monoglyme[6] and 0.5 mole of sodium hydride.[7] A solution of the appropriate amide (0.05 mole) and ester (0.125 mole)[8] in 125 ml of monoglyme was placed in the addition funnel and the system was purged with dry nitrogen, then closed to the atmosphere. The monoglyme in the reaction flask was heated to reflux and when thermal equilibrium had been established, an initial reading was taken on the gas meter. The solution of ester and amide was then added over a period of 20 min, and the resulting suspension was refluxed until hydrogen evolution had ceased[9] (Table I). The solvent was removed under reduced pressure, and the remaining pasty residue was cooled to 0°. Addition of ether (125 ml) was followed after several minutes by the cautious addition of 30 ml of water. The sodio salts of the products, which separated between the layers, were collected, and stirred with a mixture of 50 ml of concentrated hydrochloric acid and 300 g of crushed ice. The resulting solids were collected by filtration, washed with 5% sodium bicarbonate solution,[10] and recrystallized from appropriate solvents (Table I).

In the aroylation of phenylacetamide with ethyl nicotinate to form **2d**, the sodio salts, which separated between the layers, were collected by filtration and dissolved in 500 ml of cold 25% hydrochloric acid. The acidic solution was neutralized (pH 8) with solid sodium bicarbonate to precipitate β-keto imide **2d** which was then recrystallized.

Yields of β-keto imides prepared in the above manner are given in Table I. Analytical data and principal nmr absorptions for new products **1b**, **1c**, **2a–d**, **3a**, and **3b** are given in Table II. All of these compounds had infrared absorption at 3.10–3.40 (NH) and 5.80–6.00 μ (C=O).

Hydrolysis of β-Keto Imides 2a, 2b, 3a, and 3b.—A 2.0-g sample of **2a** was refluxed with 200 ml of 12 *N* hydrochloric acid for 24 hr. The hydrolysis mixture was extracted with ether, and the ethereal extracts were washed with 5% sodium bicarbonate solution. The combined bicarbonate extracts were acidified with 12 *N* hydrochloric acid to precipitate 0.69 g (97%) of benzoic acid. The ethereal extracts were dried ($MgSO_4$) and concentrated to afford 0.95 g (83%) of deoxybenzoin, mp 54–56° (lit.[11] mp 55–56°). The infrared spectrum was identical with that of an authentic sample of deoxybenzoin.

Similarly, **3a** gave nearly quantitative yields of benzoic acid and butyrophenone, and **3b** afforded caprophenone and benzoic acid.

A 1.5-g sample of **2b**, which was resistant to hydrochloric acid hydrolysis, was refluxed with a mixture of 10 ml of concentrated sulfuric acid, 10 ml of water, and 30 ml of acetic acid for 18 hr. The reaction mixture was processed as described above to yield 0.20 g (35%) of anisic acid, mp 182–184°, and 0.33 g (40%) of 2-phenyl-4′-methoxyacetophenone, mp 73°, (lit.[12] mp 76°) which was identified by comparison of its infrared spectrum with that of an authentic sample.

Cyclization of 2a with Hydrazine to Form Pyrazolone 4.—A solution of 2.0 g of **2a** and 20 drops of 95% hydrazine in 100 ml of 95% ethanol was refluxed for 1.5 hr. The reaction mixture was diluted with 100 ml of water and a few drops of 3 *N* hydrochloric acid were added. The volume was then reduced to 130 ml, and the solution was cooled to precipitate 0.50 g (37%) of 3,4-diphenylpyrazolone-5 (**4**), mp 234–236° (lit.[13] mp 234–235°). A mixture melting point determination with an authentic sample showed no depression. The infrared spectra of the two samples were identical. The aqueous solution was further reduced in volume to precipitate 0.25 g (35%) of benzamide, mp 125.5–127°.

Treatment of Acetamide and Phenylacetamide with 1 Mol Equiv of Methyl Benzoate and Sodium Hydride.—To a suspension of 0.105 mole of sodium hydride in 200 ml of refluxing monoglyme contained in the apparatus described above, was added over a period of 15 min, a solution of 0.05 mole of acetamide and 0.05 mole of methyl benzoate. The reaction mixture was allowed to reflux for 3 hr, at the end of which time 2 mol equiv of hydrogen had been evolved. The solvent was removed under reduced pressure, and the resulting residue was processed in the usual manner except that enough water was added to completely dissolve the sodio salts. The aqueous layer was acidified with cold dilute hydrochloric acid, and the acidic solution was extracted with 500 ml of ether–ethyl acetate (1:1). The extracts were dried (Na_2SO_4) and concentrated to afford a thick oil which was shown by thin layer chromatography (tlc) to consist of N-acetylbenzamide and benzamide. Concentration of the ethereal layer afforded benzamide. α-Benzoylacetamide[14] which was shown to be well-resolved from N-acetylbenzamide and benzamide by tlc on a known mixture, could not be detected.

Phenylacetamide (0.05 mole) was treated with methyl benzoate (0.05 mole) and 0.105 mole of sodium hydride in 200 ml of refluxing monoglyme for 4 hr, at the end of which time 2 mol equiv of hydrogen had been liberated. The reaction mixture was processed as described above for the reaction with acetamide. Acidification of the aqueous layer followed by extraction with ether–ethyl acetate (1:1) and concentration of the extracts afforded a light yellow oil. Tlc of this material showed the presence of two components which were identified as N-benzoylphenylacetamide[15] and α-benzoylphenylacetamide[16] by comparison of their R_f values with those of authentic samples.

Registry No.—Sodium hydride, 7646-69-7; **1a**, 15231-17-1; **1b**, 15231-18-2; **1c**, 15231-10-4; **2a**, 14072-63-0; **2b**, 15231-12-6; **2c**, 15231-13-7; **2d**, 15231-14-8; **3a**, 15231-15-9; **3b**, 15231-16-0.

(6) The monoglyme was distilled from sodium ribbon immediately before use.

(7) This reagent was used as a 55% dispersion in mineral oil as obtained from Metal Hydrides, Inc., Beverly, Mass.

(8) Although only 2 mol equiv of ester and 4 mol equiv of sodium hydride are apparently needed to effect the dicondensation reactions, consistently higher yields and purer products were obtained with the above proportions of reactants.

(9) In all cases the total volume of gas, which was corrected for temperature, pressure, and water vapor pressure, was consistent with the production of 4 mol equiv of hydrogen.

(10) Acidification of the bicarbonate washings usually produced some of the acid corresponding to the ester which was used in the aroylation.

(11) C. F. H. Allen and W. E. Barker, *Org. Syn.*, **12**, 16 (1932).

(12) E. Ney, *Ber.*, **21**, 2450 (1888).

(13) P. Gruenanger and P. V. Finzi, *Atti Accad. Nazl. Lincei Rend., Classe Sci. Fis., Mat. Nat.*, **31**, 128 (1961); *Chem. Abstr.*, **58**, 516e (1963).

(14) C. R. Hauser and C. J. Eby, *J. Am. Chem. Soc.*, **79**, 725 (1957).

(15) H. L. Wheeler, T. B. Johnson, and D. F. McFarland, *ibid.*, **25**, 795 (1903).

(16) S. D. Work, D. R. Bryant, and C. R. Hauser, *J. Org. Chem.*, **29**, 722 (1964).

Novel Formation of 11-Ketoindeno[1,2-c]isocoumarin

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The recent paper[2] which demonstrated that the structure of the compound reported earlier[3] as dibenzo[*a*,*e*]cyclooctanetrione was actually 11-ketoindeno[1,2-*c*]isocoumarin (I) suggested a report on our work which arrived at the same conclusion. Our structure assignment was based on reactions, spectra, and synthesis.

Treatment of the isocoumarin I with alkali followed by acidification gave an acid which was identical with 2-(2-carboxyphenyl)-1,3-indandione[4] (II). This acid is oxidized in basic medium by bromine to 2,2′-benzil dicarboxylic acid and upon melting or refluxing with hydrochloric acid regenerates the isocoumarin I.

Oxidation of the isocoumarin I with chromic acid gave the same lactone that is formed when the isocoumarin is treated with nitric acid.[5] This compound

(1) Abstracted in part from the Ph.D. Thesis, June 1965, of J. K. Stowell.

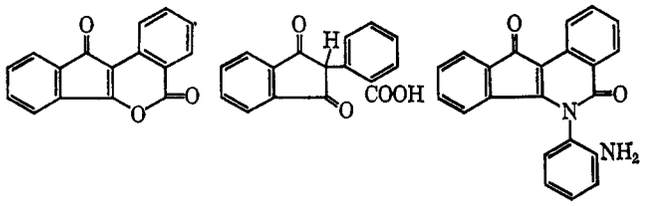
(2) P. Yates and E. Lewars, *Chem. Commun.*, 622 (1967).

(3) S. Wawzonek, *J. Am. Chem. Soc.*, **62**, 745 (1940).

(4) S. L. Shapiro, K. Geiger, and L. Freedman, *J. Org. Chem.*, **25**, 1860 (1960).

(5) M. Pailer, H. Worther, and A. Meller, *Monatsh.*, **92**, 1037 (1961).

was converted by alkali to 3-(2-carboxybenzoyl) phthalide which can be also made by the action of alkali on diphthalyl.[6]



I II III

Alkylation of 2-(2-carboxyphenyl-)-1,3-indandione with methyl iodide in alkaline solution gave 2-(2-carbomethoxyphenyl)-1,3-indandione which was identical with the ester obtained by direct esterification.[4]

Refluxing the isocoumarin I with *o*-phenylenediamine produced 5,11-diketo-6-(2-aminophenyl)indeno[1,2-*c*]-isoquinoline (III). This compound formed a N,N-diacetyl derivative with acetic anhydride and was reported in the earlier work[3] as a hydrated phenazine.

Experiment Section[7]

2-(2-Carboxyphenyl)-1,3-indandione(II).—The isocoumarin I (0.5 g) when dissolved in alkali gave a deep red solution. Acidification with dilute acid gave a theoretical amount of a white solid. Recrystallization from ethyl acetate and benzene gave 2-(2-carboxyphenyl)-1,3-indandione(II) which was identical with an authentic sample.[4]

Oxidation of 2-(2-Carboxyphenyl)-1,3-indandione.—An alkaline solution (35 ml of 20% KOH) of the isocoumarin (I) (0.2 g) containing methanol (10 ml) was treated with bromine in methanol until the red color disappeared. Acidification gave 2,2′-benzildicarboxylic acid (0.19 g) melting at 271–273° dec. Identification was made by comparison with an authentic sample.[8]

11-Ketoindeno[1,2-*c*]-isocoumarin (I).—2-(2-Carboxyphenyl)-1,3-indandione (0.5 g) was refluxed with concentrated hydrochloric acid until no more of the orange isocoumarin I was formed. The isocoumarin I (0.45 g) was recrystallized from benzene and gave orange crystals melting at 261–262°. A mixture with a sample prepared in the earlier work[3] melted at the same point.

Oxidation of 11-Ketoindeno[1,2-*c*]isocoumarin (I).—The isocoumarin I (1 g) in acetic acid (250 ml) was treated with a solution of chromium trioxide (1 g) in water (100 ml), and the resulting mixture was heated at 100° until all the solid dissolved and a color change was observed. Dilution with water and allowing the solution to stand for 2 days at 10° gave a white solid which was filtered and washed with cold benzene. Purification by crystallization from benzene gave white crystals (0.5 g) melting at 297–298° and identical with the lactone of 2-hydroxy-2-(*o*-carboxyphenyl)-1,3-indandione.[5]

1-(*o*-Carboxybenzoyl)phthalide.—The lactone of 2-hydroxy-2-(*o*-carboxyphenyl)-1,3-indandione (0.1 g) when dissolved in dilute potassium hydroxide gave a green color. Immediate acidification with dilute hydrochloric acid gave, after standing for 24 hr, a white solid (0.1 g). Recrystallization from benzene gave crystals melting at 246° followed by resolidification and remelting at 330°. This compound was identical with a sample prepared by the action of alkali on diphthalyl.[6]

2-(2-Carbomethoxyphenyl)-1,3-indandione.—The isocoumarin I (0.2 g) was dissolved in methanol (50 ml) treated previously with sodium (0.021 g), and treated with methyl iodide (3 ml); the solution was allowed to stand for 24 hr. Acidification gave a quantitative yield of a white solid which, after recrystallization from a mixture of benzene and hexane, melted at 154–155°. Continued heating at this point gave the isocoumarin I. This ester was identical with the product formed by the esterification of 2-(*o*-carboxyphenyl)-1,3-indandione.[5]

5,11-Diketo-6-(2-aminophenyl)indeno[1,2-*c*]isoquinoline (III).—The isocoumarin I (1 g) was refluxed with excess *o*-phenylenediamine and a trace of acetic acid in absolute ethanol (125 ml) for 3 hr. The red solid (1.25 g) which crystallized upon cooling melted at 289–290° after crystallization from benzene.

Anal. Calcd for $C_{22}H_{14}O_2N_2$: C, 78.11; H, 4.14; N, 8.28. Found: C, 78.30; H, 4.30; N, 8.30.

The infrared spectrum in Nujol had major peaks at 2.95, 5.91, 6.01, 6.14, and 6.48 mμ.

This compound was identified in earlier work[3] as a hydrated phenazine.

5,11-Diketo-6-(2-diacetylaminophenyl)indeno[1,2-*c*]isoquinoline.—The aminoisoquinoline III (0.34 g) was refluxed in excess acetic anhydride containing sodium acetate (0.5 g) for 24 hr. Dilution with water gave a red solid which melted at 265–266° after recrystallization from benzene to yield 0.32 g.

Anal. Calcd for $C_{26}H_{18}O_4N_2$: C, 73.93; H, 4.27; N, 6.64. Found: C, 73.74; H, 4.16; N, 6.77.

The infrared spectrum in Nujol had major peaks at 5.89, 5.99, 6.19, 6.68, and 8.11 mμ.

(6) C. Grabe and H. Schmalzigang, *Ann.*, **228**, 126 (1885).

(7) Melting points are corrected. Infrared spectra were determined on an Infracord spectrophotometer.

(8) C. Graebe and P. Juillard, *Ann.*, **242**, 214 (1887).

Synthesis of 3-Sulfopropionimide[1]

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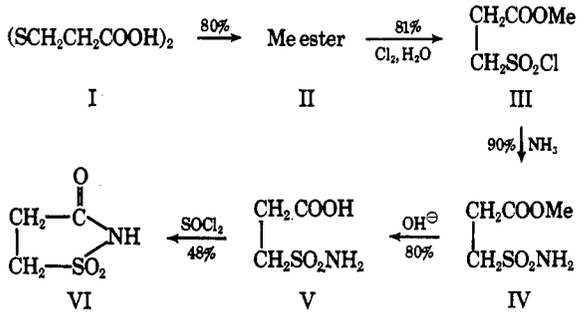
The synthesis of 3-sulfopropionimide (VI), a ring system similar to saccharin, is reported. This work culminated from efforts to prepare 4-amino-3-ketobutanesulfonamide as an analog of δ-aminolevulinic acid suggested earlier[2] for use as an anticancer agent. The synthetic pathway which resulted in 3-sulfopropionimide (VI) is outlined in Scheme I.

SCHEME I



After esterification of 3,3′-sulfopropionic acid, the sulfonyl chloride (III) was prepared by chlorine oxidation using water as an oxygen source and solvent instead of the acetic acid–water mixture which is customarily employed.[3]

By careful titration of the carbomethoxy sulfonyl chloride (III) with ammonia in ether, conversion to IV proceeded in 90% yield. Hydrolysis of the ester, methyl 3-sulfamoylpropionate (IV) with acid was accompanied by sulfonamide hydrolysis under surprisingly mild conditions (6 *N* HCl, 1 hr, reflux). When 1 *N* sodium hydroxide under carefully controlled con-

(1) This investigation was supported by U. S. Public Health Service Research Grant CAO 6520.

(2) C. C. Price and M. L. Beck, *J. Org. Chem.*, **27**, 210 (1962).

(3) S. W. Lee and G. Dougherty, *ibid.*, **5**, 81 (1940).