Synthesis and Reactions of 3-Carbethoxy and 3-Aroyl-3,4-dihydro-1*H*-2,3-benzoxazin-1-ones

Aldo Trani and Elvio Bellasio

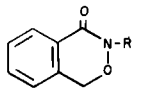
Research Laboratories of Gruppo Lepetit S.p.A., Milano, Italy

Received August 31, 1976

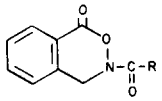
A series of 3-substituted 3,4-dihydro-1*H*-2,3-benzoxazin-1-ones (IV) (Scheme I) was prepared by reaction of 2-bromomethylbenzoyl chlorides (II) with *N*-hydroxyethylcarbamate (III) or with benzohydroxamic acids. Acid hydrolysis of 3-carbethoxy (IVa) and 3-benzoyl derivatives (IVb) afforded a mixture of 2-(hydroxyaminomethyl)benzoic acid (V) and 2,3-dihydro-2-hydroxy-1*H*-1-isoindolinone (VII). Compound IVa reacted with ethanol, amines or hydrazine to yield the ethyl ester X, amides XIV (Scheme II) and the hydrazide XII of 2-(*N*-carbethoxy-*N*-hydroxyaminomethyl)benzoic acid. Diazotization of the hydrazide XII afforded the unstable azide XIII which did not undergo the Curtius reaction but gave the benzoxazinone IVa by loss of hydrazoic acid.

J. Heterocyclic Chem., **14**, 113 (1977).

It was previously reported from our laboratories (1) that derivatives of 1*H*-2,3-benzoxazin-4(3*H*)one (I) can be prepared by reaction of 2-bromomethylbenzoic acid ethyl-ester with *N*-hydroxyethylcarbamate (III) (R = OC_2H_5 hydroxyurethane, H.U.).



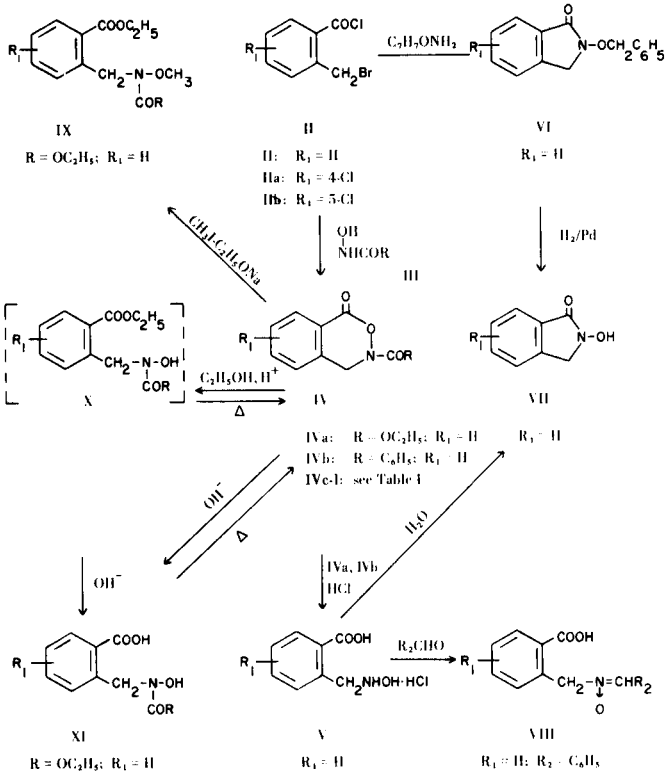
I



IV

Since it was known that aroyl chlorides react with H.U. to give *O*-derivatives (2) we have carried out the reaction of 2-bromomethylbenzoyl chloride (II) (1) with H.U. or with benzohydroxamic acids in the presence of bases to obtain 3,4-dihydro-1*H*-benzoxazin-1-ones of the type IV. The reactions proceeded in moderate yield giving the benzoxazine IVa and the 3-benzoyl analogs IVb and IVc (Scheme I). Compounds IVa and IVb were stable in boiling diluted hydrochloric acid. In concentrated hot hydrochloric acid they yielded a mixture of V and VII (3,4). Compound VII was also prepared by catalytic hydrogenation of the isoindolinone VI which was in turn obtained by reaction of II with *O*-benzylhydroxylamine (5). Compound VII and ferric chloride in ethanol gave a blue violet colour (4) whereas the hydroxy aminoacid V did not react. It was observed by means of this test that

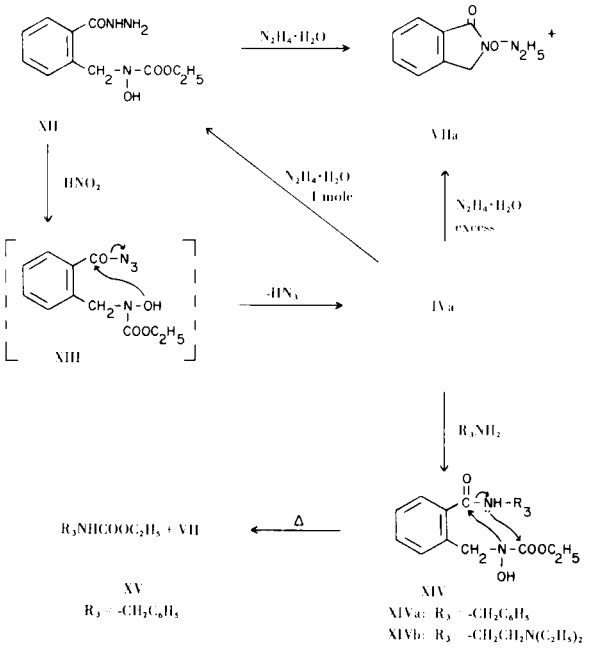
Scheme I



V gave VII after short treatment with cold water, but was quite stable in concentrated hydrochloric acid at room temperature. Hydrolysis of IVa with 1*N* sodium hydroxide at moderate temperature afforded 2-(*N*-carbethoxy-*N*-hydroxyaminomethyl)benzoic acid (XI), which melted with loss of water giving IVa. The benzoyl derivative IVb was stable towards alkaline hydrolysis either in alcohol or in water.

Compound IVa was transformed, in boiling ethanol, in the presence of catalytic amounts of diluted hydrochloric acid into X which afforded IVa by moderate heating on a water bath, or by treatment with concentrated hydrochloric acid. Mild alkaline hydrolysis of X led to the acid XI. Alcoholysis of IVa in the presence of sodium ethoxide and methyl iodide gave the ester IX. The reaction of IVa with primary amines or with hydrazine gave the amides XIV and the hydrazide XII. (Scheme II). The ir spectrum in Nujol mull of the benzylamide XIVa showed two bands at 1640 cm^{-1} (ν C=O amide) and 1530 cm^{-1} (δ NH) whereas no absorption for the ester group was noticeable. A band at 1690 cm^{-1} appeared when the spectrum was registered in chloroform solution. This can be explained with the presence of an intermolecular hydrogen bond, which disappears in solution. Pyrolysis of XIVa at 160° yielded *N*-benzylethylcarbamate (XV) and VII. Compound XII gave the hydrazinium salt VIIa when reacted with excess hydrazine hydrate in alcoholic solution. When XII was diazotized with sodium nitrite and hydrochloric acid after the reaction mixture was extracted with ether, a strong absorption, attributable to the formation of an azido group, could be observed in the ir spectrum of the ethereal solution. However, the isolation of the azido compound XIII was unsuccessful and the benzoxazinone IV was the sole compound isolated after evaporation of the solvent under reduced pressure. The same compound IV was also obtained when toluene was added to the ether solution and the resulting mixture was heated in order to effect the Curtius reaction. Compound XIII, which has the hydroxyl group in position δ to the azido group, behaves thus like δ-hydroxycarboxylic acid azides which do not undergo the Curtius rearrangement but loses hydrazoic acid with formation of δ-lactones (6).

Scheme II



3,4-Dihydro-1*H*-2,3-benzoxazin-1-ones (IVc-l) reported in Table I were obtained by reaction of 5-chloro-2-bromomethylbenzoyl chloride (IIb) (7) and 4-chloro-2-bromomethylbenzoyl chloride (IIa) with known benzohydroxamic acids.

Compound IIa was prepared, according to the general procedure used for II and IIb, starting from 5-chlorophthalide (8) which on treatment with saturated solution of hydrogen bromide in acetic acid at 60°, yielded 4-chloro-2-bromomethylbenzoic acid. The transformation of the acid into the chloride was then easily carried out with thionyl chloride. Either the carboxylic acid or the corresponding chloride were characterized only by their spectra and m.p. or b.p.

EXPERIMENTAL

Melting points were determined in open capillary tubes and are uncorrected. The ir spectra were registered with a Perkin-Elmer mod. 137 spectrophotometer as Nujol mulls. The nmr spectra were recorded on a Varian A-60 instrument. Chemical shifts are reported as δ part per million (ppm) with tetramethylsilane as internal reference (δ = 0.00). The following abbreviations were used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, b = broad band.

3,4-Dihydro-1-oxo-1*H*-2,3-benzoxazine-3-carboxylic Acid Ethyl Ester (IVa).

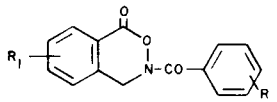
a) From II.

A solution of II (1) (51 g.) in 100 ml. of benzene was added dropwise at room temperature to a solution of IIIa (R = OC_2H_5) (23 g.) in 100 ml. of benzene. After 10 minutes a solution of triethylamine (44 g.) in 50 ml. of benzene was slowly added. The mixture was refluxed for 5 hours then it was cooled and filtered. After washing with diluted hydrochloric acid, water, sodium hydrogen carbonate and water, the organic layer was dried over sodium sulfate, filtered and evaporated. The residue was crystallized from a mixture of benzene-petroleum ether 9:1, yield 22 g., m.p. 75-77°; ir: 1770 and 1725 (C=O), 1600 and 1580 (C=C), 1220 and 1010 (C-O-C) and 750 cm^{-1} (aromatic CH); nmr (deuteriochloroform) δ: 1.26 (t, 3H, CH_3), 4.26 (q, 2H, CH_2-C), 5.01 (s, 2H, CH_2-N), 7.23-7.9 (m, 3H, H-5,6,7), 8.15 (dd, 1H, H-8).

Anal. Calcd. for $C_{11}H_{11}NO_4$: C, 59.72; H, 5.01; N, 6.33. Found: C, 59.71; H, 4.95; N, 6.27.

Table I

3-Aroyl-3,4-dihydro-1*H*-2,3-benzoxazines-1-ones



Compound	R (a)	R_1	M.p. °C crystallization solvent	Molecular formula	Analysis Calcd. % C	H	N	Cl	Found % C	H	N	Cl
IVc	3,4,5-$(CH_3O)_3$ (10)	H	171-172 Benzene	$C_{18}H_{17}NO_6$	62.97	4.99	4.08		63.10	4.95	4.03	
IVd	4-CH_3 (9)	H	127-129 Ethyl ether	$C_{16}H_{13}NO_3$	71.90	4.90	5.24		71.72	4.93	5.38	
IVe	4-Cl (9)	H	160-162 Ethanol	$C_{15}H_{10}ClNO_3$	62.62	3.50	4.87	12.32	62.40	3.61	5.03	12.44
IVf	H	6-Cl	166-169 Benzene	$C_{15}H_{10}ClNO_3$	62.62	3.50	4.87	12.32	62.81	3.66	4.98	12.24
IVg	4-CH_3 (9)	6-Cl	160 Ethyl ether	$C_{16}H_{12}ClNO_3$	63.69	4.01	4.64	11.75	63.73	3.91	4.57	11.84
IVh	4-Cl (9)	6-Cl	220-223 Benzene	$C_{15}H_9Cl_2NO_3$	55.93	2.82	4.35	22.01	55.98	2.87	4.43	21.88
IVi	3-Cl (10)	7-Cl	163 *n*-Hexane	$C_{15}H_9Cl_2NO_3$	55.93	2.82	4.35	22.01	55.86	2.77	4.26	22.13
IVl	4-NO_2 (9)	6-Cl	235-237 DMF	$C_{15}H_9ClN_2O_5$	54.15	2.73	8.42	10.66	54.28	2.85	8.06	10.32

(a) For corresponding hydroxamic, see references (9,10).

b) From X.

One g. of crude X (see below) was heated on a steam bath for 3 hours. The residue was triturated in petroleum ether, yield 0.8 g.

c) From XI.

Compound XI (1 g.) (see below) was melted in an oil bath and allowed to stand for 15 minutes. After cooling, the solid residue was triturated in petroleum ether, yield 0.9 g.

d) From XII Through XIII.

A solution of 1.19 g. (1.72 mmoles) of sodium nitrite in 10 ml. of water was added dropwise to a solution of XII (4 g., 1.58 mmoles) in 70 ml. of 5% hydrochloric acid at 0°. After 30 minutes the mixture was extracted with ether. The organic solution, which showed ir band at 2140 cm^{-1}, was dried over sodium sulphate, filtered and the filtrate was evaporated under reduced pressure over a steam bath at 30°. During the evaporation a mild decomposition took place. The residue which did not show any azide or isocyanate ir band, crystallized from benzene-petroleum ether, yield 2 g.

3-Benzoyl-3,4-dihydro-1*H*-2,3-benzoxazin-1-one (IVb).

A mixture of benzohydroxamic acid (7 g.), sodium hydride (50% in mineral oil, 2.4 g.) in 100 ml. of benzene was stirred at 70° for 20 minutes. After cooling, II (12 g.) was added dropwise and the resulting mixture was slowly heated to 60° (Caution: the reaction begins exothermically at this temperature) and then at reflux. Triethylamine (5 g.) was added over a period of 15 minutes. After 1.5 hours, the mixture was cooled and treated with water. The organic layer was separated, dried over sodium sulphate and evaporated. The residue was triturated with petroleum ether and the insoluble material was crystallized from ether, yield 6 g., m.p. 84-85°; ir: 3025 (ν aromatic CH), 1750 (ν CO cyclic), 1660 (ν C=O amide), 1600, 1580, 1500 (ν C=C aromatic), 780, 750 and 720 cm^{-1} (γ aromatic CH); nmr (DMSO-d_6) δ: 5.39 (s, 2H, CH_2), 7.40-8.05 (m, 8H, aromatic), 8.20 (dd, 1H, H-8).

Anal. Calcd. for $C_{15}H_{11}NO_3$: C, 71.14; H, 4.37; N, 5.53. Found: C, 70.88; H, 4.16; N, 5.81.

2-(Hydroxyaminomethyl)benzoic Acid (V).

a) From IVb.

A mixture of IVb (15 g.) and 60 ml. of concentrated hydrochloric acid was heated at 100° for 1 hour. After cooling the precipitate was collected and crystallized from methanol/ether to give 8 g., m.p. 189-190°; ir: 3580 (HO (N)), 2700-2300 (ν HO (CO), asym. and sym. NH_2^+), 1700 (ν C=O), 1600, 1575, 1490 (ν aromatic C=C), 1560, 1525 (δ NH_2^+) and 740 cm^{-1} (γ aromatic CH); nmr (DMSO-d_6) δ: 4.66 (s, 2H, CH_2), 7.35-7.85 (m, 3H, aromatic H-3,4,5), 7.85-8.25 (m, 1H, H-6) and 8.3-12.2 (b, 4H, mobil protons).

Anal. Calcd. for $C_8H_9NO_3 \cdot HCl$: C, 47.18; H, 4.93; N, 6.87; Cl, 17.45. Found: C, 47.05; H, 4.89; N, 6.70; Cl, 17.82.

b) From IVa.

Compound IVa (15 g.) and 60 ml. of concentrated hydrochloric acid gave in the same conditions as above 8 g. of crude V, which was washed with acetone and then crystallized. The acetone washing contains compound VII, which was identified on thin layer chromatography and compared with a pure sample prepared from VI.

2,3-Dihydro-2-(phenylmethoxy)-1*H*-1-isoindolinone (VI).

Compound II (50 g.) was added dropwise at room temperature to a solution of *O*-benzylhydroxylamine hydrochloride (6) (30 g.) and triethylamine (21 g.) in 700 ml. of benzene. After 10 minutes another portion of triethylamine (42 g.) in 100 ml. of benzene was added dropwise and the resulting mixture was refluxed for 5 hours. After cooling the suspension was filtered and the filtrate was washed with water. The organic layer was separated, dried over sodium sulphate, filtered and the solvent was evaporated under reduced pressure. The residue was crystallized from acetone-ether, yield 13 g., m.p. 138-139°; ir: 3025 (ν aromatic CH), 1700 (ν C=O), 1500 (ν aromatic C=C), 770, 730 and 697 cm^{-1} (γ aromatic CH); nmr (deuteriochloroform) δ: 4.25 (s, 2H, CH_2N), 5.16 (s, 2H, CH_2-O), 7.15-7.73 (m, 3H, aromatic H-3,4,5), 7.85 (dd, 1H, H-6).

Anal. Calcd. for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85. Found: C, 75.03; H, 5.55; N, 5.87.

2,3-Dihydro-2-hydroxy-1*H*-1-isoindolinone (VII).

a) From VI.

A solution of VI (5 g.) in 150 ml. of absolute ethanol was hydrogenated to the theoretical absorption at normal pressure in the presence of 0.5 g. of 10% palladium-carbon catalyst. After filtration, the solvent was evaporated and the residue was crystallized from acetone-ethanol 1:1, yield 2.2 g., m.p. 176-178° (lit. (3,4) m.p. 181°); ir: 3300-2500 (ν OH), 3025 (ν aromatic CH), 1680, 1640 (ν C=O), 1580, 1495 (ν C=C), 720 cm^{-1} (γ aromatic CH); nmr (DMSO-d_6) δ: 4.65 (s, 2H, CH_2), 7.3-7.9 (m, 4H, aromatic H), 10.15 (broad s, 1H, OH).

Anal. Calcd. for $C_8H_7NO_2$: C, 63.42; H, 4.73; N, 9.39. Found: C, 63.70; H, 4.85; N, 9.30.

b) From XIVa.

Compound XIVa (1 g.) was heated at 160° for 15 minutes. After cooling, the final mixture was distilled under reduced pressure. The ir spectrum of the distillate (b.p. 95°/0.4 mm.) was identical to that of *N*-benzylethylcarbamate (XV). The residue was crystallized from acetone-ethanol to give 0.3 g. of VII.

2,3-Dihydro-2-hydroxy-1*H*-1-isoindolinone Hydrazinium Salt (VIIa).

From XII.

A mixture of XII (see below) (1 g.) and 1 ml. of hydrazine hydrate in 30 ml. of ethanol was refluxed for 4 hours. After evaporation of the solvent the residue was triturated with ether, to give 0.5 g. of VIIa, m.p. 148-150°. The same compound was also obtained by treatment of a solution of VII in ether with the stechiometric amount of hydrazine. The aqueous solution of VIIa gave VII by acidification.

2-[(Phenylmethylen)aminomethyl]benzoic Acid *N*-Oxide (VIII).

Benzaldehyde (2 g.) in 3 ml. of ether was added under stirring to a solution of V (4 g.) in 20 ml. of water. After twenty minutes the precipitate was filtered and crystallized from ethanol, yield 3.7 g., m.p. 192-195°; uv: λ max (in methanol): 295 mμ (ϵ mol = 19300); ir: 3400-2300 (ν OH), 1690 (ν C=O), 1680 (ν C=N), 1600 (ν aromatic C=C) and 755, 720 cm^{-1} (γ aromatic CH); nmr (DMSO-d_6) δ: 5.55 (s, 2H, CH_2), 7.30-7.75 (m, 6H, aromatic H-3,4,5 and H-3',4',5'), 7.85-8.11 (m, 1H, H-6), 8.15 (s, 1H, -CH=), 8.20-8.50 (m, 2H, aromatic H-2',6') and 8-11 (broad s, 1H, COOH).

Anal. Calcd. for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.46; H, 5.22; N, 5.61.

2-(*N*-Carbethoxy-*N*-methoxyaminomethyl)benzoic Acid Ethyl Ester (IX).

To a stirred solution of sodium (1.05 g.) in 50 ml. of ethanol, a solution of Va (40 g.) in 50 ml. of ethanol, was added at room temperature. After 15 minutes, the solution was cooled to 10° and methyliodide (35 ml.) was added dropwise. The mixture was stirred for 0.5 hour, then it was heated at 65° for 1 hour. The solvent was evaporated and the residue was treated with 200 ml. of ether. The suspension was filtered, the filtrate was evaporated and the residue distilled, yield 10 g., b.p. 130°/0.5 mm. On standing the compound solidified (m.p. 40-42°); ir (liquid): 3030 (ν aromatic CH), 1700 (ν C=O), 1600, 1580 (ν C=C), 1260 and 1025 (ν asym. and sym. C-O-C), 740 cm^{-1} (γ aromatic CH); nmr (deuteriochloroform) δ: 1.28 (t, 3H, CH_3-(CH_2CONO)), 1.40 (t, 3H, CH_3(CH_2COOC)), 3.66 (s, 3H, CH_3O), 4.25 (q, 2H, CH_2(CONO)), 4.40 (q, 2H, CH_2COOC), 5.18 (s, 2H, CH_2), 7.20-7.80 (m, 3H, aromatic H-3,4,5), 8.0 (dd, 1H, H-6).

Anal. Calcd. for $C_{14}H_{19}NO_5$: C, 59.77; H, 6.81; N, 4.98. Found: C, 59.90; H, 6.88; N, 4.79.

2-(*N*-Carbethoxy-*N*-hydroxyaminomethyl)benzoic Acid (XI).

a) From IVa.

A mixture of Va (10 g.) and sodium hydroxide (1.8 g.) in 50 ml. of water was heated on a steam bath for 1 hour. After addition of 250 ml. of water, the mixture was filtered. The filtrate was cooled, acidified with dilute hydrochloric acid and the crystalline precipitate was collected and dried, yield 9 g., m.p. 139-140°; ir: 3180 (ν OH), 3025 (ν aromatic CH), 2700-2400 (ν OH), 1700 (ν C=O), 1600, 1580, 1500 cm^{-1} (ν aromatic C=C); nmr (deuteriochloroform/DMSO-d_6) δ: 4.66 (s, 2H, CH_2), 7.35-7.85 (m, 3H, aromatic H-3,4,5), 7.85-8.25 (m, 1H, aromatic H-6), 8.3-12.2 (broad s, 4H, mobile H).

Anal. Calcd. for $C_{11}H_{13}NO_5$: C, 55.23; H, 5.48; N, 5.86. Found: C, 55.28; H, 5.57; N, 5.80.

b) From IVa Through X.

A mixture of IVa (3 g.), ethanol (95 ml.) and dilute hydrochloric acid (1 ml.) was refluxed for 2 hours. Evaporation of the solvent under reduced pressure yielded 3 g. of crude X; ir: 3250 (ν OH), 3030 (ν aromatic CH), 1700 (ν C=O), 1600-1575 (ν C=C), 1260 and 1020 (ν asym. and sym. -C-O-C), 740 cm^{-1} (γ aromatic CH). Compound X (1 g.) was stirred with diluted sodium hydroxide at room temperature for 0.5 hour. After this time the compound gave a clear solution which was treated with dilute hydrochloric acid. The oil which separated was extracted with ether. The residue obtained after evaporation of the organic solvent was crystallized from petroleum ether (m.p. and ir spectra were identical to those of the sample of the method a).

N-[(2-Hydrazinocarbonyl)phenylmethyl]-*N*-hydroxycarbamic Acid Ethyl Ester (XII).

A suspension of IVa (10 g.) in 4.8 ml. of hydrazine hydrate and 100 ml. of ethanol was refluxed for 10 minutes. After this period the clear solution was cooled to 50° and maintained at this temperature for 7 hours. The solvent was concentrated *in vacuo* to 20 ml. and the resulting precipitate was filtered, washed with cold (0°) water and crystallized from 2-propanol; yield 8 g., m.p. 144-145°; ir: 3280 (ν NH), 3200 (ν OH), 1700 (ν C=O), 1650, 1620 (ν C=O), 1580 (ν C=C), 1530 (amide II), 1250 and 1030 (ν C-O asym. and sym.), 740 cm^{-1} (γ aromatic H); nmr (DMSO-d_6) δ: 1.26 (t, 3H, CH_3), 2.8-4.5 (broad s, 2 mobile H), 4.18 (q, 2H, CH_2(CH_3)), 4.87 (s, 2H, CH_2-N), 7.40 (broad s, 4H, aromatic H) and 9.40 (broad s, 2H, mobile protons).

Anal. Calcd. for $C_{11}H_{15}N_3O_4$: C, 52.17; H, 5.97; N, 16.59. Found: C, 52.09; H, 6.15; N, 16.78.

N-Hydroxy-*N*-[(2-phenylmethylaminocarbonyl)phenylmethyl]-carbamic Acid Ethyl Ester (XIVa).

A mixture of IVa (8.9 g.), benzylamine (4.25 ml.) in 80 ml. of benzene was heated at reflux for 2 hours and then left overnight at room temperature. The crystalline precipitate was filtered and washed with benzene, yield 13 g., m.p. 114-117°; ir: 3300 (ν NH), 3200 (ν OH), 1680 (ν C=O), 1640 (amide I), 1600, 1580 (ν C=C), 1540 (amide II), 1230, 1020 (ν asym. and sym. C-O-C), 760, 740 and 700 cm^{-1} (γ aromatic CH); nmr (deuteriochloroform) δ: 1.23 (t, 3H, CH_3), 4.10 (q, 2H, CH_2), 4.50 (d, 2H, CH_2-(NHCO), Jgem = 5.5 Hz), 4.77 (s, 2H, CH_2-(N-OH)), 6.9-7.6 (m, 10H, aromatic H and OH), 7.8-8.7 (broad s, 1H, NH-CO).

Anal. Calcd. for $C_{18}H_{20}N_2O_4$: C, 65.86; H, 6.14; N, 8.53. Found: C, 65.59; N, 6.15; N, 8.21.

N-[(2-Diethylaminoethylaminocarbonyl)phenylmethyl]-*N*-hydroxycarbamic Acid Ethyl Ester (XIVb).

A mixture of IVa (7 g.) and *N*,*N*-diethylethylendiamine (4.48 ml.) in 80 ml. of benzene was refluxed for 4 hours. After cooling, the organic solvent was washed with water, dried over sodium sulphate, filtered and evaporated. The residue was crystallized from acetone, yield 5 g., m.p. 97-98°.

Anal. Calcd. for $C_{17}H_{27}N_3O_4$: C, 60.51; H, 8.06; N, 12.45. Found: C, 60.48; H, 8.26; N, 12.60.

2-Bromomethyl-4-chlorobenzoyl Chloride (IIa).

5-Chloro-1(3*H*)isobenzofuranone (5-chlorophthalide) (8) (30 g.) was transformed, according to a general procedure already described, into crude 2-bromomethyl-4-chlorobenzoic acid (42 g.). A mixture of the crude acid (42 g.) and thionyl chloride (180 ml.) was refluxed for 3 hours. After evaporation of the thionyl-chloride the residue was distilled *in vacuo* to give IIa (25 g.), b.p. 82-85°, 0.2 mm.; ir: 1760, 1730 (γ C=O), 1585, 1550 (ν C=C aromatic), 1205, 1090, 910, 820 (γ C-H), 698 cm^{-1}.

REFERENCES AND NOTES

(1) G. Pifferi and E. Testa, *Tetrahedron*, **22**, 2107 (1966).

(2) L. W. Jones, *Chem. Zentralbl.*, **69**, I 564 (1898).

(3) J. P. Griffiths and C. K. Ingold, *J. Chem. Soc.*, **127**, 1698 (1925).

(4) O. Neunhoeffer and R. Gottschlich, *Ann. Chem.*, **736**, 100 (1970).

(5) A. Janny, *Ber.*, **16**, 170 (1883).

(6) R. A. Weerman, *Rec. Trav. Chim.*, **37**, 52 (1917).

(7) E. Bellasio and E. Arrigoni-Martelli, *Il Farmaco, Ed. Sc.*, **27**, 627 (1972).

(8) J. Tirouflet, *Bull. Soc. Sci., Bretagne Spec.*, **26**, 7 (1951).

(9) B. E. Hackley, Jr., R. Plapinger, M. Stolberg and T. Wagner-Jauregg, *J. Am. Chem. Soc.*, **77**, 3651 (1955).

(10) J. Nordmann and H. Swierkot, French Patent B.S.M. (2558), June 22, 1964; *Chem. Abstr.*, **62**, 1598a (1965).

(11) E. Urbschat and P. E. Frohberger, Belgian Patent 660,891, Sept. 10, 1965; *Chem. Abstr.*, **63**, 18966d (1965).