peak at 1090 cm^{-1} had essentially disappeared. The brown oil (13.2 g) obtained from the reaction was reduced as described above to give (after distillation) 7.28 g (0.052 mol, 71%) of 1.

Preparation of 4-Chlorotoluene.—*p*-Toluenesulfonyl chloride (15.0 g, 0.079 mol) was dissolved in 100 ml of chloroform, and the solution was stirred mechanically and irradiated by a 150-W incandescent bulb. Chlorine gas was passed through the solution until vpc analysis on a 6 ft, 3% SE-30 on Chromosorb W column showed that the *p*-toluenesulfonyl chloride was essentially completely reacted. The chlorine flow was stopped and the reaction mixture was worked up as described for the preparation of 1, to give 14.0 g of dark oil. The oil was suspended in 100 ml of rapidly stirred concentrated hydrochloric acid. Iron powder (7.0 g, 0.125 g-atom) was added slowly. The reaction mixture was stirred for 2 hr, filtered, and extracted with methylene chloride. The extract was washed with water and dilute sodium bicarbonate solution, dried over magnesium sulfate, and evaporated to give 6.1 g (0.048 mol, 61%) of brown fluid, whose ir and nmr spectra were identical with those of 4-chlorotoluene.

Registry No.—**1**, 615-60-1; **2**, 2905-30-8; bis(3,4-dimethylphenyl) sulfone, 28361-43-5; 4-chlorotoluene, 106-43-4; *o*-xylene, 95-47-6; *p*-toluenesulfonyl chloride, 98-59-9.

The Cyclization of 2-Benzamido-1-phenyl-1-propanol to 1-Phenyl-3-methylisoquinoline

STEFAN GOSZCZYŃSKI* AND TOMASZ KOPCZYŃSKI

Technical University, Poznań, pl. Skłodowskiej Curie 1, Poland

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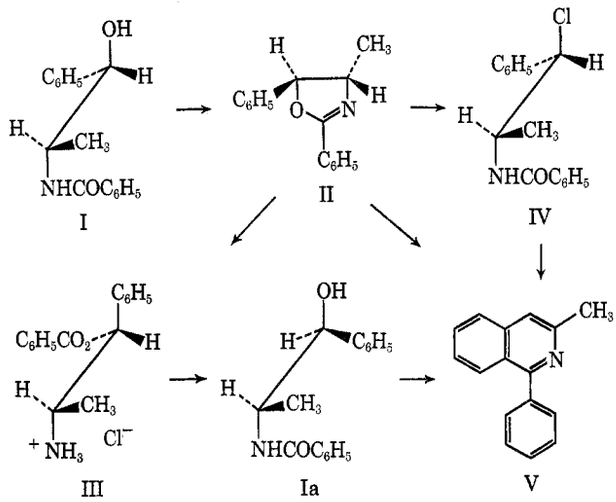
The cyclization of 3,4-diphenylbut-3-en-2-one oxime benzoate in nitrobenzene solution led unexpectedly to the formation of 1-phenyl-3-methylisoquinoline.[1] It was of great importance to us to confirm the identity of this cyclization product with a specimen obtained by a different route. The synthesis of 1-phenyl-3-methylisoquinoline by cyclization of 2-benzamido-1-phenyl-1-propanol given as a checked procedure,[2] based on the proposal earlier published,[3] furnished in our hands a product with mp 128–129°. On the other hand, our cyclization product obtained from 3,4-diphenylbut-3-en-2-one oxime benzoate had mp 89–90°, very close to that reported by Dobrovsky[4] and Gosh, *et al.*[5]

The uv, nmr, and mass spectra fully confirm the isoquinoline structure with the phenyl in the 1 and methyl in the 3 position. Our present task was to elucidate the structure of the compound obtained by Whaley and Hartung (mp 123–125°), quoted by Fitton and Smalley as having mp 126–127° and found by us to have mp 128–129°. In our opinion these were the same product, and the small differences in the melting points are caused by varying states of purity. The elemental analysis suggested the presence of oxygen and the data were in full agreement with those calculated for the starting material, 2-benzamido-1-phenyl-1-propanol. In addition the nmr spectrum was almost identical with that of starting amide and that of the product obtained after its treatment with P_2O_5 and $POCl_3$ in boiling xylene according to ref 2 and 3.

The only rational explanation is that the product claimed by Whaley and Hartung to be 1-phenyl-3-methylisoquinoline is in fact the threo isomer of the original erythro amide. The change of configuration in a series of analogous amides is well known.[6] The reaction pathways may be illustrated as follows.



The Whaley and Hartung product, in our opinion, is Ia, formed as a result of transformation I → II → III → Ia, and the reported derivatives were the hydrochloride and picrate of III. Our point of view has been confirmed by cyclization of both I and Ia in boiling decalin in the presence of phosphorus pentoxide. We have also synthesized 2,5-diphenyl-4-methyloxazoline (II) and 2-benzamido-1-chloro-1-phenylpropane (IV) and then we have refluxed them in decalin with P_2O_5. In all cases the only basic product was 1-phenyl-3-methylisoquinoline, mp 89–90°. The isolation of III after treatment of I with phosphorus oxychloride gives further support for our point of view. Our final conclusion, therefore, is that the cyclization of I does not take place under the conditions reported by Whaley and Hartung and quoted by Fitton and Smalley. The ring closure of 2-benzamido-1-phenyl-1-propanol takes place only when the amide is heated with phosphorus pentoxide at the much higher temperature of boiling decalin.

Experimental Section

Melting points were determined using a Thiele capillary melting point apparatus and are uncorrected. Uv spectra were determined with a C. Zeiss VSU-2P spectrophotometer, nmr spectra were recorded on a Tesla 80-MHz spectrometer, and ir spectra were recorded on a Unicam SP-200G spectrophotometer.

2-Benzamido-1-phenyl-1-propanol (I) was obtained from propiophenone by a three-stage synthesis according to ref 2: mp 143–144°; ir (Nujol) 3375, 3305 (NH, OH), 1640 (C=O), 1550 cm^{-1} (NH); nmr (DMSO-d_6) δ 1.05 (d, 3, CH_3), 4.13 (m, 1, C^2H), 4.69 (m, 1, C^1H), 5.39 (d, 1, OH), 7.08–7.88 (m, 10, aromatics), 8.12 (d, 1, NH).

2,5-Diphenyl-4-methyloxazoline (II) was obtained according

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to Nagai and Kanao:[7] bp 155° (5 mm); picrate mp 140–141°; nmr (CCl_4) δ 1.34 (d, 3, CH_3), 4.03 (m, 1, C^4H), 4.88 (d, 1, C^5H), 7.00–8.01 (m, 10, aromatics).

2-Benzamido-1-chloro-1-phenylpropane (IV) was prepared as described by Kojima:[8] mp 112–113°; ir (Nujol) 3375, 3305 (NH, OH), 1620 (C=O), 1550 cm^{-1} (NH).

2-Amino-1-benzoyloxy-1-phenylpropane Hydrochloride (III).—A 1-g portion of I dissolved in 10 ml of $POCl_3$ was allowed to stand at room temperature for 1 hr. Crushed ice was added, and the mixture was heated, boiled for 10 min, and cooled to give white needles. After recrystallization from water 0.9 g (79%), mp 220–221°, was obtained, ir (KBr) 2900 (NH_3^+), 1717 cm^{-1} (C=O). The hydrochloride when treated in alcoholic solution with picric acid gave picrate, mp 188–189°. The suspension of hydrochloride in water alkalized with dilute sodium hydroxide furnished Ia, mp 128–129°.

Treatment of 2-Benzamido-1-phenyl-1-propanol with P_2O_5 and $POCl_3$ in Boiling Xylene (I → Ia).—A 2-g portion of the amide was refluxed in 50 ml of xylene with 20 g of phosphorus pentoxide and 20 ml of phosphorus oxychloride for 2.5 hr. The further work-up used was similar to that described by Fitton and Smalley.[2] After recrystallization from ethanol, Ia had mp 128–129°; yield 1.3 g (65%); nmr (DMSO-d_6) δ 0.94 (d, 3, CH_3), 4.18 (m, 1, C^2H), 4.64 (m, 1, C^1H), 5.40 (d, 1, OH), 7.08–7.99 (m, 11, aromatics and NH); ir (Nujol) 3350 (NH, OH), 1637 (C=O), 1543 cm^{-1} (NH).

Anal. Calcd for $C_{15}H_{17}NO_2$: C, 75.28; H, 6.71; N, 5.48. Found: C, 75.36; H, 6.80; N, 5.44.

Cyclization of 2-Benzamido-1-phenyl-1-propanol (I, Ia) to 1-Phenyl-3-methylisoquinoline (V).—To 2.0 g of the amide I suspended in 50 ml of decalin, 20 g of phosphorus pentoxide was added. The mixture was refluxed for 3 hr, then cooled and 100 g of crushed ice was added. The decalin layer was separated and the aqueous solution was extracted with 50 ml of ether. The aqueous layer was made alkaline with 130 ml of 30% potassium hydroxide solution and then extracted with ether. The extracts were washed once with water and dried over KOH, and the solvent was removed, leaving 1.3 g (70%) of pale yellow oil which crystallized on standing.

Crystallization from ethanol gave colorless crystals, mp 89–90°, picrate mp 200–201°, hydrochloride mp 228–229°.

The free base had uv max (MeOH) 332 nm (ε 6000); uv (0.01 *N* HCl) 351 nm (ε 8900); nmr (CCl_4) δ 2.7 (s, 3, CH_3), 7.3–8.1 (m, 10, aromatics).

Anal. Calcd for $C_{16}H_{13}N$: C, 87.67; H, 5.98; N, 6.39. Found: C, 87.85; H, 6.15; N, 6.40.

The structure was further confirmed by mass spectral analysis,[9] which gave the correct molecular ion at *m/e* 219. The cyclization of the isomeric amide, mp 128–129° (Ia) (obtained after treatment of amide, mp 143–144°, with P_2O_5 and $POCl_3$ in boiling xylene or from III) gave the same result.

Cyclization of 2,5-Diphenyl-4-methyloxazoline.—A 2-g portion of II dissolved in 50 ml of decalin was treated with 20 g of P_2O_5 and refluxed for 3 hr. After cooling, 100 g of crushed ice was added, the decalin layer was removed, and the water layer was extracted several times with ether. The acidic water solution was made alkaline with 130 ml of 30% potassium hydroxide and extracted with ether. The combined ether extracts were washed with water and dried over KOH. The evaporation of ether left 1.13 g (60%) of pale yellow oil which crystallized on scratching. Recrystallization from ethanol gave colorless crystals, mp 89–90°. The uv and nmr spectra were identical as given above.

Cyclization of 2-Benzamido-1-chloro-1-phenylpropane.—A 2-g portion of IV was heated in boiling decalin with 20 g of phosphorus pentoxide for 3 hr. The further work-up was similar to that described for cyclization of II. The yield was 0.78 g (37%), mp 89–90°. The spectral data were in accordance with those found for V.

Registry No.—I, 38222-75-2; Ia, 38222-76-3; II, 38222-77-4; III, 38222-78-5; III picrate, 38222-79-6; V, 1616-50-8; V picrate, 38222-81-0; V HCl, 38222-82-1; propiophenone, 93-55-0.

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