TABLE I

ETHYL ESTERS OF SUBSTITUTED β-AMINOPROPIONIC ACIDS $RCH_2CH_2COOC_2H_5$

β-Substituent R	Yield, %	Method used	Boiling range °C.	Mm.	Picrate m. p., °C.	Refractive index $n^{20}D$	Density d^{20}	Molecular refraction Calcd.	Found	Equivalent weights Calcd.	Found
Piperidino-[a]	74	IV	124–130	25	127.5–128.0	1.4555	0.9664	51.9	51.8	184.7	185.3
	88	II									
Morpholino-	56	IV	138–140	25	106–107	1.4570	1.0484	48.5	48.8	185.6	187.1
Diethylamino-[b]	74	IV	95–98	23	75–76	1.4270	0.9005	49.4	49.4	175.1	173.3
	87	I									
	83	II									
Di-*n*-propylamino-[c]	77	IV	125–126	28	63–64	1.4313	0.8884	58.7	58.6	198.5	201.3
Di-*n*-butylamino-	66	IV	136–137	16	oil	1.4356	0.8787	68.3	67.8	229.3	230.0
	60	II									
Di-*n*-amylamino-	40[e]	IV	136–138	5	oil	1.4397	0.8779	77.2	77.0	5.67[d]	5.73[d]
Di-*n*-hexylamino-	50[e]	IV	137–145	3	oil	1.4431	0.8607	87.8	86.3	4.95[d]	4.91[d]

[a] See Wedekind, *Ber.*, **32**, 727 (1899). [b] See reference 1c. [c] Reported in ref. 3a erroneously as ethyl α-di-*n*-propylamino propionate; see ref. 1e. [d] Per cent. nitrogen by Kjeldahl method. [e] The yields with the higher members were lower mainly because of the tendency for these compounds to decompose upon prolonged heating during distillation.

Summary

The preparation of various substituted β-aminopropionic esters by three different methods has been studied and six new β-aminopropionic esters described.

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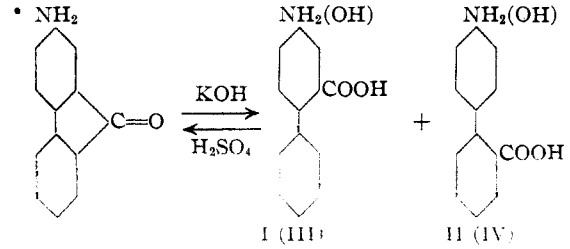
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF WELLESLEY COLLEGE]

4- and 4′-Aminobiphenyl-2-carboxylic Acids

BY MARGARET K. SEIKEL AND MARGARET F. PIERSON

In continuation of work on the cleavage of fluorenones with potassium hydroxide in diphenyl ether,[1] the cleavage of 2-aminofluorenone was repeated and a successful isolation and separation was made of the two isomeric amino acids, 4- and 4′-aminobiphenyl-2-carboxylic acids, I and II, whose formation the earlier research had already proved.[2]



The further interest in these compounds resulted from a curious anomaly existing in the literature concerning their melting points and structures. Kühling[3] prepared the first isomer, m. p. 106–110°, which he believed to be 4′-aminobiphenyl-4-carboxylic acid but which later work[4] proved to be the corresponding 2-carboxylic acid. Diels[5] isolated another *p*-aminobiphenylcarboxylic acid, m. p. *ca.* 215°, from the alkaline cleavage of 2-aminofluorenone but did not indicate the relative positions of the carboxyl and amino groups. Beilstein,[6] however, assumed it to be the 4-acid, isomeric with Kühling's acid. More recently Finzi and Mangini[7] reported an acid, m. p. 215–216°, whose structure they definitely proved to be 4′-aminobiphenyl-2-carboxylic acid, II. Therefore, two compounds have been reported to have the same structure although their melting points differ by 100°.[8]

To solve this anomaly an exhaustive search of the literature was undertaken to check on the validity of the proofs of structure offered. No errors or inconsistencies could be found and several independent lines of evidence support the structures of certain of the intermediates. The more important references in the direct lines of proof are listed below.[9]

(1) Huntress and Seikel, THIS JOURNAL, **61**, 816, 1066, 1358 (1939).
(2) Huntress and Seikel, *ibid.*, **61**, 818, 821 (1939).
(3) Kühling, *Ber.*, **29**, 166–167 (1896).
(4) Kliegl and Huber, *ibid.*, **53**, 1646–1648 (1920).
(5) Diels, *ibid.*, **34**, 1760–1771 (1901).
(6) Beilstein, Vol. 14, p. 539.
(7) Finzi and Mangini, *Gazz. chim. ital.*, **62**, 1200–1201 (1932).
(8) The authors believe that Kühling's melting point is a typographical error as a melting point of 206–210° could be observed for the 4′-acid because it is difficult to purify and melts with decomposition. The figures, 106–110°, were printed only once.
(9) (A) For Finzi and Mangini's acid, m. p. 215–216°: Finzi and Mangini, *Gazz. chim. ital.*, **62**, 1193–1203 (1932); Finzi, *ibid.*, **61**, 33–42 (1931); for *p*-amino- and *p*-hydroxybiphenyl: Latschinoff and Engelhardt, *Ber.*, **6**, 194 (1873); Schultz, *Ann.*, **174**, 209–213 (1874); **207**, 348, 363 (1881); Hübner, *ibid.*, **209**, 340–349 (1881); Kaiser, *ibid.*, **257**, 101 (1890); for *o*-hydroxybiphenyl: Graebe and Aubin, *Ann.*, **247**, 257–288 (1888); Graebe and Schestakow, *ibid.*, **284**, 310–320 (1895); Schultz, *ibid.*, **207**, 352–353 (1881); Heusler, *ibid.*, **260**,

The problem was solved by preparing the two isomeric acids, I and II, m. p. 183° and 218°, respectively, and proving their structure by conversion to the known 4- and 4′-hydroxybiphenyl-2-carboxylic acids, III and IV.[10] I is a new compound, while II checks the acid reported both by Diels and by Finzi and Mangini.

The cleavage of 2-aminofluorenone under the conditions of the experiment is practically instantaneous, markedly faster than any of the other 2-substituted fluorenones and faster than all but one of the poly-substituted fluorenones previously studied.[1] The product is a mixture of the two isomers in an approximate ratio of 1:1 to 1:2 of 4-:4′-acid (I:II) in contrast to quantitative yields of the 4′-acid from 2-chlorofluorenone, mainly the 4′-acid from 2-sulfofluorenone and mainly the 4-acid, (III), (50–70% yields) from 2-hydroxyfluorenone. The ring closure of the 4-acid to 2-aminofluorenone by concentrated sulfuric acid occurred more readily than that of the 4′-acid; the same relationship was found to hold for the 4- and 4′-chloro- and hydroxybiphenyl-2-carboxylic acids.

Experimental[11]

Cleavage of 2-Aminofluorenone.—The procedure followed was essentially that described earlier.[12]

In order to ensure sufficient material for fractional crystallization of the isomeric products, 3 g. samples of the deep wine-red 2-aminofluorenone, m. p. 158–160° (recorded 160°[13]), were used. Less decomposition and dark gummy by-products resulted when the amine was dissolved in the least volume of hot diphenyl ether (75 ml.), added to the previously heated, well-stirred emulsion of 8 g. of potassium hydroxide in diphenyl ether (25 ml.) and with immediate contact thus achieved allowed to react for only ninety seconds. Completion of the reaction, usually judged by disappearance of the color of the ketone, was almost impossible to ascertain because of by-products, but rapid decrease in color coupled with 80% yields indicated fast cleavage.

Separation of the Isomeric Acids.—The precipitated potassium salts of the acids were extracted from the cool diphenyl ether reaction mixture with water (total volume, 160 ml.). Addition of 20 ml. of 6 *N* hydrochloric acid to this extract precipitated 1.14 g. of a dirty brown product, m. p. 188–190°, while a second lot of similar but far lighter colored material was obtained by an additional 2 ml. of acid: 0.78 g., m. p. 185–190°.[14] These precipitates were later proved to be mainly the high melting 4′-acid and represented a 58% yield. Since further acidification was unproductive, the orange filtrate was evaporated to one-half, traces of black gum removed and the acidity gradually reduced by addition of 6 *N* sodium hydroxide. While still acid, a finely divided precipitate began to settle, was coagulated by heating, and was isolated: *ca.* 0.75 g., m. p. 177–185°. This was the more soluble 4-acid, a 20–24% yield.

The high melting 4′-acid was purified by a series of recrystallizations and decolorizations, using first 50% acetone as a solvent, then 66% alcohol twice, 25% acetic acid and finally 66% alcohol. The colorless plates then melted at 217.5–218.5° dec.,[15] (recorded, 215–216°[7]), and weighed 0.24 g., a 7.5% yield.

The low melting 4-acid was similarly purified using 50% acetone, 25% acetic acid and finally 50% alcohol. The recrystallization from dilute acetic acid is imperative with this isomer as it alone served to sharpen the melting point. An 8.5% yield (0.27 g.) of material, also colorless plates, m. p. 182.5–183°, was thus isolated.

Evidence for the Structure of I and II.—*Anal.* Calcd. for $C_{13}H_{11}NO_2$: N, 6.57; neut. equiv., 213. Found: for the high melting 4′-acid, N, 6 71, 6.81; neut. equiv., 211, 214; for the low melting 4-acid, N, 6.81, 6.86; neut. equiv., 212, 214.

Both acids were reconverted to 2-aminofluorenone. The low melting 4-acid developed a red color almost immediately in cold concentrated sulfuric acid but the solution was allowed to stand for one-half hour to ensure complete ring closure. Dilution with water precipitated the yellow amine sulfate which alkali converted to the free amine, m. p. and mixed m. p. with authentic 2-aminofluorenone 158–159° (recorded 160°[13]). The high melting 4′-acid required slight warming of the concentrated sulfuric acid solution to produce the color[16]; m. p. of the resultant amine 157–158° and mixed m. p. 157–159°.

Both amino acids were converted into the corresponding hydroxy acids, III and IV, by diazotizing 0.1-g. samples and boiling. The impure products were purified by decolorization and recrystallization from water and identified by mixed melting points with authentic samples of 4- and 4′-hydroxybiphenyl-2-carboxylic acids[10] (see Table I). These new samples of the hydroxy acids showed their characteristic crystal structures.

TABLE I

SUMMARY OF MELTING POINTS

Biphenyl-2-carboxylic acids		4-Series, °C.	4′-Series, °C.
Amino-	recorded[7]	.....	215–216 dec.
Amino-	experimental	182.5–183	217.5–218.5 dec.
Hydroxy-	recorded[10]	202–202.5	206.5 cor.
Hydroxy-	from amino acid		
Hydroxy-	authentic sample[10]	201–201.5	206–207
Hydroxy-	mixture		

235–237 (1890); Graebe and Rateanu, *ibid.*, **279**, 257–267 (1894); Hönigschmid, *Monatsh.*, **22**, 566–569 (1901).

(B) For Kühling's acid, m. p. 106–110°: Kühling, *Ber.*, **28**, 41–43, 523–527 (1895); **29**, 165–169 (1896); Kliegl and Huber, *ibid.*, **53**, 1646–1655 (1920).

(10) The 4′-acid was synthesized from phenol and anthranilic acid [Graebe and Schestakow, *Ann.*, **284**, 323–324 (1895)]; its structure is substantiated by this preparation and by its conversion to *p*-hydroxybiphenyl[9A] [Courtot and Geoffroy, *Compt. rend.*, **178**, 2261 (1924)]. The 4-acid was obtained by cleavage of 2-hydroxyfluorenone [Huntress and Seikel, THIS JOURNAL, **61**, 817, 820–821 (1939)]; structure of this ketone is evidenced by its preparation from the 4′-acid [Courtot and Geoffroy, *loc. cit.*, and Huntress and Seikel, *loc. cit.*], and from 2-nitrofluorenone [Diels, *Ber.*, **34**, 1758–1768 (1901)] which has a well-substantiated structure [*i. e.*, Schultz, *Ann.*, **203**, 95–118 (1880); Heilbron, Hey and Wilkinson, *J. Chem. Soc.*, 113–116 (1938)].

(11) All melting points reported are uncorrected and were taken according to Mulliken, "Identification of Organic Compounds," Vol. 1, p. 218, on a 360° thermometer immersed in sulfuric acid to the −10° point.

(12) Huntress and Seikel, THIS JOURNAL, **61**, 819 (1939).

(13) Diels, *Ber.*, **34**, 1764–1765 (1901).

(14) In another run all the insoluble material precipitated at the first addition of acid: 1.77 g., m. p. 186–192°.

(15) Before the acid melts, it shows considerable darkening and decomposition so that the exact melting point is uncertain.

(16) Comparative tests were carried out later to obtain a qualitative idea of the effect of position and type of substituent on speed of ring closure of the 4- and 4′-substituted biphenyl-2-carboxylic acids. A few milligrams of each acid were dissolved in *ca.* 1 ml. of cold concentrated sulfuric acid and the time elapsing before the appearance of the color characteristic of the resultant ketone in sulfuric acid solution was noted: 4-chloro-, immediately; 4-hydroxy-, less than 1 minute; 4-amino-, 1 minute; 4′-chloro-, 10–15 minutes; 4′-hydroxy-, 10–30 minutes; 4′-amino-, several hours.

Summary

1. Both 4- and 4′-aminobiphenyl-2-carboxylic acids have been isolated from the alkaline cleavage of 2-aminofluorenone in diphenyl ether.

2. Proof of the structure of these compounds resolves an anomaly in the literature.

WELLESLEY, MASS. RECEIVED MARCH 15, 1945

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING OF THE UNIVERSITY OF PENNSYLVANIA]

Preparation of 2-Phenylnaphth[1,2]imidazole and 2-Methylnaphth[1,2]imidazole

BY CHARLES F. KELLY AND ALLAN R. DAY

The isolation of two isomeric forms of 2-phenylnaphth[1,2]imidazole was reported by Galimberti in 1933.[1] The so-called isomers were prepared by reducing N-(2-nitro-1-naphthyl)-benzamide and N-(1-nitro-2-naphthyl)-benzamide, respectively, with zinc and hydrochloric acid. The melting points of the resulting naphthimidazoles, 214 and 296°, appeared to indicate that the two compounds were not identical.

In view of the considerable amount of evidence in favor of the active tautomeric character of the imidazole ring system, the isolation of stable isomeric forms should be of interest. It seemed desirable, therefore, to repeat Galimberti's work using carefully prepared intermediates. At the same time it was decided to prepare 2-phenylnaphth[1,2]imidazole in a neutral non-aqueous medium. If identical results are obtained from both methods then any specific effects which might be attributed to the media would be eliminated. The second method consisted of heating dry N-(2-amino-1-naphthyl)-benzamide and N-(1-amino-2-naphthyl)-benzamide, respectively, in an atmosphere of nitrogen.

N-(2-Nitro-1-naphthyl)-benzamide and N-(1-nitro-2-naphthyl)-benzamide were converted into 2-phenylnaphth[1,2]imidazole by reduction with zinc and hydrochloric acid. The corresponding amino compounds were converted into 2-phenylnaphth[1,2]imidazole by heating in a nitrogen atmosphere. Analyses, melting points, and mixed melting points indicated that the 2-phenylnaphth[1,2]imidazoles obtained from the four starting compounds were identical. Similarly, the 2-methylnaphth[1,2]imidazoles prepared from N-(2-amino-1-naphthyl)-acetamide and N-(1-amino-2-naphthyl)-acetamide proved to be identical. In view of these results it would appear that Galimberti's claim to have isolated two isomeric forms of 2-phenylnaphth[1,2]imidazole is not correct.

Both N-(1-amino-2-naphthyl)-benzamide and 2-phenylnaphth[1,2]imidazole melt at 217–218°. The same behavior was noted for N-(1-amino-2-naphthyl)-acetamide and 2-methylnaphth[1,2]-imidazole, both melting at 170.5–171.5°. It is probable that the 1-amino derivatives are converted into the corresponding naphthimidazoles during the melting point determinations, thus accounting for these observations. It is not clear, however, why the 2-amino derivatives do not behave similarly.

(1) Galimberti, *Gazz. chim. ital.*, **63**, 96 (1933).

Experimental

N-(2-Nitro-1-naphthyl)-acetamide and N-(2-Nitro-1-naphthyl)-benzamide.—2-Nitro-1-naphthol was converted into 2-nitro-1-naphthylamine by a modification of the method described by Hodgson and Kilner.[2] Best results were obtained by heating the mixture of 2-nitro-1-naphthol, ammonium carbonate, and ammonium hydroxide for six hours at 130–140° in an autoclave. The crude 2-nitro-1-naphthylamine was recrystallized from dilute alcohol, yield 50–60%, m. p. 144° cor.

N-(2-Nitro-1-naphthyl)acetamide was prepared from 2-nitro-1-naphthylamine by treatment with acetic anhydride to which a drop of concentrated sulfuric acid had been added. The crude product was recrystallized from alcohol, yield 90%, m. p. 199° cor.[3]

N-(2-Nitro-1-naphthyl)-benzamide could not be prepared by any of the usual methods of acylation. The following procedure was finally adopted. Seven grams (0.037 mole) of 2-nitro-1-naphthylamine, 4.8 cc. (0.0415 mole) of benzoyl chloride and 3.2 cc. (0.0415 mole) of pyridine were dissolved in 150 cc. of dry xylene and refluxed for six hours. On cooling, a small amount of unchanged 2-nitro-1-naphthylamine separated as an oil which solidified on further cooling. The xylene solution was decanted and allowed to stand overnight during which time the benzoyl derivative separated. The product was recrystallized from xylene, yield 68%, m. p. 197–198° cor.[4]

Anal. Calcd. for $C_{17}H_{12}N_2O_3$: N, 9.59. Found: N, 9.54.

N-(1-Nitro-2-naphthyl)-acetamide and N-(1-Nitro-2-naphthyl)-benzamide.—N-2-Naphthylacetamide was converted into N-(1-nitro-2-naphthyl)-acetamide by nitration in glacial acetic acid[5]; yield 53%, m. p. 123–124° cor.

The acetyl derivative was hydrolyzed to 1-nitro-2-naphthylamine by treatment with alcoholic potassium hydroxide[6]; yield 91%, m. p. 125.5° cor.

N-(1-Nitro-2-naphthyl)-benzamide was prepared by the following procedure: 1-nitro-2-naphthylamine (32.5 g., 0.17 mole) was dissolved in 200 cc. of dry acetone and 13.9 cc. (0.17 mole) of pyridine and 19.9 cc. (0.17 mole) of benzoyl chloride added. After standing for two days the mixture was cooled and filtered. The filtrate was refluxed for several hours and on cooling more of the benzoyl derivative was obtained. The product was recrystallized from acetone and water, yield 33%, m. p. 170–171° cor. Unchanged 1-nitro-2-naphthylamine may be recovered by diluting the original filtrate with water.

N-(2-Amino-1-naphthyl)-acetamide.—Five grams (0.022 mole) of N-(2-nitro-1-naphthyl)-acetamide was dis-

(2) Hodgson and Kilner, *J. Chem. Soc.*, **129**, 7 (1926).

(3) Lellman and Remy, *Ber.*, **19**, 796 (1886).

(4) Worms [*ibid.*, **15**, 1815 (1881)] reported m. p. 174°.

(5) "Organic Syntheses," **13**, 72 (1933).

(6) Liebermann and Jacobsen, *Ann.* **211**, 36 (1892).