

relative positions of the groups have a marked effect on the stability of the molecule. The rate of racemization is modified by the solvent used.

A comparison of the rates of racemization of

optically active 6-nitrodiphenic acid with optically active 2,2'-dinitro-6-carboxybiphenyl also has been made. The latter is the more stable.

URBANA, ILLINOIS

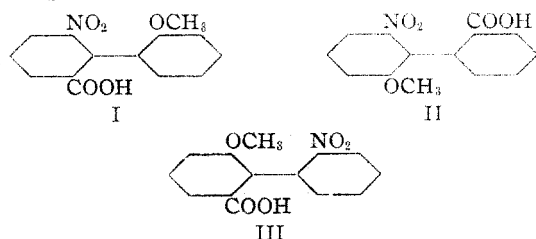
RECEIVED JULY 24, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Stereochemistry of Biphenyls. XLIX. Comparison of the Racemization Rates of the 2,2',6-Nitro-, Carboxy- and Methoxy-biphenyl¹

BY ROGER ADAMS AND G. C. FINGER²

In the previous paper the relative stabilities of biphenyls containing nitro, methyl and carboxyl in the three possible combinations in the 2,2',6-positions were described. Another similar series has been prepared now in which the nitro, methoxy and carboxyl groups occupy the three possible positions in biphenyl.



Based upon the expectations from the relative size of the groups, compounds I and II (CH₃O, COOH collision) should have essentially the same stability and compound III should be more stable.

mal, and the yields of the acid were poor. It is likely, therefore, that the half-life period is more in error than usual.

The variation in stability of these molecules is concordant with the results described in the previous paper¹ in which the methyl group was present in place of the methoxyl.

Experimental

2-Methoxy-6-carboxy-2'-nitrobiphenyl.—The 1-methoxy-2-iodo-3-carbomethoxybenzene was prepared by the method of Stanley, McMahon and Adams.³

In a large Pyrex test-tube a mixture of 5 g. of 1-methoxy-2-iodo-3-carbomethoxybenzene, 4.3 g. of *o*-iodonitrobenzene and 10 g. of copper-bronze powder was heated under reflux in an oil-bath for two hours at 200°. The reaction mixture was extracted with acetone, the acetone solution refluxed with norit, and the solvent concentrated to small volume.

The crude material, which separated, was refluxed for eighteen hours with a mixture of 2 g. of sodium hydroxide

TABLE I
RACEMIZATION OF ACTIVE ACIDS

Compound	Wt. in g. made up to 10 cc. in abs. ethanol	Minutes before initial reading	Initial α_D ($t = 27^\circ$)	Final α_D	Calcd. for zero time α_D	Final α_D	Av. K^a	Av. dev. K	Half-life period, min.
I	0.0557	7	+0.21	0.0	+0.33	+59.4	0.02936	± 0.00081	10.2 ^b
II	.0430	31	-.50	.0	-0.55	-127.9	.001364	$\pm .000048$	219 ^c
III	.0473	120	-.76	.0	-1.01	-213.3	.00111	$\pm .00006$	271

^a The K value was calculated by the formula $K = \frac{1}{t} \log \frac{\alpha_0 - \alpha_f}{\alpha_t - \alpha_f}$. ^b Stoughton and Adams first prepared this active acid [THIS JOURNAL, 54, 4406 (1932)] and reported 9.4 minutes; Li and Adams found 12.2 minutes [Li and Adams, *ibid.* 57, 1565 (1935)]. ^c *l*-Acid from hydrochloric acid hydrolysis gave 288 minutes.

Experimentally compound I proved to be very unstable while compounds II and III were much more stable. The value of the half-life period obtained for compound II is possibly unreliable due to the fact that the formation of the salt and the decomposition to the active acid was abnormal.

(1) For previous paper see Adams and Hale, THIS JOURNAL, 61, 2826 (1939).

(2) An abstract of a thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in chemistry.

and 8 g. of sodium carbonate in 350 cc. of water and 50 cc. of ethanol. The saponification mixture was filtered from the alkali-insoluble 2,2'-dinitrobiphenyl. The alkaline filtrate was diluted to 1500 cc. and acidified with dilute sulfuric acid to precipitate the product. The crude material which amounted to about 5 g. was crystallized from 80% ethanol, from which it formed white needles, m. p. 234–236°.

Anal. Calcd. for C₁₄H₁₁O₅: C, 61.53; H, 4.03; N, 34.44.

(3) Stanley, McMahon and Adams, THIS JOURNAL, 65, 708 (1933).

5.16; neut. equiv., 273. Found: C, 61.58; H, 4.1; N, 5.24; neut. equiv., 269, 273.

Resolution of 2-Methoxy-6-carboxy-2'-nitrobiphenyl.—

To a warm solution of 0.72 g. of 2-methoxy-6-carboxy-2'-nitrobiphenyl in 35 cc. of ethanol was added a solution of 1.05 g. of anhydrous brucine in 50 cc. of ethanol. The mixture was allowed to stand in the ice box for two days. The brucine salt separated as white powdery crystals; m. p. 222–225°, yield 0.92 g.

Anal. Calcd. for $C_{17}H_{13}N_3O_6$: C, 66.54; H, 5.59. Found: C, 66.30; H, 5.54.

Mutarotation. 0.1060 g. of brucine salt was made up to 20 cc. in dry chloroform. α_D (after six minutes) -0.49 ; $l = 2$; $[\alpha]^{27}_D -47.1^\circ$.

The rotation was read at first every two minutes then every ten and finally every hour until seven hundred forty-five minutes had elapsed: $\alpha_D -0.16$; $[\alpha]^{27}_D -15.1^\circ$. The half-life period calculated on the basis of a monomolecular reaction is 99 ± 11 min.

1-2-Methoxy-6-carboxy-2'-nitrobiphenyl.—A mixture of 0.4 g. of brucine salt and 25 cc. of dilute hydrochloric acid (1:1) was kept in an ice-bath and shaken occasionally over a period of an hour. The mixture was filtered rapidly and washed with a small amount of ice-cold water. The precipitate was again treated with 25 cc. of dilute acid and allowed to stand overnight at 0°. The active acid was washed with ice-cold dilute hydrochloric acid and water until completely free from brucine and chloride ion. The acid weighed 0.14 g. and had a melting point of 229–232°.

2-Methoxy-6-nitro-2'-carboxybiphenyl

1-Methoxy-2-chloro-3-nitrobenzene.—The 2-chloro-3-nitrophenol was made by the method of Erp⁴ and esterified by the method described below.

To a hot solution of 39 g. of 2-chloro-3-nitrophenol in 250 cc. of hot xylene was added slowly with rapid stirring 40 g. of finely powdered anhydrous potassium carbonate. The red phenol salt separated and in some instances it was necessary to add more xylene to facilitate the agitation. To this mixture was now added 30 cc. of dimethyl sulfate at such a rate that the reaction mixture boiled rather vigorously. After continued stirring and refluxing for an hour, the mixture was treated with a little dilute sodium hydroxide and then steam distilled. After all the xylene had come over, the distillation was stopped and the residual material cooled. The crude 1-methoxy-2-chloro-3-nitrobenzene solidified, yield, 39 g. (92%). It was purified from 40% ethanol and formed white flake-like crystals, m. p. 93–94°. Erp reported m. p. 94°.

A mixture of 14 g. of 1-methoxy-2-chloro-3-nitrobenzene and 20 g. of methyl *o*-iodobenzoate was heated in an oil-bath to 255°. The temperature was raised gradually to 275° over a period of one hour and during this period 32 g. of copper-bronze powder was added in about 5-g. quantities at regular intervals. The mixture was stirred rapidly during the addition. After the addition was completed, the temperature was raised to 280° for about five to ten minutes and then allowed to drop.

The reaction product was refluxed with ethanol for two

hours, the solvent decanted and the residual material again extracted for several hours with fresh ethanol.

After evaporation of the solvent, a black semi-solid mass was obtained weighing 13 g. This was refluxed for ten to twelve hours with a mixture of 5 g. of sodium hydroxide, 10 g. of sodium carbonate, 50 cc. of ethanol and 200 cc. of water. After cooling, the mixture was filtered and the insoluble residue separated from the alkaline solution. It proved to be 2,2'-dimethoxy-6,6'-dinitrobiphenyl. The alkaline solution was refluxed with norit for two hours, then filtered and acidified with dilute hydrochloric acid. The precipitated product was extracted with ether, the ether solution dried over anhydrous magnesium sulfate and the solvent evaporated. The product thus obtained which appeared to be a mixture of a solid and a very viscous oil was heated with successive portions of 25 cc. of benzene, the extracts were combined and allowed to cool. Diphenic acid separated. The benzene was evaporated gradually and intermittently cooled. When a volume of about 20 cc. had been reached, crude 2-methoxy-6-nitro-2'-carboxybiphenyl separated and by further evaporation of the filtrate a second crop could be obtained. The product was purified by recrystallization from 50% methanol: pale cream colored crystals, m. p. 196–198°; yield, 1.5 g.

Anal. Calcd. for $C_{14}H_{11}NO_6$: C, 61.53; H, 4.03; N, 5.16; neut. equiv., 273. Found: C, 61.76; H, 4.02; N, 5.24; neut. equiv., 271, 272.

2,2'-Dimethoxy-6,6'-dinitrobiphenyl.—The alkali-insoluble material obtained in the condensation of 1-methoxy-2-chloro-3-nitrobenzene and methyl *o*-iodobenzoate was purified by crystallization from ethanol in the presence of norit. It formed yellow crystals.

The same product was prepared by heating a mixture of 5 g. of 1-methoxy-2-chloro-3-nitrobenzene in 30 g. of anhydrous nitrobenzene at 180° and adding gradually with stirring 5 g. of copper-bronze powder. The reaction mixture was then maintained at a temperature of 200–210° for five hours, cooled and filtered. The copper residue was extracted carefully with acetone.

The nitrobenzene solution and acetone extracts were subjected to steam distillation, whereupon the solvent was removed as well as some of the unreacted chloro compound. The crude residual product was filtered and dissolved in acetone. This solution was then heated with norit, filtered, and evaporated on a steam cone. Upon treatment of this residue with 50 cc. of hot ethanol, the oily material went into solution and yellow crystals of the 2,2'-dimethoxy-6,6'-dinitrobiphenyl remained undissolved; yield 2.8 g. from ethanol, m. p. 226–228°. The compound can also be purified very satisfactorily from hot glacial acetic acid.

Anal. Calcd. for $C_{14}H_{12}O_6N_2$: N, 9.2. Found: N, 9.13.

Resolution of 2-Methoxy-6-nitro-2'-carboxybiphenyl.—

To a warm solution of 0.72 g. of 2-methoxy-6-nitro-2'-carboxybiphenyl in 25 cc. of absolute ethanol was added a warm solution of 1.05 g. of brucine in 50 cc. of absolute ethanol. After filtration, the mixture was allowed to stand at 0° for thirty hours. Yellow needle-like crystals separated; yield, 0.83 g. A second crop could be obtained by allowing the mother liquor to stand at 0° for several days.

(4) Erp, *J. prakt. Chem.*, **127**, 20 (1930).

The product was purified by dissolving 0.91 g. in 40 cc. of hot absolute ethanol and allowing to stand at 0° for thirty hours. Cream colored crystals were thus obtained.

The melting point of the brucine salt showed unusual irregularity, some samples partially melting around 70°, others at 80 or 90°. The decomposition points ranged from 108–125°.

The brucine salt had practically a zero rotation and no mutarotation was observed over a period of several hours. In spite of this, active acid was obtained from the salt by hydrolysis. Although the salt was well crystallized, the analyses did not indicate absolute purity.

l-2-Methoxy-6-nitro-2'-carboxybiphenyl

A. Hydrolysis with Acid.—The brucine salt was hydrolyzed with dilute hydrochloric acid (1:1) as described previously for 2-methoxy-6-carboxy-2'-nitrobiphenyl. An exceedingly low yield of active acid resulted.

B. Hydrolysis with Dilute Sodium Hydroxide.—At 0° 0.1 g. of brucine salt was shaken with 15 cc. of aqueous 10% sodium hydroxide for one hour. Extraction with chloroform served to remove the brucine. After filtering the alkaline solution, it was acidified with dilute hydro-

chloric acid (1:1) at 0°. The *l*-acid separated but, as it was too fine for filtrations, it was extracted with ether. The solvent was evaporated at a low temperature and the residue dried in a vacuum desiccator at room temperature; weight, 0.022 g., m. p. 195–199°.

Anal. Calcd. for C₁₃H₁₁O₅N: N, 5.16. Found: N, 5.10.

Summary

The following compounds have been prepared: 2-methoxy-6-carboxy-2'-nitrobiphenyl, 2-nitro-6-carboxy-2'-methoxybiphenyl, and 2-methoxy-6-nitro-2'-carboxybiphenyl. The 2-nitro-6-carboxy-2'-methoxybiphenyl proved to be unstable and the least stable of the three. The other two were relatively stable compounds. A more exact comparison of the stability of the latter two was impossible due to the fact that the purity of one of them appeared to be questionable.

URBANA, ILLINOIS

RECEIVED JULY 24, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Synthesis in the 1,2,3,4-Tetrahydroquinoline Series

BY WILLIAM S. EMERSON AND J. W. DAVIS

The N-alkyl-1,2,3,4-tetrahydroquinolines represent an interesting and but little studied group of compounds. Very few containing alkyl groups in the benzene ring have ever been prepared, much less, thoroughly examined.

These compounds can be prepared readily from the corresponding quinolines either by reduction of the quinoline methiodides¹ or by first reducing the quinolines and then treating the tetrahydro compounds with methyl iodide.^{1,2} In examining the second method we were surprised to find that 1,2,3,4-tetrahydroquinolines vary markedly in their stability and reactivity. This paper reports the great differences in these respects between 2,6- and 2,8-dimethyl-1,2,3,4-tetrahydroquinoline.

While the 2,8-compound is relatively stable, forming a well defined picrate and zinc chloride-hydrochloric acid double salt, the corresponding derivatives of the 2,6-compound are unstable, decomposing when attempts are made to crystallize them. In the case of the picrate, 2,6-dimethylquinoline picrate subsequently was isolated from the filtrate. The 2,6-compound also reacted much more violently with methyl iodide

than the 2,8-compound. On the other hand, the N-methyl derivative of 2,6-dimethyl-1,2,3,4-tetrahydroquinoline was found to be stable and normal in its reactions.

Reduction studies of alkyl and aryl quinolines³ showed that 2,6-dimethylquinoline was reduced readily with nickel and hydrogen at 105°. At the same pressure three monomethylquinolines were reduced at 120°, while a temperature of at least 150° was required in all other cases. 2-Methylquinoline could be reduced at temperatures as low as 110°, but the reaction proceeded more smoothly at 150°. Since this type of hydrogenation is reversible, it is interesting that the tetrahydroquinoline which we have found to be unstable was prepared at the lowest temperature in these reduction studies.

Experimental

2,8-Dimethylquinoline was prepared by the method of Doebner and v. Miller; b. p. 245–255°; *n*_D²⁰ 1.5955; *d*₄²⁰ 1.036; *M*_D calcd. 51.73; *M*_D found 51.60. Its identity was checked by means of the picrate, m. p. 177–179° (180°).⁴

(3) Von Braun, Petzold and Seemann, *ibid.*, **55**, 3779 (1922); v. Braun, Gmelin and Schultheiss, *ibid.*, **56**, 1338 (1923); v. Braun, Petzold and Schultheiss, *ibid.*, **56**, 1347 (1923); v. Braun, Gmelin and Petzold, *ibid.*, **57**, 382 (1924).

(4) Eibner, *ibid.*, **34**, 2450 (1901).

(1) Möller, *Ann.*, **242**, 313 (1887).

(2) Doebner and v. Miller, *Ber.*, **16**, 2464 (1883).