546. *The Disproportionation of Dihydro*iso*quinolines.*

By C. I. Brodrick and W. F. Short.

1-Phenyl-3 : 4-dihydro*iso*quinoline yields 1-phenyl*iso*quinoline and 1-phenyl-1 : 2 : 3 : 4-tetrahydro*iso*quinoline on distillation at atmospheric pressure and this has led to some confusion in the literature. 1-Benzyl-3 : 4-dihydro*iso*quinoline similarly affords 1-benzyl*iso*quinoline and *iso*quinoline.

During the course of synthetical experiments in the *iso*quinoline group the authors required a reference specimen of 1-phenyl-3 : 4-dihydro*iso*quinoline and observed curious discrepancies in the descriptions of the properties of this base and its derivatives. The compound has been prepared from benzo-2-phenylethylamide by various modifications of the original Bischler–Napieralski method (Bischler and Napieralski, *Ber.*, 1893, **26**, 1907; Pictet and Kay, *ibid.*, 1909, **42**, 1975; Decker and Kropp, *ibid.*, 1909, **42**, 2075; Decker, Kropp, Hoyer, and Becker, *Annalen*, 1913, **395**, 299; Späth, Berger, and Kuntara, *Ber.*, 1930, **63**, 134) and is generally described as an oil; however, Bischler and Napieralski (*loc. cit.*), who carried out the dehydration of the amide at a temperature (250—260°) higher than that used by subsequent investigators, report a " dark semi-solid product," Pictet and Kay (*loc. cit.*), obtained a product, m. p. 73—74° (but only after the oily base initially obtained had been distilled at atmospheric pressure), and Decker and Kropp (*loc. cit.*) stated that the product in one preparation crystallised after some time. On repeating the work of Pictet and Kay we obtained a liquid base, b. p. 146—149·5°/1·2 mm., having the composition $C_{15}H_{13}N$, which, after distillation at atmospheric pressure, afforded a solid, m. p. 70—75°, which also gave analytical figures agreeing with this formula. The original liquid base did not solidify on being seeded with the solid, indicating that the distillation had produced some transformation, most probably a disproportionation. Confirmation of the view that the solid consists of an equimolecular mixture of 1-phenyl*iso*quinoline, m. p. 94—96°, and 1-phenyl-1 : 2 : 3 : 4-tetrahydro*iso*quinone, m. p. 97·5—98·5°, was obtained by a Zerewitinoff determination, which indicated the presence of only 0·5 atom of active hydrogen, and by the isolation of *ca.* 20% of each of these bases from the solid by chromatographic separation on alumina. 2-*Acetyl*-1-*phenyl*-1 : 2 : 3 : 4-*tetrahydro*iso*quinoline* (42%) and 1-phenyl*iso*quinoline (49%) were isolated from the mixture obtained by the action of acetic anhydride on the solid. 1-Phenyl*iso*quinolinium picrate, m. p. and mixed m. p. 167—167·5°, was obtained from the solid and alcoholic picric acid, and is most probably the compound described by Pictet and Kay (*loc. cit.*) as the picrate of 1-phenyl-3 : 4-dihydro*iso*-quinoline. The sparingly soluble hydrochloride isolated by these authors was likewise probably 1-*phenyl*-1 : 2 : 3 : 4-*tetrahydro*iso*quinolinium chloride,* since we obtained this salt from our solid mixture and ethereal hydrogen chloride, and the hydrochloride of the dihydro-base is readily soluble in cold water. Dr. W. F. Elvidge and Mr. L. Brealey kindly examined the absorption spectra of 1-phenyl-3 : 4-dihydro*iso*quinoline, 1-phenyl-1 : 2 : 3 : 4-tetrahydro*iso*quinoline, 1-phenyl*iso*quinoline, and of the solid, m. p. 70—75°, and the results (see Table) are in complete agreement with the chemical evidence.

Light-absorption data.

	In 0·1N-hydrochloric acid.				In alcohol.			
	Maxima.		Minima.		Maxima.		Minima.	
Substance.	mμ.	$E^{1\%}_{1\,cm.}$	mμ.	$E^{1\%}_{1\,cm.}$	mμ.	$E^{1\%}_{1\,cm.}$	mμ.	$E^{1\%}_{1\,cm.}$
1-Phenyl-3 : 4-dihydro*iso*quinoline	285	950	243	98	247	588	237	493
Product *A*, m. p. 70—75°	232	1275	249—250	167	273—277	215	260—263	190
	270	297	—	—	—	—	—	—
1-Phenyl*iso*quinoline	230	2170	251	313	278	374	260	313
	270	497	300	98	323—327	303	300	190
	342	428	—	—	—	—	—	—
1-Phenyl-1 : 2 : 3 : 4-tetrahydro*iso*quinoline	General absorption only				265	22·7	245	12·0
1-Benzyl-3 : 4-dihydro*iso*quinoline	276	502	240	170	252	405	230	300
Product *E*, b. p. 145—148°/0·7 mm. (see Experimental)	228	1116	255	216	253	215	245	202
	271—274	251	304	89	284	112	280	110
	310	94	315	91	296	59	294	58
	326—328	129	—	—	309	80	300	57
	—	—	—	—	322	92	316	67
1-Benzyl*iso*quinoline	228	2160	253	141	271	261	249	168
	267	156	295	53	310	162	294	90·5
	333	258	—	—	321	181	315	150

The remarkably ready disproportionation of 1-phenyl-3 : 4-dihydro*iso*quinoline caused by heat is doubtless exhibited by other dihydro-bases and we have made a cursory examination of the behaviour of 1-benzyl-3 : 4-dihydro*iso*quinoline. On distillation at atmospheric pressure, this compound affords *iso*quinoline and a mixture of bases, containing 0·33 atom of active hydrogen, in which 1-benzyl*iso*quinoline was definitely identified. The absorption spectrum (see Table) indicated the presence of 1-benzyl*iso*quinoline and possibly of unchanged base. After the completion of our experiments, Huntress and Shaw (*J. Org. Chem.*, 1948, **13**, 679) observed that 1-benzyl-3 : 4-dihydro*iso*quinoline is completely decomposed into toluene and *iso*quinoline by potassium hydroxide at 200°.

EXPERIMENTAL.

1-*Phenyl*-3 : 4-*dihydro*iso*quinoline.*—Benzo-2-phenylethylamide (54 g.) was cyclised according to Pictet and Kay (*loc. cit.*) to give 1-phenyl-3 : 4-dihydro*iso*quinoline, b. p. 146—149·5°/1·2 mm. (32·8 g., 66%) as an almost colourless oil (Found : C, 86·4; H, 6·2; N, 6·65. Calc. for $C_{15}H_{13}N$: C, 86·95; H, 6·3; N, 6·8%). The picrate consisted of yellow prismatic needles (from ethanol), m. p. 174—175°. The hydrochloride formed colourless needles (from methanol–ether), m. p. 236—238° (Found, on material dried at 100°/1 mm. : C, 73·4; H, 5·8; N, 5·9. Calc. for $C_{15}H_{14}NCl$: C, 73·9; H, 5·75; N, 5·75%), and was readily soluble in cold water. (Pictet and Kay, *loc. cit.*, record m. p. 222—223°, and Decker, Kropp, Hoyer, and Becker, *loc. cit.*, m. p. 225°.)

When the foregoing base (21·8 g.) was distilled at atmospheric pressure (b. p. 340—345°) (21·0 g.), it crystallised readily. Redistillation (b. p. 148—155°/1·2—1·4 mm.) (19·7 g.) and crystallisation from light petroleum (b. p. 40—60°) gave colourless prisms, m. p. 70—75° (14·1 g.) (product *A*) (Found : C, 87·0; H, 6·2; N, 7·1%; active H, 0·47 atom. Calc. for $C_{15}H_{11}N,C_{15}H_{15}N$: C, 86·95; H, 6·3; N, 6·8%; active H, 0·5 atom). A second crop (3·3 g.) had m. p. 73—77°.

Reactions of Product A.—(*a*) With alcoholic or ethereal picric acid yellow needles, m. p. 167—167·5°, were obtained, undepressed on admixture with an authentic specimen of 1-phenyl*iso*quinolinium picrate [m. p.s varying from 164° (Pictet and Kay, *loc. cit.*) to 165—166° (Späth *et al.*, *loc. cit.*) are given in the literature] prepared from 1-phenyl*iso*quinoline, obtained from the dihydro-base by dehydrogenation with palladium (Späth *et al., loc. cit.*) or by oxidation with potassium permanganate (Pictet and Kay, *loc. cit.*).

(*b*) The action of dry ethereal hydrogen chloride, followed by repeated crystallisation of the product from methanol–ether, gave slender, colourless needles, m. p. 227—229° (Found : C, 73·2; H, 6·5; N, 5·7. $C_{15}H_{16}NCl$ requires C, 73·3; H, 6·5; N, 5·7%), which did not depress the m. p. of an authentic specimen of 1-*phenyl*-1 : 2 : 3 : 4-*tetrahydro*iso*quinolinium chloride*, prepared from the base, m. p. 97·5—98·5° (Leithe, *Monatsh.*, 1929, **53**, 956 gives m. p. 97°).

(*c*) When *A* (5 g.) was dissolved in chloroform (7 c.c.), and light petroleum (125 c.c.) was added, 1·03 g. of 1-phenyl-1 : 2 : 3 : 4-tetrahydro*iso*quinoline, m. p. 96—98° alone or admixed with an authentic specimen, separated. Concentration of the mother-liquor gave crops of m. p. around 70°.

(*d*) Adsorption of *A* (1 g.) in light petroleum (150 c.c.) on activated alumina and elution with the same solvent gave first almost pure 1-phenyl*iso*quinoline (0·28 g.), then a small amount of impure material, and finally, when eluted with 50% (v/v) chloroform–light petroleum, almost pure tetrahydro-base (0·2 g.).

(*e*) Acetic anhydride (37·5 c.c.) and *A* (5 g.) were heated for 3 hours at 100°. Volatile material was removed under diminished pressure, and the residue separated into basic and neutral fractions with ether and hydrochloric acid. The basic fraction (2·46 g.), on recrystallisation from light petroleum, gave 1-phenyl*iso*quinoline, m. p. 95—96°, and the neutral fraction (2·5 g.), m. p. 89·5—91°, separated from light petroleum in colourless needles or from aqueous acetone in dense prisms of 2-*acetyl*-1-*phenyl*-1 : 2 : 3 : 4-*tetrahydro*iso*quinoline*, m. p. 91·5—92·5° (Found : C, 81·5; H, 7·0; N, 5·7. $C_{17}H_{17}ON$ requires C, 81·3; H, 6·8; N, 5·6%). There was no depression in m. p. on admixture with a specimen prepared from 1-phenyl-1 : 2 : 3 : 4-tetrahydro*iso*quinoline.

1-*Benzyl*-3 : 4-*dihydro*iso*quinoline*.—Phenylaceto-2-phenylethylamide (42 g.) was cyclised according to Pictet and Kay (*loc. cit.*) to give the base (20·1 g.), b. p. 158—161°/1·2 mm., n_D^{21} 1·6201. The picrate had m. p. 178—179·5° [m. p.s varying from 173—175° (Späth, *et al., loc. cit.*) to 182° (Decker *et al., loc. cit.*) are given in the literature], and the *hydrochloride* (from methanol–ether) m. p. 227—229° (Found : C, 72·0; H, 6·5; N, 5·5°; loss at 30°/1 mm., 3·3. $C_{16}H_{16}NCl,\frac{1}{2}H_2O$ requires C, 72·1; H, 6·75; N, 5·25; H_2O, 3·4%).

When the base (16·4 g.) was distilled at atmospheric pressure some decomposition occurred but the main fraction had b. p. 315—340°. The distillate (12·2 g.) was redistilled giving three fractions, (*B*) b. p. 70—80°/1 mm. (2·6 g.), (*C*) b. p. *ca.* 120—150°/1 mm. (1·8 g.), and (*D*) b. p. 148—155°/0·8—1 mm. (8·55 g.). On redistillation, (*B*) gave *iso*quinoline, b. p. 65—68°/1 mm. (Found : N, 10·7. Calc. for C_9H_7N : N, 10·85%), identified by comparison of the picrate, m. p. 227—229° (Found : C, 50·4; H, 3·3; N, 15·7. Calc. for $C_{15}H_{10}O_7N_4$: C, 50·3; H, 2·8; N, 15·6%), with an authentic specimen. Fraction (*D*), redistilled, had b. p. 145—148°/0·7 mm., n_D^{21} 1·6252 [product *E*] (Found : C, 86·1; H, 6·4; N, 6·5%; active H, 0·33 atom).

Reactions of Product E.—(*a*) With picric acid a mixture of picrates was obtained which on repeated crystallisation from alcohol and from acetone gave a small amount of yellow prisms, m. p. 180—182° (Found : N, 12·3. Calc. for $C_{22}H_{16}O_7N_4$: N, 12·5%), identical (mixed m. p.) with 1-benzyl*iso*quinolinium picrate, m. p. 182—183·5°, obtained from the base, m. p. 55°, prepared according to von Braun and Nelles (*Ber.*, 1937, **70**, 1767; for other references see Huntress and Shaw, *loc. cit.*, who give the m. p. of the picrate as 179—181°).

(*b*) The action of ethereal hydrogen chloride and repeated crystallisation from methanol–ether gave colourless needles, m. p. around 100°, containing solvent (Found : loss at 55°/1 mm. : 12·6. Calc. for $C_{16}H_{14}NCl,2H_2O$: H_2O, 12·3%). The dried product had m. p. 188—190° (Found : C, 74·8; H, 5·9; N, 5·8. Calc. for $C_{16}H_{14}NCl$: C, 75·1; H, 5·8; N, 5·5%), and was identified as 1-benzyl*iso*quinolinium chloride by mixed m. p. with an authentic specimen prepared from the pure base (Forsyth, Kelly, and Pyman, *J.*, 1925, **127**, 1662, record m. p. 185—187° for the anhydrous salt and below 100° for the dihydrate).

(*c*) Reaction with acetic anhydride as for the phenyl homologue gave a basic fraction which formed a hydrochloride sparingly soluble in water, identical with 1-benzyl*iso*quinolinium chloride. The neutral fraction was a gum which could not be crystallised.

The authors are indebted to Mr. R. J. Kemp for experimental assistance and to Miss M. Birchmore and Miss F. Skidmore for the semi-microanalyses.

RESEARCH LABORATORIES, MESSRS. BOOTS PURE DRUG CO. LTD., NOTTINGHAM.

[*Received, May 21st*, 1949.]