Anal. Calcd. for $C_{25}H_{34}O_7$ (446.52): C, 67.24; H, 7.68. Found: C, 67.65; H, 7.50.

21-Acetoxy-3,20-bisethylenedioxypregnane-5β,6β,11β,17α-tetrol (VIII) *and 21-acetoxy-3,20-bisethylenedioxypregnane-5α,6α,11β,17α-tetrol* (IXa). A solution of 2.33 g. of 21-acetoxy-3,20-bisethylenedioxy-5-pregnene-11β,17α-diol (VIIb) and 1.5 g. of osmic acid in 60 ml. of benzene and 1.5 ml. of pyridine was allowed to stand at room temperature for 5 days with occasional stirring. After the addition of 100 ml. of water, 70 ml. of methanol, and 10.8 g. each of sodium sulfite and potassium bicarbonate, the mixture was stirred for an additional 7 hr. The inorganic precipitate was collected by filtration and washed with chloroform. The combined filtrates were washed with saturated saline, dried, and evaporated. The resulting glass was chromatographed on 130 of silica gel. The fractions eluted with 20–40% acetone in ether gave, after crystallizations from acetone-ether, 700 mg. of a white powder, m.p. 178–184°. Four crystallizations of a small portion from acetone-ether gave the pure 5β,6β-diol VIII, m.p. 194–195°; $[\alpha]^{25}_{D} + 34°$; ν_{max} 3520, 1750, and 1250 cm.$^{-1}$

Anal. Calcd. for $C_{27}H_{42}O_{10}$ (526.61): C, 61.58; H, 8.04. Found: C, 61.80; H, 8.26.

The fractions eluted with 80% acetone in ether gave, after crystallization from acetone–petroleum ether, 450 mg. of crystals, m.p. 231–234°. Two further crystallizations of a small portion from acetone–petroleum ether gave the pure 5α,6α-diol IXa, m.p. 236–237°; $[\alpha]^{25}_{D} + 9°$; ν_{max} 3520, 1750 and 1240 cm.$^{-1}$

Anal. Found: C, 61.53; H, 8.40.

6α,21-Diacetoxy-3,20-bisethylenedioxypregnane-5α,11β,17α-triol (IXb). A solution of 200 mg. of 21-acetoxy-3,20-bisethylenedioxypregnane-5α,6α,11β,17α-tetrol (IXa) in 1.5 ml. of acetic anhydride and 4 ml. of pyridine was allowed to stand at room temperature for 18 hr., when it was poured into water. The resulting precipitate was collected by filtration to give 165 mg., m.p. 234–236°. Four crystallizations from acetone–petroleum ether gave the pure diacetate IXb, m.p. 231–232°; $[\alpha]^{25}_{D} + 5°$; ν_{max} 3450, 1740, and 1250 cm.$^{-1}$

Anal. Calcd. for $C_{29}H_{44}O_{11}$ (568.64): C, 61.25; H, 7.80; Ac, 15.13. Found: C, 60.96; H, 7.93; Ac, 15.48.

Attempted reduction of 5β,6β-epoxides with lithium aluminum hydride. A. To a solution of 250 mg. of 21-acetoxy-3,20-bisethylenedioxy-5β,6β-epoxy-9(11)-pregnen-17α-ol (II) in 20 ml. of tetrahydrofuran was added 500 mg. of lithium aluminum hydride and the mixture was heated under reflux for 3 hr. The mixture was cooled, water was added, and the resulting precipitate was separated by filtration and washed several times with chloroform. The combined filtrates were washed with water, dried, and evaporated. The crude glass so obtained was treated with 2 ml. of acetic anhydride in 5 ml. of pyridine at room temperature for 60 hr. Evaporation of the solvents followed by crystallization of the residue from acetone–petroleum ether gave 190 mg. (76%) of starting material II, m.p. 200–204°. Infrared spectral analysis showed the product to be identical with the starting material.

B. A solution of 250 mg. of 21-acetoxy-3,20-bisethylenedioxy-5β,6β,9α,11α-diepoxypregnan-17α-ol (IV) in 20 ml. of tetrahydrofuran containing 500 mg. of lithium aluminum hydride was heated under reflux for 8 hr. and allowed to stand at room temperature overnight. The crude product, isolated as described in *B* above, was treated with 1 ml. of acetic anhydride in 3 ml. of pyridine at room temperature overnight. After the addition of methanol the reaction mixture was concentrated, ether was added, and 50 mg. (20%) of crystals, m.p. 230–232°, was obtained. Admixture melting point with IV gave no depression. A crystallization from chloroform-ether gave 28 mg. of material, m.p. 235–236° whose infrared spectrum was identical with that of IV.

C. To a solution of 250 mg. of 21-acetoxy-3,20-bisethylenedioxy-5β,6β-epoxypregnane-11β,17α-diol (IIIb) in 35 ml. of tetrahydrofuran was added 750 mg. of lithium aluminum hydride. The mixture was refluxed for 4 hr., then was allowed to stand at room temperature overnight. After cautious addition of water to decompose excess reagent the residue was filtered, and the filtrate was evaporated to give 205 mg. of a low melting solid. The crude residue was treated with 0.8 ml. of acetic anhydride in 4 ml. of pyridine for 20 hr. at room temperature. The mixture was extracted with ethyl acetate, and the extract was washed with dilute sodium bicarbonate solution and dried. Evaporation gave 180 mg. (72%) of crystalline product, m.p. 194–198°. Crystallization from acetone–petroleum ether gave pure IIIb, m.p. 204–205°, $[\alpha]^{25}_{D} + 21°$. Infrared spectral analysis showed the product to be identical with an authentic sample[3] of starting material.

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Hammett Sigma Constants for *m*- and *p*-Benzoyl Groups[1a]

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During the course of a recent investigation,[1b] the Hammett sigma constants for *m*- and *p*-benzoyl groups were required. Values of these constants based upon ionization constant data[2] were not available. Furthermore, as the benzoyl group is often easily introduced into molecules and in certain situations might be a more convenient (*e.g.*, less reactive) substituent than some of the other carbonyl functions, we considered that a knowledge of the σ constants for the benzoyl group might be of value in substituent effect studies. The isomeric *m*- and *p*-benzoylbenzoic acids were therefore prepared, and their ionization constants were determined and compared with those of five other acids having substituents with well established σ values.

EXPERIMENTAL

p-Methylbenzophenone. A mixture of 15 g. of anhydrous aluminum chloride, 80 cc. of carbon disulfide and 14.1 g. of benzoyl chloride was refluxed until homogeneous. Then 10.0 g. of dry toluene was added. After refluxing for 30 min., the solvent was distilled. The mixture obtained by stirring this residue into ice and concd. hydrochloric acid was extracted with ether. The ether solution was washed with 10% hydrochloric acid and water and dried over calcium chloride. Distillation of the residue obtained by evaporation of the ether solution gave 14.2 g. (72%) of *p*-methylbenzophenone as a colorless oil, b.p. 140–145° at 6.5 mm. (reported[3] b.p. 327–328°) which solidified on standing. It was crystallized from petroleum ether (b.p. 30–65°) to obtain 10.5 g. (53%)

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(1) (a) This research was sponsored by a Frederick Gardner Cottrell grant from the Research Corporation. (b) W. N. White, D. Gwynn, R. Schlitt, C. Girard, and W. Fife, *J. Am. Chem. Soc.*, **80**, 3271 (1958).

(2) D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, **23**, 420 (1958).

(3) K. v. Auwers and P. Strodter, *Ber.*, **59**, 533 (1926).

of the ketone as small white needles, m.p. 56.0–57.2° (lit.[3] m.p. 59°).

p-Benzoylbenzoic acid. A solution of 35 g. of chromium trioxide and 25 cc. of concd. sulfuric acid in 80 cc. of water and 130 cc. of glacial acetic acid was added dropwise to a hot solution of 25.0 g. of *p*-methylbenzophenone in 130 cc. of glacial acetic acid at such a rate as just to maintain boiling. Then the mixture was refluxed 45 min., cooled, and poured into 2 l. of water. The solid was collected, washed well with water, and dissolved in a 100 cc. of 10% aqueous potassium hydroxide. The basic solution was filtered and acidified with concd. hydrochloric acid. The solid was filtered off, washed with water, and dried. After three recrystallizations from toluene there was obtained 21.2 g. (73%) of *p*-benzoylbenzoic acid as fine, white crystals, m.p. 195.0–195.5° (lit.[4] m.p. 194°).

m-Toluyl chloride. A solution of 20.4 g. of *m*-toluic acid in 36.0 g. (22.0 cc.) of thionyl chloride was refluxed 3 hr. Distillation gave 21.5 g. (92%) of *m*-tolyl chloride as a colorless oil, b.p. 78–79° at 4 mm. (reported[5] b.p. 105° at 20 mm.).

m-Methylbenzophenone. This compound was prepared in the manner described above for *p*-methylbenzophenone using *m*-toluyl chloride and benzene instead of benzoyl chloride and toluene, respectively. There was obtained after distillation a 55% yield of *m*-methylbenzophenone as a colorless oil, b.p. 140–141° at 3.5 mm. (lit.[6] b.p. 183–185° at 16 mm.).

m-Benzoylbenzoic acid. *m*-Methylbenzophenone was oxidized in the same way as described for *p*-methylbenzophenone to obtain a 73% yield of thrice-recrystallized fine white crystals, m.p. 162.5–163.2° (lit.[4] m.p. 161–162°).

p-Acetaminobenzoic acid. To a boiling solution of 10.0 g. of *p*-aminobenzoic acid in 100 cc. of water was added slowly 8.7 g. of acetic anhydride. The semisolid mixture was cooled and the product was filtered and washed with water. It was dissolved in hot aqueous acetone, clarified with charcoal, and allowed to crystallize. The crystallization was repeated twice to give 3.98 g. (31%) of *p*-acetaminobenzoic acid as white plates, m.p. 263.8–264.8° (reported[7] m.p. 256.5°).

m-Acetaminobenzoic acid. This compound was prepared from *m*-aminobenzoic acid by the procedure described above for conversion of *p*-aminobenzoic acid to *p*-acetaminobenzoic acid. There was obtained a 37% yield of fine white needles, m.p. 257.2–257.8° (lit.[7] m.p. 250°).

Substituted acids. Samples of *p*-bromobenzoic acid, *p*-nitrobenzoic acid, *p*-anisic acid, and benzoic acid obtained from commercial sources were purified by several crystallizations from aqueous ethanol. The melting points of these are listed in Table I.

TABLE I

X-Benzoic Acids

X	M.P.	Lit. M.P.
p-Br	254.4–255.6	254.5[a]
p-NO_2	239.8–241.7	239.2[b]
p-CH_3O	182.7–184.0	185[c]
p-CH_3	177.2–177.9	179.6[b]
H	121.0–121.8	122.4[d]
p-C_6H_5CO	195.0–195.5	194[e]
m-C_6H_5CO	162.5–163.2	161–162[2]
p-CH_3CONH	263.8–264.8	256.5[f]
m-CH_3CONH	257.2–257.8	250[f]

[a] P. J. Montague, *Rec. trav. chim.*, **43**, 642 (1924). [b] D. H. Andrews, G. Lynn, and J. Johnston, *J. Am. Chem. Soc.*, **48**, 1285 (1926). [c] E. E. Harris and G. B. Frankforter, *J. Am. Chem. Soc.*, **43**, 3149 (1926). [d] F. W. Schwab and E. Wickers, *J. Res. Natl. Bur. Stand.*, **34**, 333 (1945). [e] Ref. 4. [f] Ref. 7.

Determination of the pK$_a$'s of the acids. The solvent for these studies was prepared by mixing 1500 cc. of boiled methanol and 500 cc. of boiled distilled water. A solution of $0.05021N$ carbonate-free sodium hydroxide was prepared by the dissolution of about 0.50 g. of freshly cut sodium in 500 cc. of this solvent (it was standardized against potassium acid phthalate using phenolphthalein as indicator).

About 0.002 mole of the acid was accurately weighed into a 100-cc. volumetric flask and was diluted to volume with the solvent. Aliquots (25.00 cc.) of this solution were pipetted into three glass-stoppered flasks and to the first, second, and third of these was added 2.00 cc., 5.00 cc., and 7.00 cc., respectively, of the sodium hydroxide solution. These solutions were poured into electrolytic beakers set in a constant temperature bath (39.80° ± 0.02°) and allowed to stand ten minutes with occasional swirling to attain temperature equilibrium. The *p*H's of these solutions were determined using a set of calomel and glass electrodes in conjunction with a Beckman Model GS pH-meter. After the electrodes were introduced into a solution about 10 min. were allowed to elapse before taking any measurements so that equilibrium could be reached. The meter was set at high sensitivity and readings were made using the duodial after the latter had been set using a standard buffer solution. After each unknown solution was read the meter and electrodes were rechecked against the standard buffer to insure that there was no change in the operating characteristics of the instrument system. In addition the *p*H of each solution was double-checked using a different set of electrodes. All of the values obtained agreed within one part in 500.

The *p*H of each solution, obtained from the meter readings, was used together with the concentrations of acid and acid salt (calculated from the weight of acid and the volumes of acid and base used) in the solution to find the *p*K$_a$. For this purpose Henderson's equation[8] was employed. The results are shown in Table II.

TABLE II

*p*K$_a$'s of X-Benzoic Acids in 1:3 v./v. Water-Methanol at 39.8°

X	*p*K$_a$
p-Br	5.579 ± 0.012
p-NO_2	4.920 ± 0.004
p-CH_3O	6.304 ± 0.016
p-CH_3	6.169 ± 0.022
H	5.995 ± 0.013
p-C_6H_5CO	5.373 ± 0.004
m-C_6H_5CO	5.486 ± 0.003
p-CH_3CONH	6.033 ± 0.011
m-CH_3CONH	5.811 ± 0.007

RESULTS AND DISCUSSION

The ionization constants of *m*- and *p*-benzoyl benzoic acids (and also of *p*-bromobenzoic, *p*-nitrobenzoic, *p*-toluic, *p*-anisic, and benzoic acids) were determined at 39.8° in 75% methanol- 25% water by volume. The use of a solvent containing but little water was made necessary by the low solubility of the benzoylbenzoic acids, even though the concentrations used were low (about $0.02M$).

The average of the average deviations of the measured *p*K$_a$'s is ±0.010 *p*K$_a$ unit. The deviations

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(4) M. E. Smith, *J. Am. Chem. Soc.*, **43**, 1921 (1921).

(5) G. T. Morgan and C. R. Porter, *J. Chem. Soc.*, 1258 (1925)

(6) J. v. Braun, G. Manz, and E. Reinsch, *Ann.*, **468**, 285 (1929).

(7) F. Ullmann and J. Bex Vzbachian, *Ber.*, **36**, 1801 (1903).

(8) S. Glasstone, *Textbook of Physical Chemistry*, Van Nostrand, New York, 1940, p. 982.

for an individual acid showed no systematic variation even though the salt concentration varied from about 0.0037*M* to 0.022*M*.

Using the σ values for *p*-Br, *p*-NO_2, *p*-CH_3O, *p*-CH_3, and H tabulated by McDaniel and Brown[2] the following relation between σ and pK_a for the ionization of substituted benzoic acids in 25% water- 75% methanol by volume at 39.8° was determined using the least squares procedure.

$$pK^x_a = -1.339\,\sigma_x + 5.947$$

This equation can be used to calculate σ values from pK_a's. Inserting the pK_a values of *m*- and *p*-benzoylbenzoic acids, one obtains[9]:

$$\sigma(m\text{-}C_6H_5CO) = +0.343$$

$$\sigma(p\text{-}C_6H_5CO) = +0.429$$

Comparing these with the σ values for *m*- and *p*-acetyl[2] (+0.376 and +0.502, respectively) it is obvious that the benzoyl group is not quite as strong an electron-withdrawing substituent as the acetyl group. This may be due to reduction of the electronegative character of the carbonyl in the benzoyl group by its conjugation with the phenyl ring from which it can withdraw electrons by resonance.

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[9] The constants obtained for acetamino groups using the same equation are σ (*p*-CH_3CONH) = −0.086 and σ (*m*-CH_3CONH) = +0.102. The values reported by McDaniel and Brown (Ref. 2) are 0.00 and +0.21 respectively.

Communications TO THE EDITOR

Hydrazine Reduction of α,β-Epoxy Ketones to Allylic Alcohols

Sir:

A preliminary investigation has demonstrated a useful, general, and previously unobserved reductive reaction of hydrazine with α,β-epoxy ketones.[1] The reaction is, in effect, an eliminative Kishner reduction of an α-substituted ketone,[2] *proceeding rapidly at room temperature* with the evolution of nitrogen and formation of an allylic alcohol.

Although optimum conditions remain to be determined, the reduction can be carried out in alcohol solution containing two to three equivalents of hydrazine hydrate and *ca.* 0.2 equivalents of acetic acid. Under these conditions the reaction mixture becomes slightly warm and evolution of nitrogen is effectively complete *in five minutes:* isophorone oxide[3] (89%),[4] 2,3-epoxycyclohexanone[5] (75%), 2,3-epoxybutanone[5a] (50%), glycidaldehyde[6] (20%). A useful alternative procedure, simply treating with excess hydrazine hydrate, can be applied to the reduction of α,β-epoxy ketones only slightly soluble in hydrazine hydrate: 4β,5-epoxy-3-coprostanone[7] (90%), isophorone oxide (69%). However, using this procedure the more soluble epoxy ketones give relatively poor yields: 2,3-epoxycyclohexanone (26%), 2,3-epoxybutanone (5%).

The reaction of hydrazine with α,β-epoxy ketones was investigated when a current study necessitated the preparation of certain sesquiterpenoid precursors containing the $\Delta^{1,2}$-9-octalol system. It was thought that an effective route[8] to this system might be a simple oxidation-reduction sequence starting from the available $\Delta^{1,9}$-2-octalones.[9] The oxidation step, epoxidation of the enone to the epoxy ketone, is an established synthetic method,[10] and the reduction step, the subject of this communication, was therefore first attempted with a known model compound, 4β,5-epoxy-3-coprostanone (I).

A two-phase mixture of I (7 g.) and excess hydrazine hydrate, with no added solvent or base, rapidly evolved a gas (90% yield) on heating to

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[1] The only products isolated from reported reactions of α,β-epoxy ketones with hydrazine itself are of the same type as those obtained from substituted hydrazines, namely pyrazolines and pyrazoles. See T. L. Jacobs, *Heterocyclic Compounds*, Vol. 5, R. C. Elderfield, ed., Wiley, New York, 1957, p. 68.

[2] For a review of the eliminative Kishner reduction of α-substituted ketones see N. J. Leonard and S. Gelfand, *J. Am. Chem. Soc.*, **77**, 3272 (1955).

[3] G. B. Payne, *J. Org. Chem.*, **24**, 719 (1959); R. L. Wasson and H. O. House, *Org. Syntheses*, **37**, 58 (1957).

[4] Yields are based on nitrogen evolution unless otherwise specified. Nitrogen was identified mass spectroscopically and measured volumetrically.

[5] (a) N. C. Yang and R. A. Finnegan, *J. Am. Chem. Soc.*, **80**, 5845 (1958); (b) H. O. House and R. L. Wasson, *J. Am. Chem. Soc.*, **79**, 1488 (1957).

[6] Supplied by Shell Development Co., Emeryville, Calif.; purity not established.

[7] J. I. Shaw and R. Stevenson, *J. Chem. Soc.*, 3549 (1955).

[8] A reasonable but more involved synthesis might be: $\Delta(1,9)$-2-octalone → $\Delta(1,9)$-octalin → $\Delta(1,2)$-9-octalol. See V. Georgian, R. Harrisson, and N. Gubisch, *J. Am. Chem. Soc.*, **81**, 5834 (1959) and G. O. Schenk and O. A. Neumüller, *Ann.*, **618**, 194 (1958).

[9] E. D. Bergmann, *Org. Reactions*, **X**, 179 (1959).

[10] First investigated by E. Weitz and A. Scheffer, *Ber.*, **54**, 2327 (1921). See also refs. 3 and 5 and G. B. Payne, *J. Org. Chem.*, **26**, 250 (1961).