower and the corresponding protons give rise to an A_2B_2 pattern.[4,9] The signal at lowest field (δ 11.2) in the spectrum of 12 corresponds to one proton, thus providing firm support for the enolic structure 12.



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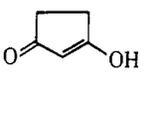

13

Attempts to condense the diketo ester 12 with the phenol 1 as well as with simpler phenols in the presence of acidic catalysts did not lead to more than trace amounts of the coumarin 3 or analogous cyclopentenone[2,3-*c*]coumarins. We attribute this situation to instability of the diketo ester 12 which in the presence of acids is rapidly transformed to cyclopentane-1,3-dione (13).

Experimental Section

Elemental analyses were performed by Midwest Microlabs, Inc., Indianapolis, Ind., and Dr. S. M. Nagy and associates at the Massachusetts Institute of Technology. Melting points (mp) were determined on a hot-stage microscope and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 237 instrument; only selected high-intensity bands are listed. Ultraviolet spectra were obtained on a Cary Model 14 recording spectrophotometer. All nuclear magnetic resonance (nmr) spectra were measured on a Varian A-60 instrument and chemical shifts are presented in parts per million downfield from an internal tetramethylsilane standard.

Methyl *t*-Butyl Succinate.—Using the method of Backer and Homan,[10] β-carbomethoxypropionyl chloride[11] (124.6 g, 0.83 mole) was dissolved in twice its own volume of chloroform and this solution was added slowly to a stirred mixture of anhydrous *t*-butyl alcohol (148 g, 2.0 moles) and freshly distilled dimethylaniline (145 g, 1.2 moles). The reaction vessel and contents were cooled during the addition to maintain the temperature below 50°. The flask contents were then warmed in a hot-water bath (80°) for 2.5 hr, after which the flask was cooled and its contents were poured over crushed ice. To this was added 2 *N* sulfuric acid (0°) and the mixture was shaken in a separatory funnel. An additional portion of cold sulfuric acid was added until, after thorough mixing, the aqueous solution showed pH 1. The aqueous solution was extracted with three 200-ml portions of methylene chloride and all the organic solutions were combined. These combined solutions were washed with six 100-ml portions of cold 2 *N* sulfuric acid, until the acidic washings were completely colorless, and then with sodium bicarbonate solution, and water until the washings were neutral. After drying over sodium sulfate, solvents were removed *in vacuo* and the liquid residue was distilled. A colorless liquid resulted: yield, 117 g (0.62 mole,

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(7) Kindly measured by Miss L. Foley, Massachusetts Institute of Technology.

(8) H. Muxfeldt and R. S. Schneider, *J. Org. Chem.*, in press. We are indebted to these investigators for a friendly exchange of data. *Cf.* W. R. Chan and C. H. Hassall, *J. Chem. Soc.*, 3495 (1956).

(9) S. Forsén, F. Merényi, and M. Nilsson, *Acta Chem. Scand.*, **18**, 1208 (1964).

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(11) J. Cason, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p 169.

75%); bp 53–54° (0.65 mm) and 43–44° (0.13 mm); ν_{max} ($CHCl_3$) 1725, 1445, 1375, 1265, 1160 cm^{-1}; nmr (CCl_4), 3.63 (3 H, singlet), 2.48 (4 H, multiplet), 1.43 (9 H, singlet).

Anal. Calcd for $C_9H_{16}O_4$: C, 57.43; H, 8.57. Found: C, 57.47; H, 8.62.

t-Butyl Hydrogen Succinate.—Methyl *t*-butyl succinate (94 g, 0.5 mole) was dissolved in 1150 ml of dioxane and an aqueous sodium hydroxide solution (20 g, 0.5 mole in 1100 ml of water) was added. The resulting clear solution was stirred for 40 hr at room temperature and then concentrated *in vacuo* until entirely aqueous. This barely alkaline solution was extracted with ether once, poured over ice, acidified with cold 2 *N* sulfuric acid (0°), and extracted six times with ether. The ethereal solution was washed with water and dried over sodium sulfate, and the solvent was removed *in vacuo*. The resulting solid was recrystallized once from petroleum ether (bp 30–60°) giving crystals: yield, 57.4 g (0.33 mole, 66%); mp 49–52° (lit.[10] mp 51.5–52°).

Diethyl 3-Carbo-t-butoxypropionylmalonate (6).—Diethyl ethoxymagnesiomalonate was prepared according to Price and Tarbell[12] by adding 0.5 ml of carbon tetrachloride, 5 ml of absolute ethanol, and 6 ml of a mixture of diethyl malonate (24 g, 0.15 mole) and ethanol (11 ml) to a flask containing 3.7 g (0.15 g-atom) of magnesium turnings. The vigorous reaction was moderated by cooling before dropwise addition of the remainder of the mixture. After complete addition, 60 ml of anhydrous ether was added and the flask contents were warmed to reflux for several hours until almost all the magnesium was consumed. All volatile material was removed *in vacuo* and replaced with benzene. The benzene was also distilled *in vacuo* and the solid residue was dissolved in 60 ml of anhydrous ether for addition to the mixed anhydride prepared simultaneously.

The mixed anhydride was prepared by the dropwise addition of ethyl chloroformate (16.3 g, 0.15 mole) to a stirred solution containing *t*-butyl hydrogen succinate (26.5 g, 0.15 mole), triethylamine (15.2 g, 0.15 mole), and anhydrous toluene (150 ml). The reaction flask was cooled in an ice–salt slurry and its contents were maintained just below 0°. After this addition was complete, the flask contents were stirred for 30 min prior to the addition of the diethyl ethoxymagnesiomalonate. The flask remained in the ice–salt slurry and the addition was again slow enough to maintain the contents below 0°. After addition, the reaction was stirred overnight at room temperature. The flask contents were poured over ice and acidified cautiously with cold 2 *N* sulfuric acid (0°). The mixture was shaken in a separatory funnel until clear and the solution was ascertained to be acidic before extracting twice with ether. The combined organic solutions were washed twice with cold 2 *N* sulfuric acid (0°), with sodium bicarbonate solution, and then with water until the washings were neutral. After drying over sodium sulfate, the solvents were removed *in vacuo*, leaving a liquid residue (positive ferric chloride test). The residue was distilled and a colorless, viscous liquid resulted: yield, 30 g (0.095 mole, 63%); bp 112–113° (0.03 mm); ν_{max} ($CHCl_3$) 1760, 1725, 1648, 1615, 1372, 1245, 1152, 1090, 1029 cm^{-1}; nmr ($CDCl_3$), 14.03 (1/3 H, singlet), 4.55 (2/3 H, singlet), 4.23 (4 H, quartet), 2.73 (4 H, multiplet), 1.45 (singlet), 1.30 (triplet) (bands at 1.45 and 1.30 represent 15 H; when shaken with D_2O, the 14.03 band disappeared; on addition of sodium carbonate, the 4.55 band also disappeared).

Anal. Calcd for $C_{15}H_{24}O_7$: C, 56.95; H, 7.65. Found: C, 57.21; H, 7.53.

2-Carbethoxy-4-carbo-t-butoxycyclopentane-1,3-dione (7).—In a 500-ml, three-necked, round-bottom flask, equipped with dropping funnel, mechanical stirrer, and reflux condenser fitted with drying tude, were placed 200 ml of anhydrous benzene, 30 ml of anhydrous *t*-butyl alcohol, and 6.0 g (0.15 g-atom) of potassium metal. The potassium was allowed to react using no external heat and when the reaction was complete, the slurry was brought to gentle reflux by means of an oil bath heated to 95–100°. To this off-white slurry was added a solution of 15.8 g (0.05 mole) of diethyl 3-carbo-*t*-butoxypropionylmalonate in 50 ml of benzene, over a period of 30 min. After addition was complete, the mixture was allowed to reflux for an additional 1.75 hr and then allowed to stir at room temperature overnight. The reaction flask contents were poured over crushed ice and acidified with cold 2 *N* sulfuric acid (0°). The mixture was shaken with ethyl acetate in a separatory funnel. The aqueous solution was ascertained to be acidic, separated, saturated with sodium chloride, and extracted with three 200-ml portions of ethyl acetate. The combined ethyl acetate solutions were extracted with saturated aqueous sodium bicarbonate solution, using four 200-ml portions. The aqueous extracts were washed once with benzene, poured over crushed ice, and carefully acidified with cold 2 *N* sulfuric acid (0°) before saturating with sodium chloride and extracting with four 300-ml portions of ethyl acetate. The ethyl acetate solutions were combined and washed with saturated sodium chloride solution until the washings showed a pH increase. The solution was dried and the solvent was removed *in vacuo* leaving an orange oil which crystallized on standing (11.8 g, 0.044 mole, 87% crude yield). An earlier cyclization using the same conditions had produced a similar product (11.4 g, 0.042 mole, 84% crude yield) of comparable purity (tlc, silica gel G developed with 5% methanol in chloroform). The crude product (11.8 g) was recrystallized from warm benzene by adding petroleum ether and cooling this solution to 0° for 2 days. Much of the material had to be recrystallized twice to free it from an oily impurity. The white, crystalline beads obtained had mp 81–84°: yield, 7.3 g (54%). A small sample was recrystallized further in the same manner and the white solid resulting had mp 84–85°; ν_{max} ($CHCl_3$), 3300–2700 (broad), 1714, 1660, 1610, 1474, 1437, 1385, 1377, 1340, 1230, 1160, 1052; λ_{max} (0.1 *N* HCl) 248 mμ (ε 21,000); λ_{max} (0.1 *N* NaOH) 250 mμ (ε 27,000); nmr ($CDCl_3$), 11.67 (1 H, broad), 4.53 (2 H, quartet), 3.70 (1 H, four lines), 3.04 (2 H, unresolved multiplet), 1.53 (singlet), 1.43 (two lines of triplet, third line under 1.53 band), bands at 1.53 and 1.43 represent a total of 12 H.

Anal. Calcd for $C_{13}H_{18}O_6$: C, 57.77; H, 6.71. Found: C, 57.95; H, 6.75.

2-Carbethoxycyclopentane-1,3-dione (12).—The cyclic diketo diester **7** (2.70 g, 0.01 mole) was dissolved in 200 ml of anhydrous benzene along with 0.4 g of fused *p*-toluenesulfonic acid and the suspension was heated at reflux in an oil bath for 10 hr. The solid obtained after filtration and solvent evaporation was sublimed at 0.05 mm and 55°. The white sublimate (1.04 g, 61%) had mp 95–96°. A small amount of this material was purified further by tlc on silica gel plates (Mallinckrodt TLC-7) developed with 5% ethanol in ethyl acetate, followed by resublimation. The white solid resulting had mp 104°; λ_{max} (0.1 *N* HCl) 243 mμ (ε 22,200); λ_{max} (0.1 *N* NaOH) 252 mμ (ε 29,800); nmr ($CDCl_3$), 11.2 (1 H, singlet), 4.42 (2 H, quartet), 2.65 (4 H, singlet), 1.37 (3 H, triplet); infrared absorptions ($CHCl_3$) 1714, 1656, and 1609 cm^{-1}.

Anal. Calcd for $C_8H_{10}O_4$: C, 56.47; H, 5.93. Found: C, 56.65; H, 6.07.

Cyclopentane-1,3-dione (13). A. From 2-Carbethoxy-4-carbo-t-butoxycyclopentane-1,3-dione (7).—A solution of **7** (270 mg, 1 mmole) in 60 ml of 6 *N* hydrochloric acid was heated on a steam cone for 5 hr. The solid obtained after solvent evaporation was sublimed at 0.5 mm and 100° to give white crystals: yield, 49 mg (50%); mp 150–151° (lit.[6] mp 151–152°). Identity was confirmed by comparison of infrared spectra.

B. From 2-Carbethoxycyclopentane-1,3-dione (12).—A solution of **12** was hydrolyzed and worked up as above. The white sublimate had mp 151–152°, yield 65 mg (73%).

Registry No.—**7**, 14734-23-7; **12** enol, 14734-24-8; methyl *t*-butyl succinate, 14734-25-9.

Acknowledgment.—We are indebted to the National Cancer Institute for financial support.

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A New Isoflavone Glycoside from *Baptisia australis*

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Received July 17, 1967

We wish to report the isolation and structure determination of a new isoflavone glycoside which belongs