2-Phenylphthalimidine Derivatives. A Probable Formation Mechanism of Adducts from 3-Benzylidenephthalide and Aniline

Valerio Scartoni* and Tiziana Tognetti

Istituto di Chimica Farmaceutica e Tossicologica dell'Università,
via Bonanno 6, 56100 Pisa, Italy

Received January 12, 1984

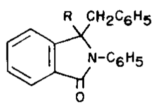
3-Benzyl-3-hydroxy-2-phenylphthalimidine (**1**) and 3-anilino-3-benzyl-2-phenylphthalimidine (**2**), the unusual adduct, are obtained from the title compounds. 3-Alkoxy-3-benzyl-2-phenylphthalimidines **3** are synthesized. The behaviour of **1**, 3-benzylidene-2-phenylphthalimidines (**4** and **5**), 3-(α-bromobenzylidene)-2-phenylphthalimidines (**6** and **7**) with respect to bases and the preparation of the open tautomer **13** of **1** and its hydrochloride are described. A hypothetical mechanism about the formation of **1** and **2** is suggested.

J. Heterocyclic Chem., **21**, 1499 (1984).

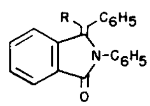
For a long period we have been interested in the chemistry and the eventual biological activity of phthalimidine derivatives, some of which were prepared in the past by using Gabriel's method [1] and which were widely studied [2,4-10].

This paper deals mainly with 3-benzyl-2-phenyl- and 3-benzylidene-2-phenylphthalimidines, which deserve to be mentioned owing to their peculiar chemical behaviour.

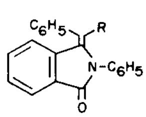
While primary alkyl and aralkylamines with 3-benzylidenephthalide readily gave an adduct, aniline slowly reacted yielding compounds **1** and **2**, the last one being the prevalent product when an excess of base was used. The



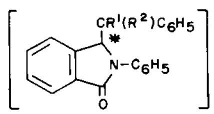
1, R = OH
2, R = NHC_6H_5
3a R = OCH_3
3b R = OC_2H_5



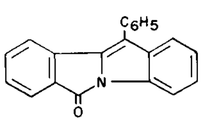
4, R = H(Z)
6, R = Br(E)



5, R = H(E)
7, R = Br(Z)



A, $R^1 = R^2 = H$, * = +
B, $R^1 = H$, $R^2 = Br$, * = +
C, $R^1 = R^2 = Br$, * = ·



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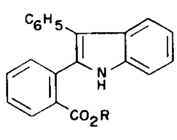
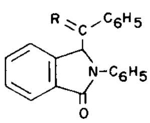
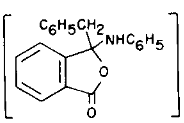


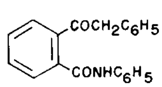
9, R = H
10, R = CH_3



11, R = O
12, R = H + OH



E



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elemental analysis and spectral characteristics were in agreement with these structures; the nmr spectrum of both compounds showed a quartet (see Experimental), attributable to two diastereotopic hydrogens of a methylene group attached to a chiral carbon [2].

When **1** and **2** were submitted to the action of aqueous mineral acids in alcoholic medium, compounds **3**, **4**, and **5** were isolated, the first one, probably originated from the solvent interaction on the intermediate carbocation **A** [3], was the sole product when the reaction was performed with hydrogen chloride in anhydrous alcohol. Previously we isolated an analogous compound [4].

On the other hand, **4** and **5** were obtained as the only products by conducting the reaction in an aqueous mixture of mineral acid or by bubbling hydrogen chloride at 0° into an aprotic solvent solution of **1** or **2**, the ratio of isomers (**4**:**5** ≅ 5:1) being dependent on their relative thermodynamic stabilities [5-6]. The configurations assigned to these geometrical isomers as well as to **6** and **7** (**6**:**7** ≅ 2:3), which were obtained by treatment of the first ones with bromine, were based on their spectroscopic evidence.

The constance of composition of the bromination mixture, in accordance with results previously reported [5], and the fact that **6** and **7** were isomerised by contact with sulphuric acid or with a chloroform solution of bromine could suggest these *cis-trans* interconversions would proceed through both an ionic (**B**) or a radical (**C**) intermediate [3].

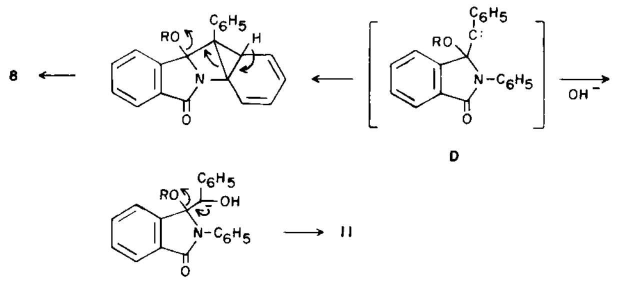
Successively we investigated the behaviour of **1**, **4**, **5**, **6**, **7** with respect to bases. When **6** and **7** were refluxed in ethylene glycol in the presence of sodium acetate, 11-phenylisoindolo[2,1-*a*]indol-6-one (**8**) [4], 2-phenylphthalimidine and benzoic acid were obtained. Incidentally, **8** yielded with alkali acid **9**, from which ester **10** was prepared.

Considering that compound **8** was also obtained by photolysis of **6** and **7** in methanol we assumed that in these conditions its formation probably followed a free-radical mechanism after the homolytic cleavage of the C-Br bond [7-10].

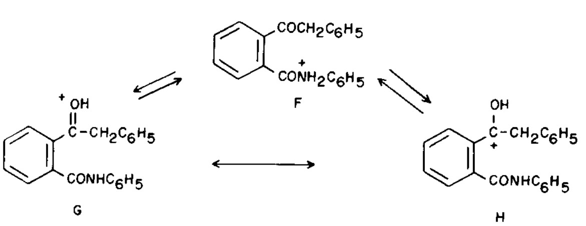
However, in the presence of bases an alternative mechanism could be considered. In fact, **6** and **7** were converted after a rather short time of contact with a hot ethanolic potassium hydroxide solution in **11**, which was easily soluble in strong bases and led to, by heating with these reagents, 2-phenylphthalimidine and benzoic acid. The structure of **11** was confirmed on the basis of spectral characteristics of its reduction product **12**, obtained with sodium borohydride, whose nmr spectrum showed the presence of a 1,2,2-trisubstituted ethanol in the molecule.

In addition, according to the general behaviour of 2-alkyl or 2-aralkyl-3-(α-bromobenzylidene)phthalimidines, **6** and **7** did not react appreciably with alcoholic silver nitrate, and were recovered unchanged after prolonged boiling with a methanolic solution of sodium azide or with two equivalents of dilute methanolic potassium methoxide. These facts mean the formation of **11** from **6** and **7** in the presence of bases could not be merely explained following Grob monomolecular mechanism [11].

SCHEME 1



SCHEME 2



Therefore, regarding the obtainment of **8** and **11** in the presence of bases (RO^-:AcO^-, OH^-) we could consider the intervention of a carbenoid intermediate as **D**, originated from the attack of the base on C-3 (Scheme 1) [12].

Concerning the reaction with bases, both **4** and **5** showed an interesting behaviour. While 2-alkyl-3-benzylidenephthalimidines were recovered unchanged after treatment with strong bases in high boiling mediums, compounds **4** and **5** with ethanolic potassium hydroxide afforded *o*-phenylacetylbenzoic acid anilide **13**. Probably the phenyl group bound to the nitrogen atom favours the nucleophilic attack of the hydroxide ion on C-3 of the phthalimidine nucleus.

Adduct **1** reacted neither in these conditions nor with aniline. Furthermore, it was remarkable that *o*-phenylacetylbenzoic acid, whereas with primary amines usually gave adducts alike **1**, with aniline yielded **13** [13].

Compound **13**, soluble and fairly stable in dilute alkaline solution or in aniline, was easily converted with hydroxylamine into 4-benzylbenzoxazin-1-one [2,14]; in contrast, adduct **1** did not condense with this reagent showing the absence of ring-chain tautomerism.

Both the direct preparation of **13** and the fact that this compound did not condense with aniline proved that the intermediate formation of **13** in the reaction between 3-benzylidenephthalide and aniline did not occur, and led to the conclusion that the nucleophilic attack of aniline could first involve C-3 rather than C-1. A second attack of aniline on the hypothetical species **E**, preferentially when it was present in excess could compete with the intramolecular one to give **2**. Without kinetic data, we could consider this picture moderately realistic.

Treatment of **13** with hydrogen chloride in dichloromethane-ethyl ether afforded the slightly soluble hydrochloride. It was difficult to understand *a priori* the atom to which the proton was bound; in fact three sites of protonation were present in the molecule. In accordance with general considerations [15-16] the protonation of the oxygen atom of the amide carbonyl should be the most probable route. However, the nmr spectrum of this salt recorded in dimethyl sulphoxide showed that the signal attributed to the methylene hydrogens was unimportantly shifted downfield with respect to that one of **13**, but a broad double intensity signal was present at low field. These facts might indicate that a N protonation occurred in these conditions to give the species **F**.

Nevertheless, the **13** hydrochloride slowly changed into a mixture of **4** and **5** on standing at room temperature in dimethyl sulphoxide or in methanol [17], whereas it gave solely 3-benzylidenephthalide by refluxing with hydrochloric acid. The first result suggested the species **F** was in equilibrium with the protonated keto group forms **G** and **H**, which were important for the formation of **4** and **5** by a nucleophilic intramolecular attack (Scheme 2). Furthermore, compounds **4** and **5** were quickly obtained from **13** by treatment with acetic anhydride. In the end, the formation of 3-benzylidenephthalide in refluxing hydrochloric acid was probably obtained through the intermediate production of *o*-phenylacetylbenzoic acid.

Work is in progress to establish the synthetic feasibility to introduce a group at C-3 of the phthalimidine nucleus by trapping ionic species **A** and **B** alike with a suitable reagent. In a next paper we shall report these results.

EXPERIMENTAL

Melting points were determined with a Kofler apparatus and are uncorrected. The ir spectra were recorded for Nujol mulls with a Perkin Elmer 137 and absorption maxima are quoted in cm^{-1}. The uv spectra were recorded for solutions in 95% ethanol with a Zeiss PMQ II and a Perkin Elmer 575 spectrophotometers and absorption maxima are quoted in nm. The pmr spectra were recorded for solutions in deuteriochloroform (unless otherwise indicated) with a Jeol C-60 HL spectrometer; each line of the most significant signals is quoted in δ ppm from tetramethylsilane and multiplicity is designed s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet).

3-Benzyl-3-hydroxy-2-phenylphthalimidine (**1**).

To a stirred suspension of 25 g (1.13×10^{-1} mole) of 3-benzylidenephthalide in 15 ml of methanol and 5 ml of water, 25 ml (2.7×10^{-1} mole) of aniline was dropwise added in 5 hours at 100°. Heating was continued for 20 hours. The reaction mixture was diluted with 40 ml of methanol and left overnight at room temperature. The precipitate was filtered and recrystallised from methanol to give 27.5 g (77%) of 3-benzyl-3-hydroxy-2-phenylphthalimidine (**1**), mp 178-180°; ir: 3140 (OH), 1650 (CO); nmr (deuteriochloroform/DMSO-d_6): 3.4 (q, 2H, J = 13.5 Hz), 6.58-8.0 (m, 15H).

Anal. Calcd. for $C_{21}H_{17}NO_2$: C, 80.00; H, 5.45; N, 4.45. Found: C, 80.20; H, 5.55; N, 4.50.

3-Anilino-3-benzyl-2-phenylphthalimidine (**2**).

To 5 ml (5.4×10^{-2} mole) of aniline, 1.0 g (4.5×10^{-3} mole) of 3-benzylidenephthalide was added portionwise at 100°. After 20 hours of heating the reaction mixture was diluted with 30 ml of aqueous ethanol (1:1) causing separation of 1.1 g (63%) of 3-anilino-3-benzyl-2-phenylphthalimidine (**2**), which was crystallised from ethanol, mp 137-139°; ir: 3330 (NH), 1680 (CO); nmr (deuteriochloroform/DMSO-d_6): 3.48 (q, 2H, J = 13.5 Hz), 6.3-7.9 (m, 20H).

Anal. Calcd. for $C_{27}H_{22}N_2O$: C, 83.05; H, 5.70; N, 7.10. Found: C, 83.20; H, 5.55; N, 7.15.

3-Benzyl-3-methoxy-2-phenylphthalimidine (**3a**).

Into 50 ml of a methanolic solution of 2 g (6.35×10^{-3} mole) of **1** a stream of hydrogen chloride was bubbled at 0° for 15 minutes, and the reaction mixture was kept at this temperature for 2 hours. Addition of 200 g of ice allowed collection of a white crude material which was washed with water, suspended in 5% sodium bicarbonate and extracted with dichloromethane. The organic layer, washed with water, dried and evaporated under reduced pressure, was then diluted with petroleum ether to give 1.7 g (81%) of **3a**, mp 124-126°; ir: 1670 (CO); nmr: 3.05 (s, 3H), 3.36 (q, 2H, J = 13.5 Hz), 6.5-8.0 (m, 14H).

Anal. Calcd. for $C_{22}H_{19}NO_2$: C, 80.40; H, 5.80; N, 4.25. Found: C, 80.60; H, 5.95; N, 4.20.

3-Benzyl-3-ethoxy-2-phenylphthalimidine (**3b**).

With the same procedure described above, 10 g (3.17×10^{-2} mole) of **1** in anhydrous ethanol gave 5.2 g (48%) of **3b**, mp 130-132°; ir: 1675 (CO); nmr: 1.22 (t, 3H, J = 7 Hz), 3.22 (q, 2H, J = 7 Hz), 3.42 (q, 2H, J = 13.5 Hz), 6.62-8.0 (m, 14H).

Anal. Calcd. for $C_{23}H_{21}NO_2$: C, 80.45; H, 6.15; N, 4.10. Found: C, 80.70; H, 6.20; N, 4.10.

3-Benzylidene-2-phenylphthalimidines **4** and **5**.

a) From 3-Benzyl-3-hydroxy-2-phenylphthalimidine (**1**).

To a solution of 45 ml of acetic acid and 5 ml of hydrochloric acid 10 g (3.17×10^{-2} mole) of **1** was added and the mixture was heated at 100° for 30 minutes. Dilution with 10 ml of water caused separation of 6.3 g (67%) of **4**, which was crystallised from benzene as pale yellow prisms, mp 201-203°; ir: 1680 (CO); nmr: 6.77 (s, 1H), 6.8-8.0 (m, 14H).

Anal. Calcd. for $C_{21}H_{15}NO$: C, 84.80; H, 5.10; N, 4.70. Found: C, 85.05; H, 5.30; N, 4.85.

Further addition of water allowed to collect 1.35 g (14%) of **5**, which was crystallised from benzene-petroleum ether, mp 113-116°; ir 1685 (CO); nmr: 6.31 (s, 1H), 6.8-7.6 (m, 13H), 7.87 (m, 1H).

Anal. Calcd. for $C_{21}H_{15}NO$: C, 84.80; H, 5.10; N, 4.70. Found: C, 84.80; H, 5.00; N, 4.60.

b) From 3-Anilino-3-benzyl-2-phenylphthalimidine (**2**).

Into a solution of 1 g (2.56×10^{-3} mole) of **2** in 20 ml of ethyl ether and 80 ml of dichloromethane hydrogen chloride was bubbled at 0° for 15 minutes. Aniline hydrochloride formed during this time was filtered off. The organic solution was washed with water, sodium bicarbonate solution, dried and evaporated. The oily residue by addition with petroleum ether gave 0.7 g (92%) of a mixture of **4** and **5** (ratio 5:1).

Treatment of **1** and **2** with Hydrochloric Acid in Alcohols.

This reaction allowed us to isolate 5.3 g (56%) of **4**, 1.1 g (12%) of **5** and 1.2 g (11%) of **3a** or 1.0 g (9%) of **3b** respectively, by diluting with care the reaction mixture obtained from 10 g (3.17×10^{-2} mole) of **1** or 12.4 g (3.17×10^{-2} mole) of **2**, in 45 ml of alcohol (methanol or ethanol) and 5 ml of hydrochloric acid, with the same procedure reported above when acetic acid was used as solvent.

3-(α-Bromobenzylidene)-2-phenylphthalimidines **6** and **7**.

To a stirred solution of 29.7 g (10^{-1} mole) of **4** and **5** in 100 ml of chloroform, 5.5 ml (10^{-1} mole) of bromine in 50 ml of chloroform was slowly added. The mixture was heated at 100° for some minutes favouring evolution of hydrogen bromide, then washed with water, sodium metabisulphite solution, and evaporated to an oily residue which solidified with petroleum ether to give 34.0 g of a mixture of **6** and **7** [ratio (40 ± 5):(60 ± 5)]. A tedious crystallisation with dichloromethane-petroleum ether gave **6**, pale red platelets, mp 146-148°; ir 1680 (CO); nmr: 6.9-8.25 (m, 13H), 9.11 (m, 1H).

Anal. Calcd. for $C_{21}H_{14}BrNO$: C, 67.05; H, 3.75; N, 3.70. Found: C, 66.85; H, 3.65; N, 3.65.

The isomer **7** was obtained by crystallisation from methanol, mp 144-146°; ir: 1680 (CO); nmr: 6.22 (m, 1H), 7.02-7.68 (m, 12H), 7.88 (m, 1H).

Anal. Calcd. for $C_{21}H_{14}BrNO$: C, 67.05; H, 3.75; N, 3.70. Found: C, 67.15; H, 3.75; N, 3.55.

11-Phenylisoindolo[2,1-*a*]indol-6-one (**8**).

a) By Thermal Rearrangement.

A mixture of 1.1 g (2.9×10^{-3} mole) in 10 ml of ethylene glycol containing 1 g of sodium acetate was refluxed for 1 hour. After cooling, dilution with 40 ml of water caused separation of 0.50 g of a crude product which crystallised from methanol to give 0.30 g (35%) of **8**, mp 223-226° [4]. By evaporation of the mother liquor, 0.2 g of *N*-phenylphthalimidine was obtained; weak acidification of the aqueous solution with acetic acid permitted another crop of this compound to be obtained (0.15 g, entire yield 55%). Exhaustive addition of hydrochloric acid, extraction with ethyl ether and evaporation of solvent gave 0.1 g (28%) of benzoic acid.

b) By Photolysis.

A solution of 4.3 g (1.15×10^{-2} mole) of **6** and **7** in 400 ml of methanol containing 2 g of sodium acetate was irradiated with a 70 W high-pressure mercury lamp (Hanau TQ 81), equipped with an immersion well system (Pyrex glass), at room temperature for 3 hours. The mixture was evaporated, the residue was suspended in dichloromethane and washed with water. The solvent was evaporated and the oily residue treated with methanol gave 0.85 g (25%) of **8**.

2-(*o*-Carboxyphenyl)-3-phenylindole (**9**).

A solution of 0.5 g (1.7×10^{-3} mole) of **8** in 10 ml of ethanol containing 0.5 g of potassium hydroxide was refluxed for 1 hour. Dilution with 100 ml of water and addition of acetic acid gave 0.3 g (56%) of **9**, which crystallised from chloroform-petroleum ether, mp 98-101°; ir: 3310 (NH), 1650 (CO); nmr: 6.3 (broad s, 1H), 7.2-8.1 (m, 13H), 11.12 (broad s, 1H).

Anal. Calcd. for $C_{21}H_{15}NO_2$: C, 80.50; H, 4.80; N, 4.45. Found: C, 80.30; H, 4.95; N, 4.55.

Treatment of **9** with Acids.

A mixture of 5 ml of acetic acid, 1 ml of hydrochloric acid and 0.5 g (1.6×10^{-3} mole) was heated at 100° for 30 minutes. Addition of 5 ml of water afforded 0.4 g (85%) of **8**.

2-(*o*-Carbomethoxyphenyl)-3-phenylindole (**10**).

To a 0.5 g (1.6×10^{-3} mole) of **9** an ethereal solution of diazomethane was added. Evaporation of solvent gave 0.45 g (86%) of crude **10**, which was crystallised from chloroform-petroleum ether, mp 130-132°; ir 3250 (NH), 1680 (CO); nmr: 3.6 (s, 3H), 7.1-8.0 (m, 13H), 8.77 (broad s, 1H).

Anal. Calcd. for $C_{22}H_{17}NO_2$: C, 80.70; H, 5.25; N, 4.30. Found: C, 80.90; H, 5.3; N, 4.25.

3-Benzoyl-2-phenylphthalimidine (**11**).

A solution of 5 g (1.33×10^{-2} mole) of **6** and **7** in 40 ml of ethanol containing 5 g of potassium hydroxide was refluxed for 30 minutes. Addition of 150 ml of water and extraction with ethyl ether gave an organic layer which was dried and evaporated to leave 0.7 g (25%) of *N*-phenylphthalimidine. The aqueous layer acidified with acetic acid gave 1.2 g (29%) of **11**, which was crystallised from methanol, mp 182-184°; ir 1670, 1690 (CO); uv 236 (log ϵ 4.28), 2.51 (4.25), 273 infl (4.07), 280.5 sh (4.04) [in ethanolic potassium hydroxide 2.2×10^{-2} *M*: 263 (log ϵ 4.06), 413 (3.95)]; nmr: 6.62 (s, 1H), 7.0-8.1 (m, 14H).

Anal. Calcd. for $C_{15}H_{15}NO_2$: C, 80.5; H, 4.85; N, 4.45. Found: C, 80.30; H, 4.90; N, 4.70.

Addition of an excess of mineral acid to the solution and extraction with ethyl ether gave by evaporating the organic solvent an oily residue which solidified with petroleum ether affording 0.15 g (9%) of benzoic acid.

Compound **11** was completely converted into *N*-phenylphthalimidine and benzoic acid by heating with 10% ethanolic potassium hydroxide for 30 minutes.

3-(α-Hydroxybenzyl)-2-phenylphthalimidine (**12**).

To a stirred solution of 0.2 g (6.4×10^{-4} mole) of **11** in 20 ml of ethanol 0.3 g of sodium borohydride was portionwise added at room temperature. After 1 hour the mixture was diluted with 200 ml of water and 5 ml of 10% sodium hydroxide, obtaining 0.12 g (60%) of **12**, which was crystallised from methanol, mp 209-211°; ir 3270 (OH), 1640 (CO); nmr: 5.35 (m, 1H), 5.89 (d, 1H), 6.06 (d, 1H) [after deuterium oxide 5.35 (d, 1H), 5.89 (d, 1H)], 6.72-8.37 (m, 14H).

Anal. Calcd. for $C_{21}H_{17}NO_2$: C, 80.00; H, 5.45; N, 4.45. Found: C, 80.20; H, 5.70; N, 4.60.

o-Phenylacetylbenzoic Acid Anilide (**13**).

a) From **4** and **5**.

A solution of 10 g (3.37×10^{-2} mole) of **4** and **5** in 100 ml of 10% ethanolic potassium hydroxide was boiled under reflux for 1 hour. After cooling, 200 ml of water and 15 ml of acetic acid was added and the precipitate **13** collected, which crystallised from ethyl ether, mp 154-156°; ir: 3330 (NH), 1720 (CO); uv 234 (log ϵ 4.31), 278 (3.45); nmr (DMSO-d_6): 3.5 (broad s, 1H), 3.7 (s, 2H), 6.3-8.0 (m, 14H).

Anal. Calcd. for $C_{21}H_{17}NO_2$: C, 80.00; H, 5.45; N, 4.45. Found: C, 79.95; H, 5.50; N, 4.45.

b) From *o*-Phenylacetylbenzoic Acid.

A mixture of 1 g (4.16×10^{-3} moles) of acid and 1 ml of aniline was heated at 100° for 1 hour. Addition of aqueous ethanol and acetic acid caused separation of 0.85 g (65%) of **13**.

o-Phenylacetylbenzoic Acid and *N*-Methylaniline.

A mixture of 1 g (4.16×10^{-3} mole) of *o*-phenylacetylbenzoic acid and 1 ml of amine was heated at 150° for 1 hour. Addition of aqueous ethanol and acetic acid allowed us to obtain 0.8 g (87%) of 3-benzylidenephthalide.

If this reaction was performed at 100° only 0.05 g of this product was obtained.

Some Reactions of *o*-Phenylacetylbenzoic Acid Anilide (**13**).

a) With Hydroxylamine.

A stirred solution of 0.5 g (1.6×10^{-3} mole) of **13** in 10 ml of ethanol and 1 ml of pyridine was treated with 1 g of hydroxylamine hydrochloride at room temperature and stirring was continued for 30 minutes. Dilution with 10 ml of 5% sulphuric acid caused precipitation of 0.3 g (79%) of 4-benzylbenzoxazin-1-one, mp 115-117° [14].

b) With Acetic Anhydride.

A solution of 0.5 g (1.6×10^{-3} mole) of **13** in 1 ml of pyridine and 1 ml of acetic anhydride was heated at 100° for 10 minutes. Dilution with 10 ml of cold 10% sulphuric acid allowed us to collect 0.4 g (84%) of **4** and **5**.

c) With Hydrogen Chloride.

Into a solution of 2 g (6.35×10^{-3} mole) of **13** in 50 ml of dichloromethane and 50 ml of ethyl ether hydrogen chloride was bubbled at 0° for 30 minutes. The white dust consisting in 1.5 g (67%) of *o*-phenylacetylbenzoic acid anilide hydrochloride (**13**·HCl) was collected, mp 195-200°; ir: 2570, 2430 (NH_2^+), 1660, 1625 (CO); nmr (DMSO-d_6): 3.82 (s, 2H), 6.4-8.0 (m, 14H), 10.87 (broad s, 2H).

Anal. Calcd. for $C_{21}H_{18}ClNO_2$: C, 71.70; H, 5.15; N, 4.00. Found: C, 71.65; H, 5.25; N, 3.95.

Some Reactions of **13**·HCl.

a) In Dimethylsulphoxide.

A solution of 0.5 g (1.4×10^{-3} mole) of **13**·HCl in 5 ml of dimethylsulphoxide was heated at 100° for 1 hour. Dilution with 30 ml of water afforded 0.35 g (83%) of a mixture of **4** and **5**.

b) In Methanol.

A solution of 0.5 g (1.42×10^{-3} mole) of **13**·HCl in 5 ml of methanol was refluxed for 1 hour. Dilution with 30 ml of water afforded 0.4 g of **3a**, **4** and **5**.

These last two reactions occurred also by keeping the solutions at room temperature for several days.

c) In Hydrochloric Acid.

A suspension of 0.5 g (1.42×10^{-3} mole) of **13**·HCl in 10 ml of hydrochloric acid was refluxed for 4 hours. After cooling 0.25 g (79%) of 3-benzylidenephthalide was collected.

REFERENCES AND NOTES

[1] S. Gabriel, *Ber.*, **18**, 1251 (1885).

[2] A. Marsili and V. Scartoni, *Gazz. Chim. Ital.*, **102**, 507 (1972).

[3] In forthcoming papers we shall give further evidence of these ionic intermediates.

[4] V. Scartoni, I. Morelli, A. Marsili and S. Catalano, *J. Chem. Soc., Perkin Trans. I*, 2332 (1977).

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[6] The ratio of isomers was determined by the nmr method on the basis of relative intensity of signals attributed to proton at C-8 for **4** and **5**, and to proton at C-4 for **6** and **7**, therefore data were not accurate (see Experimental and, for numbering system, reference [5]).

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[12] This hypothesis constituted a tentative explanation of experimental results based only on the nature of reagents and products and on reaction conditions.

[13] *o*-Phenylacetylbenzoic acid reacted with *N*-methylaniline to give 3-benzylidenephthalide.

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[17] In methanol a little **3a** was also obtained.