In calculating the compositions of the menthene mixtures, the relation $\alpha_{obs} = \alpha_3 x + \alpha_2 y$ was used,[19] where α_{obs} = observed rotation; α_3 and α_2 = rotations of pure *d-p*-3-menthene and pure *d-trans-p*-2-menthene, respectively; x and y = mole fractions of 3-menthene and 2-menthene, respectively. After racemization of the 3-menthene present, $\alpha_{obs} = \alpha_2 y$. The 2-menthene obtained from N,N-dimethyl-*d*-neomenthylamine oxide had α_D +109.06°; since this is the highest value reported and vapor-phase chromatography indicated this 2-menthene was pure, α_2 = +109.06° was used subsequently in the calculation of its mole fraction, y. Then, x can be calculated as $1 - y$, or as $\alpha_3 x$ = the drop in rotation on racemization of 3-menthene, using α_3 = +88.0°. Pure *d-p*-3-menthene has not been prepared, and this value is one which was calculated by Hückel.[5] The results are listed in Table I, and show values of x in excellent agreement when calculated by both methods.

It will be observed that there was a small loss of rotation on treatment of pure 2-menthene with alcoholic *p*-toluenesulfonic acid, which corresponds to a value of 0.994 for y. By difference, x = 0.006 for the material racemized. The rotation of the material racemized can be calculated as α_3 = drop in rotation/x, giving α_3 = 103.2°. Since this is nearly the rotation of 2-menthene, it may mean that a small amount of the 2-menthene was racemized rather than indicating the presence of 3-menthene. Correction of the other results to allow for 0.6% racemization of 2-menthene does not appreciably change the figures. Composition of the menthenes given in Table I was calculated from the rotations listed in Table II.

Analysis of Menthenes. (b) Gas Chromatography.—Approximately 0.005 ml. samples of the olefin mixtures were injected into a column (200 × 0.6-cm.) containing 48–100 mesh firebrick impregnated in a 5/2 ratio with tetraethylene glycol that had been saturated with silver nitrate at 100°. The column was heated to 88° and equipped with a preheater at 150°. The carrier gas was helium at a pressure of 12.7 p.s.i. A thermal conductivity cell was used as detector. The composition of each olefin mixture was computed from a chromatogram by determining the ratio of individual peak areas, obtained from the product of the peak height and its half-band width.[12] The 2-menthene obtained from N,N-dimethyl-*d*-neomenthylamine oxide showed only a single peak. The olefins obtained from the other three pyrolyses showed but two peaks, those for 2-menthene and 3-menthene, varying only in relative size.

(19) H. Landolt, "Optical Rotating Power of Organic Substances and Its Applications," 2nd ed., Chemical Publishing Co., Easton, Pa., 1902 (translated), p. 240.

TABLE II

OPTICAL ROTATION OF MENTHENES FORMED BY PYROLYSES

Compound pyrolyzed	Rotations of menthenes produced ($\alpha^{25}D$, pure liq., l = 1 dm.) Before racemization	After racemization
Dimethyl-*d*-neomenthylamine oxide	109.06°	108.44°
Dimethyl-*l*-menthylamine oxide	101.28	70.64
Trimethyl-*l*-menthylammonium hydroxide	106.55	95.31
Trimethyl-*d*-neomenthylammonium hydroxide	89.62	10.50

Attempted Isomerization of 2-Menthene to 3-Menthene—A mixture of 2- and 3-menthene (3 ml.), having $\alpha^{25}D$ + 106.34° (pure liq., l = 1 dm.), was heated in a sealed tube with 0.5 ml. of 50% aqueous tetramethylammonium hydroxide at 150° for 2 days. The reaction mixture was diluted with 50 ml. of pentane, the aqueous phase was separated, and the pentane solution was dried over magnesium sulfate. Distillation and redistillation of the olefin obtained afforded a menthene mixture having α_D +105.64° (pure liq., l = 1 dm.). Calculations based on values of α_3 = 88.0° for *d*-3-menthene, and α_2 = 109.06° for *d*-2-menthene, indicated that the composition of the mixture was shifted from 87.1% 2-menthene and 12.9% 3-menthene to 83.8% 2-menthene and 16.2% 3-menthene. If the drop in rotation was caused by double-bond migration, this corresponds to a conversion of 4% of the 2-menthene originally present into optically inactive 3-menthene. Apparently 2-menthene is not appreciably converted into 3-menthene under the conditions of the Hofmann decomposition.

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[CONTRIBUTION FROM AVERY LABORATORY, THE UNIVERSITY OF NEBRASKA]

Esters of β-Diazopropionic Acid. A New Synthesis of β-Aryloxypropionic Acids[1,2]

BY LOREN L. BRAUN[3] AND J. H. LOOKER

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Ethyl and benzyl β-diazopropionate have been prepared *ex situ* from the corresponding nitrosocarbamate by a novel procedure. Reaction of several phenolic and enolic compounds with the diazopropionic ester in methanolic ether has led to the β-aryloxypropionic ester, which upon acid hydrolysis (or hydrogenolysis when appropriate) gave the corresponding β-aryloxypropionic acid. Cyclization of β-(6-bromo-2-naphthoxy)-propionic acid with polyphosphoric acid resulted in 8-bromo-1-benzo[f]chromanone.

Esters of diazoacetic acid and their application to a variety of organic syntheses are well-known.[4] However, diazo esters in which diazo and carbonyl functions are separated by one or more methylene groups appear to have been prepared infrequently.[5] The present paper describes the preparation of ethyl and benzyl β-diazopropionate by a simple but novel *ex situ* procedure which does not involve a distillation step, and the utility of these diazo esters in syntheses of β-aryloxypropionic acids and esters.

The synthesis of diazopropionic esters was investigated by both *in situ* and *ex situ* procedures.[6] The necessary starting material in each case was the N-nitrosocarbamate ($C_2H_5O_2CN(NO)CH_2CH_2CO_2R$, R = C_2H_5 or $CH_2C_6H_5$), which was obtained by nitrosation of ethyl or benzyl N-carbethoxy-β-aminopropionate (N-carbethoxy-β-alanine ethyl or benzyl ester) and used without purification. A classical *in situ* procedure[7] utilizing

(1) Abstracted from a portion of a thesis submitted in partial fulfillment of requirements for the Ph.D. degree at the University of Nebraska by Loren L. Braun, 1956.

(2) Financial support of this investigation through a Frederick Gardner Cottrell Grant to the University of Nebraska by the Research Corporation of New York is gratefully acknowledged.

(3) Department of Chemistry, Idaho State College, Pocatello, Idaho.

(4) (a) N. C. Hancox, *Roy. Australian Chem. Inst. J. and Proc.*, **16**, 282 (1949); (b) C. D. Gutsche in "Organic Reactions," Vol. VIII, John Wiley and Sons, Inc., New York, N. Y., 1954, p. 364; (c) R. Huisgen, *Angew. Chem.*, **67**, 439 (1955).

(5) Ethyl 6-diazohexanoate has been prepared *in situ* by D. W. Adamson and J. Kenner, *J. Chem. Soc.*, 184 (1939).

(6) For a discussion of the terms *in situ* and *ex situ*, see reference 4b, p. 394.

(7) For a discussion of the various procedures available for the synthesis of diazoalkanes, see reference 4; also, W. E. Bachmann and

TABLE I

ALKYLATION WITH ETHYL β-DIAZOPROPIONATE *ex situ*

$$ArOH + CHN_2CH_2CO_2C_2H_5 \longrightarrow ArOCH_2CH_2CO_2C_2H_5 + N_2$$

ArOH	Yield,[a] %	M.p.,[f] °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
I	5.1[b]	95–97[b,c,h]	$C_9H_{10}O_3$[b]						
II	50	55.5–58[e]	$C_{11}H_{13}NO_5$	55.25	55.33	5.48	5.42	5.86	6.14
III	60	59–60[f]	$C_{11}H_{12}BrNO_5$	41.52	41.59	3.80	3.81	4.40	4.41
IV	53	49–51[e]	$C_{11}H_{12}BrNO_5$	41.52	41.46	3.80	3.56	4.40	4.57
V[g]	23[b]	122–124[b,d,e]	$C_9H_8N_2O_7$[b]	42.20[b]	42.63[b]	3.15[b]	3.27[b]	10.94[b]	11.06[b]
				Bromine, %					
VI	69	46.5–47[f]	$C_{15}H_{15}BrO_3$	55.74	55.44	4.68	4.67	24.73	25.26
VII	33	87–89[e,h]	$C_{15}H_{15}BrO_3$	55.74	55.89	4.68	4.96	24.73	25.02

[a] Of ester, unless otherwise noted; corrected for phenol recovered by acidification of NaOH extracts of ethereal reaction mixture. [b] Of the free acid; ester not isolated in pure state. [c] Lit.[11a] m.p. 97–98°. [d] Melted partially at 113–114°; double m.p. persisted after recrystn. from water, chloroform and benzene–petr. ether. [e] Recrytsd. from benzene–petr. ether (b.p. 30–60°). [f] Recrystd. from 95% ethanol. [g] Added in benzene soln. to ethereal soln. of ethyl β-diazopropionate. [h] Uncorr. [i] Corrected, unless otherwise noted.

phenol and the nitrosourethan in alkaline ethanolic solution gave 6 and 14% yields of β-phenoxypropionic acid based on the ethyl and benzyl carbamate, respectively. Benzyl β-phenoxypropionate was isolated and characterized, and converted in 66% yield to the free acid by a hydrogenolysis procedure. In our hands, the modification of Samour and Mason[8] did not lead to any detectable quantity of β-diazopropionic ester.

A satisfactory *ex situ* preparation of esters of β-diazopropionic acid was developed, only after considerable unsuccessful experimentation,[9] through a novel approach to decomposition of the nitrosourethan. An ether solution of the ethyl or benzyl N-nitroso-N-carbethoxy-β-aminopropionate was placed over a solution of 10–12% aqueous potassium hydroxide solution and treated with methanol. Upon vigorous shaking of the heterogeneous reaction mixture, a stable deep yellow color appeared in the supernatant methanolic ether layer. The quantity of methanol to be added was determined by withdrawing a small portion of the ethereal solution, which was treated with acetic acid. After nitrogen evolution subsided, a green color (presumably due to unreacted nitrosourethan) indicated further addition of methanol to be necessary. No attempt was made to isolate the β-diazopropionic esters in a pure condition because of their possible explosive character. Evidence for the existence of ethyl β-diazopropionate rests on the method of synthesis, yellow color of the ethereal solution, lability in acid, and reaction with phenolic compounds to give β-phenoxypropionic esters, which were hydrolyzed to the free acid (including the known β-phenoxypropionic acid). Although less thoroughly characterized, benzyl β-diazopropionate showed similar properties and reactivity.

In Table I are presented data relating to the reaction of ethyl β-diazopropionate *ex situ* with the following phenols and naphthols: phenol (I), *p*-nitrophenol (II), 2-bromo-4-nitrophenol (III), 4-bromo-2-nitrophenol (IV), 2,4-dinitrophenol (V), 1-bromo-2-naphthol (VI) and 6-bromo-2-naphthol (VII). The detailed reaction conditions employed are outlined in the Experimental section (on Ethyl β - (2 - Bromo - 4 - nitrophenoxy) - propionate). β-Aryloxypropionic acids have been prepared previously by the action of metallic salts of phenols on β-halopropionic acids,[10] by the addition of phenols to acrylates and subsequent hydrolysis of the products,[11] and by the reaction of β-propiolactone with phenols or the metallic salts of phenols.[12] In the present study, the phenolic compound in ether (solution I) was added to a methanolic ether solution of the β-diazopropionic ester until gas evolution ceased. After the reaction was complete, the depleted ethereal solution of the phenol (solution II) was retained. The quantity of the phenol added was then calculated by difference, as described in Experimental. Because of difficulty in estimating the exact instant when gas evolution ceased, excess phenolic compound usually was added. The yields of β-phenoxypropionic esters reported in Table I are based on the phenol which actually reacted, a quantity obtained by determining the excess phenol recovered upon extraction of the ethereal reaction mixture with 1% sodium hydroxide and making a suitable correction. Even thus corrected, in several instances the yields reported remain minimum approximations because the moderate water solubility of the phenol

W. S. Struve in "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 38; B. Eistert (translated and revised by F. W. Spangler) in "Newer Methods of Preparative Organic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1948, p. 513.

(8) C. M. Samour and J. P. Mason, THIS JOURNAL, **76**, 441 (1954), decomposed the nitrosourethan in ethanol solution by the addition of sodium hydroxide pellets, decanted the resulting diazo solution from the remaining base, and added it slowly to an alcohol or ether solution of acid or phenol.

(9) Thus both addition of an absolute isopropyl alcohol solution of the nitrosourethan to absolute isopropyl alcohol containing 3–4 pellets of sodium hydroxide and addition of the nitrosourethan in absolute isopropyl alcohol to 3% sodium hydroxide in isopropyl alcohol gave transient yellow colors, presumably indicative of decomposition of the initially formed β-diazopropionic ester. Simultaneous addition of the nitrosourethan in abs. isopropyl alcohol and 3% NaOH in abs. isopropyl alcohol to the reaction mixture so as to maintain a *p*H of 8–10 gave a stable yellow colored solution, but also a large amount of finely divided white solid which could not be removed by any means studied.

(10) (a) F. Arndt and B. Kallner, *Ber.*, **57B**, 202 (1924); (b) W. H. Perkin, Jr., J. Ray and R. Robinson, *J. Chem. Soc.*, 941 (1926); (c) P. F. Wiley, THIS JOURNAL, **73**, 4205 (1951).

(11) (a) R. H. Hall and E. S. Stern, *J. Chem. Soc.*, 2035 (1949); (b) G. B. Bachman and H. A. Levine, THIS JOURNAL, **70**, 599 (1948).

(12) (a) T. L. Gresham and F. W. Shaver, U. S. Patent 2,449,991; *C. A.*, **43**, 1054 (1949); (b) T. L. Gresham, J. E. Jansen, F. W. Shaver, R. A. Bankert, W. L. Beears and M. G. Prendergast, THIS JOURNAL, **71**, 661 (1949).

TABLE II

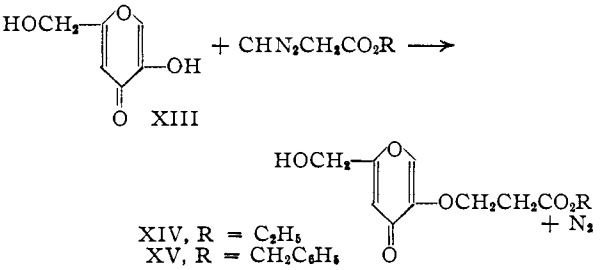
β-ARYLOXYPROPIONIC ACIDS FROM HYDROLYSIS OF ETHYL ESTER

Acid	Yield,[a] %	M.p.,[b] °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
VIII[c]	78	142–143.5[i]	$C_9H_8BrNO_5$	37.26	37.38	2.78	2.87	4.83	4.89
IX[d]	24	138–139.5[j]	$C_9H_8BrNO_5$	37.26	37.56	2.78	2.68	4.83	4.96
X[e]	23[h]	122–124	$C_9H_8N_2O_7$	See Table I					
								Bromine, %	
XI[f]	73	158–160[k]	$C_{13}H_{11}BrO_3$	52.90	53.25	3.76	4.18	27.08	27.07
XII[g]	58	182–185[i,l]	$C_{13}H_{11}BrO_3$	52.90	53.13	3.76	3.94	27.08	27.54

[a] Based on ethyl ester of the β-aryloxypropionic acid. [b] Corrected. [c] For hydrolysis procedure, see Experimental. [d] Hydrolysis medium, 4 *N* aq. HCl; reflux period 3 hr.; crude acid isolated direct from reaction mixture. [e] Hydrolysis conditions as in *d*; isolation of acid by ether extraction of hydrolysis mixture and subsequent extraction of ether extract with 10% Na_2CO_3. [f] Hydrolysis medium, concd. HCl; reflux period 2.5 hr.; crude acid isolated direct from reaction mixture. [g] Hydrolysis as in *f*, except for 7 hr. reflux. [h] Based on 2,4-dinitrophenol; ester not isolated in pure state. [i] Recrystd. from benzene. [j] Recrystd. from chloroform. [k] Recrystd. from benzene–petr. ether (b.p. 30–60°). [l] Previously described by M. N. Green, *et al.*, THIS JOURNAL, **76**, 48 (1954), as melting 179–181°.

made quantitative recovery a practical impossibility. The apparent low yield of β-phenoxypropionic acid can be attributed partly to the latter factor. It is interesting to note that attempted alkylation of *p*-nitrophenol and 2-bromo-4-nitrophenol with ethyl β-diazopropionate *in situ* failed. In our hands, reaction of 1-bromo-2-naphthol with β-propiolactone[12] gave a 15% yield of β-(1-bromo-2-naphthoxy)-propionic acid, which can be compared with a 50% yield obtained in the present procedure. A reaction between 2-bromo-4-nitrophenol and β-propiolactone proved unsatisfactory because of difficulty encountered in separating the product from the unreacted, strongly acidic phenol with sodium bicarbonate,

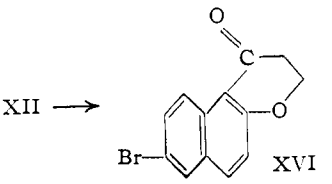
The following β-aryloxypropionic acids have been prepared by acid-catalyzed hydrolysis of the appropriate ethyl ester: β-(2-bromo-4-nitrophenoxy)-propionic acid (VIII), β-(4-bromo-2-nitrophenoxy)-propionic acid (IX), β-(2,4-dinitrophenoxy)-propionic acid (X), β-(1-bromo-2-naphthoxy)-propionic acid (XI), and β-(6-bromo-2-naphthoxy)-propionic acid (XII). Yield data and properties of the acids VIII–XII are presented in Table II.



A reaction between kojic acid (XIII) and the β-diazopropionic esters was observed only when XIII was added in dry, powdered form. Structures XIV and XV are advanced for the reaction products on the basis of combustion analyses and negative ferric chloride tests. This result of O-alkylation is particularly interesting since Woods has shown that in the cyanoethylation of kojic acid, C-alkylation takes place.[13] Attempted hydrolysis of XIV with 4 *N* hydrochloric acid gave a small yield of material giving a positive ferric chloride test, Catalytic debenzylation of XV gave an oil which resisted all attempts at crystallization.

(13) L. L. Woods, THIS JOURNAL, **74**, 3959 (1952).

Possible cyclization of all acids in Table II to the chromanone with polyphosphoric acid[14] was investigated. β-(6-Bromo-2-naphthoxy)-propionic acid (XII) gave 8-bromo-1-benzo(f)chromanone (XVI)[11b] in 13.7% yield.



β-(1-Bromo-2-naphthoxy)-propionic acid gave a minute yield of unidentified crystalline yellow solid. All other acids in Table II gave products, the infrared spectra of which showed absorption bands in the region 1764–1775 cm.$^{-1}$, which probably are due to carboxylic anhydride carbonyl groups.[15] The reaction product from β-(2,4-dinitrophenoxy)-propionic acid gave carbon–hydrogen values in fair agreement with theory for the carboxylic anhydride.

There was no band in the region 3520–3730 cm.$^{-1}$, indicating the absence of a free hydroxyl group. A band at 3140 cm.$^{-1}$ was weak but sharp, thus excluding an associated hydroxyl group, which exhibits a broad band in this region, Also there was no weak broad band in the region 2500–2900 cm.$^{-1}$.

The infrared spectrum for the product of the attempted cyclization of β-(2,4-dinitrophenoxy)-propionic acid exhibited bands at 3140w, 1790sh, 1775s, 1614s, 1542m, 1517m, 1347s, 1315w, 1291m, 1252m, 1245sh, 1214m, 1144s, 1070s, 1020s, 995w, 907w, 890w, 832s, 757w, 740m, 702w, 676w, and 642w cm.$^{-1}$ (where sh = shoulder, s = strong, m = medium, w = weak).

Experimental[16]

N-Carbethoxy-β-aminopropionic Acid (N-Carbethoxy-β-alanine).—The method of preparation employed was a modification of the synthesis of N-carbobenzoxy-β-aminopro-

(14) J. D. Loudon and R. D. Razdan, *J. Chem. Soc.*, 4299 (1954).

(15) F. A. Miller in "Organic Chemistry," Vol. III, edited by H. Gilman, John Wiley and Sons, Inc., New York, N. Y., 1953, pp. 140–141, 143–150.

(16) Melting points are uncorrected except where otherwise noted. Infrared spectra of Nujol mulls in sodium chloride cells were recorded with a Perkin–Elmer model 21 spectrophotometer.

pionate.[17] A few drops of phenolphthalein solution were added to a solution of 356 g. (4.0 moles) of β-alanine in 500 ml. of water. Then 10% sodium hydroxide solution was added dropwise until the mixture became basic to phenolphthalein. The reaction flask was then cooled in an ice-bath, and the dropwise addition of 10% sodium hydroxide continued simultaneously with the dropwise addition of 466.5 g. (4.3 moles) of ethyl chlorocarbonate to the stirred mixture at such a rate that it remained basic to phenolphthalein. The addition required about six hours.

The reaction mixture was acidified with concentrated hydrochloric acid to a *p*H of less than one, and was then extracted with two 500-ml. portions and four 200-ml. portions of chloroform. The combined extracts were dried over anhyd. sodium sulfate. After solvent removal (last traces under water-pump vacuum) the solid residue was recrystallized from benzene to give white crystalline N-carbethoxy-β-alanine, m.p. 57–59° (lit.[18] m.p. 59°), yield 553.0 g. (85.8%).

Ethyl N-Carbethoxy-β-aminopropionate.—A solution of 200 g. (1.24 moles) of N-carbethoxy-β-aminopropionic acid in 500 ml. of absolute ethanol was cooled in an ice-bath, and saturated with dry hydrogen chloride. After standing overnight the excess ethanol was removed (water-pump) leaving a clear, colorless oil. The oil was redissolved in 400 ml. of absolute ethanol and the above process repeated. The residual oil was distilled through a 14 × 0.5 in. Vigreux column. Three fractions were collected: (a) b.p. 111–112° (1.6 mm.) contained an unidentified white solid which gave it a cloudy appearance; (b) b.p. 108–110° (1.4–1.5 mm.) was less cloudy; (c) b.p. 99–107° (0.8–1.3 mm.), $n^{23}D$ 1.4398, appeared clear and colorless and weighed 202.8 g. (86.3%). A sample of fraction c from a similar run, further purified by distillation, gave analytically pure ethyl N-carbethoxy-β-aminopropionate, b.p. 150–154° (30 mm.), $n^{20}D$ 1.4408.

Anal. Calcd. for $C_8H_{15}NO_4$: C, 50.78; H, 7.99; N, 7.40. Found: C, 51.12; H, 8.18; N, 7.64.

Benzyl N-Carbethoxy-β-aminopropionate.—A mixture of 88.5 g. (0.55 mole) of N-carbethoxy-β-aminopropionic acid, 80 g. (0.63 mole) of benzyl chloride, 200 ml. of 10% sodium hydroxide solution and 350 ml. of 95% ethanol was heated under reflux for 2.5 hours. The mixture was then distilled at atmospheric pressure until about 400 ml. of distillate had been collected. The two-phase residue was extracted with ether, the ether extract dried over anhydrous magnesium sulfate, and the solvent removed under reduced pressure. During a preliminary distillation of the residual oil, through a 14 × 0.5 in. Vigreux column, gaseous decomposition of some unidentified product made high vacuum difficult to maintain. Six fractions were collected: (a) b.p. 70–74° (1.1–4.6 mm.), (b) b.p. 75–78° (1.1–1.3 mm.), (c) b.p. 56–110° (0.8–5.0 mm.), (d) b.p. 110–168° (2.9–5.0 mm.), (e) b.p. 165–171° (1.6–1.7 mm.), (f) b.p. 168–171° (1.4–1.6 mm.). Only fraction f on redistillation through a 24-in. Podbielniak column yielded a product (fractions f-2 and f-3) sufficiently pure for subsequent reactions. Three fractions were collected: (f-1) b.p. 170–175° (1.5–2.0 mm.), $n^{23}D$ 1.5002; (f-2) 6.81 g., b.p. 170–174° (1.5 mm.), $n^{23}D$ 1.5062; (f-3) 9.79 g., b.p. 170–174° (1.5 mm.), $n^{23}D$ 1.5070. Analytically pure benzyl N-carbethoxy-β-aminopropionate was prepared from a similar run, b.p. 170° (0.5–0.8 mm.), $n^{20}D$ 1.5073.

Anal. Calcd. for $C_{13}H_{17}NO_4$: C, 62.12; H, 6.82; N, 5.57. Found: C, 61.80; H, 6.87; N, 5.45.

Nitrosation of Ethyl N-Carbethoxy-β-aminopropionate.—*Caution is necessary in carrying out this reaction, and subsequent reactions in which the product is involved, since serious skin irritation may result.* A 15-g. (0.08 mole) quantity of ethyl N-carbethoxy-β-aminopropionate was dissolved in a solution of 42 ml. of concd. sulfuric acid and 51 ml. of water. The mixture was cooled in an ice-bath and a solution of 12 g. (0.17 mole) of sodium nitrite in 18 ml. of water was added dropwise with stirring over a period of 15 minutes. A green liquid layer formed on the surface of the mixture. The product was extracted with ether, and the ether extract washed free of acid with 5% sodium bicarbonate. The ether extract was retained for *ex situ* procedures. For *in situ* procedures, the ether solution was dried over anhyd. magnesium sulfate and the solvent was removed under reduced pressure. The residual oil was used without further purification.

Benzyl β-Phenoxypropionate.—Benzyl N-carbethoxy-β-aminopropionate (12.6 g., 0.05 mole) was nitrosated in the same manner as ethyl N-carbethoxy-β-aminopropionate (described immediately above). The resulting ether solution was dried over anhyd. magnesium sulfate and the solvent removed under reduced pressure. The residual oil was dissolved in *ca.* 200 ml. of absolute ethanol (distilled from sodium), 8 g. (0.085 mole) of phenol added and the resulting solution cooled in an ice-bath. On the addition of two pellets of sodium hydroxide a slow evolution of gas began. Stirring was begun, and after 90 minutes (during which time two more pellets of sodium hydroxide were added) gas evolution ceased. The solution was decanted from the remaining pellets of sodium hydroxide and neutralized with a few drops of concd. hydrochloric acid. The solvent was removed under reduced pressure. The residual oil was dissolved in ether, extracted with 2% sodium hydroxide, washed with 5% sodium bicarbonate, and dried over anhyd. magnesium sulfate. The solvent was removed under reduced pressure and the residual oil distilled through a 1 × 0.25 in. Vigreux column. Three fractions were collected: (a) 3.67 g., b.p. 72–86° (0.8–1.2 mm.); (b) 2.18 g., b.p. 86–170° (0.8 mm.); (c) 2.81 g., b.p. 170–180° (0.8 mm.). Fraction c solidified in the receiver. An analytical sample of benzyl β-phenoxypropionate was prepared by recrystallization of fraction c from 95% ethanol; m.p. 49–50°.

Anal. Calcd. for $C_{16}H_{16}O_3$: C, 74.98; H, 6.30. Found: C, 74.71; H, 6.32.

β-Phenoxypropionic Acid. (a) From Ethyl N-Carbethoxy-N-nitroso-β-aminopropionate.—When phenol (12.0 g., 0.13 mole) was treated with the nitrosation product from 15 g. (0.08 mole) of ethyl N-carbethoxy-β-aminopropionate in alcoholic alkaline solution in the same manner as with the benzyl ester, an oil was obtained which was distilled through a 1 × 0.25 in. Vigreux column. Three fractions were collected at 15 mm.: (a) 1.90 g., b.p. 50–86°, $n^{24}D$ 1.4165; (b) 4.48 g., b.p. 86–120°, $n^{24}D$ 1.4818; (c) 5.52 g., b.p. 120–146°, $n^{24}D$ 1.4952. The literature[11a] gives b.p. 142° (11 mm.), $n^{18}D$ 1.5007, for ethyl β-phenoxypropionate.

A 1.0-g. quantity of fraction c was placed in 25 ml. of 1 *N* potassium hydroxide in 50% aqueous ethanol. The mixture was shaken for three minutes and then acidified with 25 ml. of cold 2 *N* hydrochloric acid. The solution was reduced to about half its volume (under water-pump vacuum) and then extracted with ether. The ether solution was extracted with 5% sodium bicarbonate which, on acidification, yielded 0.15 g. (18.5%)[19] of β-phenoxypropionic acid, m.p. 95–97° (lit.[11a] m.p. 97–98°).

(b) From Benzyl β-Phenoxypropionate.—A 1.0-g. quantity of crude benzyl β-phenoxypropionate (fraction c) was dissolved in 50 ml. of dioxane and hydrogenated at 40 p.s.i.g. over 1.0 g. of 10% palladium-on-charcoal for 8 hr. at 50°. The catalyst was removed by filtration, and the solvent removed from the filtrate by distillation under reduced pressure. The residual white solid was dissolved in ether and extracted with 5% sodium bicarbonate. Upon acidification of the sodium bicarbonate extract, β-phenoxypropionic acid (0.43 g., 66.4% based on the crude ester) precipitated, m.p. 95–98° (lit.[11a] m.p. 97–98°).

Ethyl β-(2-Bromo-4-nitrophenoxy)-propionate (III).—A 4.7-g. (0.025 mole) quantity of ethyl N-carbethoxy-β-aminopropionate was nitrosated as previously described. The light green ether solution (*ca.* 120 ml.) was placed in a separatory funnel over a previously ice-cooled solution of 10 g. of potassium hydroxide in 90 ml. of water. Methanol then was added to the mixture in 5- to 10-ml. portions with intermittent shaking. Gas evolution during this addition was vigorous, and it was necessary to release the pressure frequently while shaking the mixture. When about 40 ml. of methanol had been added, a deep yellow color appeared in the ether layer. To determine whether the addition of more methanol was necessary, a 1- to 2-ml. sample of the ether layer was withdrawn and treated with acetic acid. After the ensuing evolution of gas and disappearance of the yellow color, a light green color, presumably due to unreacted

(17) R. H. Sifferd and V. du Vigneaud, *J. Biol. Chem.*, **108**, 757 (1935).

(18) F. Lengfeld and J. Stieglitz, *Am. Chem. J.*, **15**, 513 (1893).

(19) R. H. Hall and E. S. Stern (ref. 11a) report a 70% yield of the acid on hydrolysis for 5 min. in 1 *N* potassium hydroxide, in aqueous ethanol (50%). Variations in length of the hydrolysis period did not increase our yields.

nitrosourethan, remained. Hence, more methanol was added to the reaction mixture. Methanol addition was terminated when an acid-treated sample of the ethereal mixture became colorless. The ethereal solution of ethyl β-diazopropionate was separated and washed by swirling with cold water. Dropwise addition to this ethereal solution of the diazo ester from a solution of 3.0 g. of 2-bromo-4-nitrophenol in 50 ml. of ether (solution I) was begun and continued as long as an evolution of gas resulted (*ca.* 30 minutes). The reaction mixture was cooled in an ice-bath when gas evolution became violent. The remainder of the ethereal solution of 2-bromo-4-nitrophenol, which had not reacted with the diazo ester, was retained (solution II).

After standing for about an hour at room temperature, the reaction mixture was extracted with 100 ml. of 1% sodium hydroxide solution (in three portions; extracts retained), washed with 5% sodium bicarbonate and dried over anhyd. magnesium sulfate. The solvent was removed under reduced pressure leaving the ethyl β-(2-bromo-4-nitrophenoxy)-propionate as a residue which, after recrystallization from ethanol, weighed 1.4 g., m.p. 58–60° (cor.).

Evaporation of the solvent from solution II (second preceding paragraph) left as a residue 1.3 g. of 2-bromo-4-nitrophenol. Hence 1.7 g. of the phenol had been added to the diazo ester solution.

Ether extraction of the acidified sodium hydroxide extracts of the reaction mixture (second preceding paragraph) resulted in the recovery of 0.1 g. of 2-bromo-4-nitrophenol. The yield (60%) is based on the 1.6 g. (0.0073 mole) of phenolic compound which actually reacted.

β-(2-Bromo-4-nitrophenoxy)-propionic Acid (VIII).—A 1.4-g. (0.0064 mole) quantity of ethyl β-(2-bromo-4-nitrophenoxy)-propionate (III) was placed in 40 ml. of 4 *N* hydrochloric acid and the mixture was heated under reflux for 3 hr. On cooling white crystals appeared and were collected by filtration. Recrystallization from ethanol yielded 1.0 g. of product, m.p. 137–138°. Further recrystallization from benzene gave the analytically pure β-(2-bromo-4-nitrophenoxy)-propionic acid, m.p. 142–143.5° (cor.).

Ethyl β-(2-Hydroxymethyl-4-pyrone-5-oxy)-propionate (XIV).—A 3.8-g. (0.02 mole) quantity of ethyl N-carbethoxy-β-aminopropionate was nitrosated as previously described. The resulting ether solution of the nitrosation product was treated with methanol over aqueous potassium hydroxide as in the preparation of ethyl β-(2-bromo-4-nitrophenoxy)-propionate. To the resulting yellow diazo ester solution was added, little by little, dry, powdered kojic acid (XIII) until gas evolution ceased (0.25 g., 0.00176 mole, required over a period of two hours). The reaction mixture was allowed to stand for a few hours and then was dried over anhyd. magnesium sulfate. The solvent was removed under reduced pressure and the residual solid recrystallized five times from benzene; yield 0.09 g. (21.1%), m.p. 103–107°, of product giving a negative ferric chloride test. An analytical sample, m.p. 108–110.5° (cor.), was prepared by further recrystallization from benzene.

Anal. Calcd. for $C_{11}H_{14}O_6$: C, 54.54; H, 5.83. Found: C, 54.32; H, 6.01.

Since the product was soluble in water and only slightly soluble in ether, excess kojic acid added to the reaction mixture could not be extracted with water or aqueous alkali. When kojic acid was present in the final product (as shown by positive ferric chloride tests), purification was effected with chloroform, in which only the product was soluble.

An attempt was made to hydrolyze 90 mg. of ethyl β-(2-hydroxymethyl-4-pyrone-5-oxy)-propionate by heating under reflux with 9 ml. of 4 *N* hydrochloric acid for 50 minutes. On removal of the solvent under reduced pressure, there remained only a brown solid which gave a purple color on addition of ferric chloride. The quantity of product was considered too small for further study.

Benzyl β-(2-hydroxymethyl-4-pyrone-5-oxy)-propionate (XV) was prepared in the same way as ethyl β-(2-hydroxymethyl-4-pyrone-5-oxypropionate. To the intermediate ethereal solution of benzyl β-diazopropionate (prepared from 6.27 g., 0.25 mole, of benzyl N-carbethoxy-β-aminopropionate) was added 1.05 g. (0.0074 mole) of dry, powdered kojic acid. The reaction mixture was dried over anhyd. magnesium sulfate, and the solvent was removed under reduced pressure. The residual solid was recrystallized from benzene; yield 0.67 g. (29.8%), m.p. 100–107°. An analytical sample, m.p. 100–108° (cor.), was prepared by recrystallization from benzene. The product gave a negative ferric chloride test.

Anal. Calcd. for $C_{16}H_{16}O_6$: C, 63.15; H, 5.65. Found: C, 62.85; H, 5.29.

An attempt to debenzylate 0.195 g. (0.00064 mole) of benzyl β-(2-hydroxymethyl-4-pyrone-5-oxy)-propionate over 10% palladium-on-charcoal in 50 ml. of dioxane at 50° and 40–44 p.s.i.g. for 6 hr. yielded only an oil, which resisted all attempts at crystallization.

8-Bromo-1-benzo[f]chromanone (XVI).—A 0.7-g. (0.0237 mole) quantity of β-(6-bromo-2-naphthoxy)-propionic acid (XII) was placed in 7 g. of polyphosphoric acid and the mixture heated at 70–80° for 2 hr. with stirring and with the exclusion of moisture. The mixture was poured into cold water and extracted with benzene. The benzene solution was extracted with 5% sodium bicarbonate and dried over anhyd. magnesium sulfate. The solvent was removed under reduced pressure and the residual white solid recrystallized from 50% ethanol; yield 0.09 g. (13.7%), m.p. 125–127.5° (cor.) (lit.[11b] m.p. 123°). The infrared spectrum (Nujol) possessed a strong band at 1655 cm.$^{-1}$, which is attributed to the conjugated carbonyl group[16] of the chromanone ring system.

Attempted Cyclization of β-(2,4-Dinitrophenoxy)-propionic Acid (X).—An attempt was made to cyclize β-(2,4-dinitrophenoxy)-propionic acid (X, 0.55 g. 0.0022 mole) to 6,8-dinitrochromanone with polyphosphoric acid (7.5 g.) by the procedure employed in the preparation of 8-bromo-1-benzo[f]chromanone (XVI). The product on recrystallization from ethanol melted at 119.5–121.5° (cor.), yield 0.1 g. A mixed m.p. with β-(2,4-dinitrophenoxy)-propionic acid was 93–105°. The infrared spectrum (Nujol) contained a strong band at 1775 cm.$^{-1}$, which is attributed to probable presence of a carbonyl group of a carboxylic anhydride.[15]

Anal. Calcd. for 6,8-dinitrochromanone, $C_9H_6N_2O_6$: C, 45.01; H, 3.36. Calcd. for β-(2,4-dinitrophenoxy)-propionic anhydride, $C_{18}H_{14}N_4O_{13}$: C, 43.73; H, 2.85. Found: C, 43.33; H, 2.45.

Similar results were obtained in the attempted cyclization of β-(2-bromo-4-nitrophenoxy)-propionic acid (VIII) and β-(4-bromo-2-nitrophenoxy)-propionic acid (IX). The infrared spectra (Nujol) of the products from VIII and IX contained strong bands at 1775 and 1764 cm.$^{-1}$, respectively.

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