[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

A New Route to 1-Aryl Pyrroles[1]

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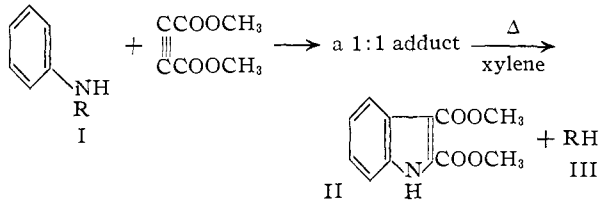
RECEIVED JUNE 27, 1955

Reaction of arylhydroxylamines with dimethyl acetylenedicarboxylate resulted in three products: a 1,2-adduct, a 1,1-adduct and an orange oil. The 1,2-adduct was readily converted to the corresponding tetramethyl 1-arylpyrrole-2,3,4,5-tetracarboxylate, and the orange oil (in the two cases tried) to the corresponding monomethyl indole-2,3-dicarboxylate. The 1:1-adduct was not stable but reverted to its components on standing at room temperature.

An interest[3] in the reaction of dimethyl acetylenedicarboxylate with hydrazobenzene (I, R = C_6H_5-NH) to form dimethyl indole-2,3-dicarboxylate (II)[4] led us to investigate the same reaction using N-phenylhydroxylamine in place of hydrazobenzene. By analogy, N-phenylhydroxylamine (I, R = OH) should give the desired indole derivative by loss of water (III, R = OH) instead of aniline (III, R = C_6H_5NH) thus:



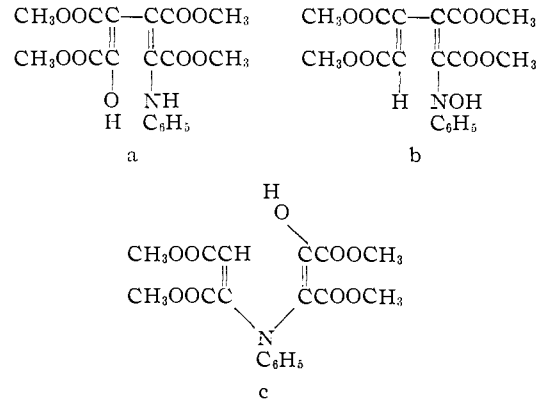
Under suitable conditions, dimethyl acetylenedicarboxylate and N-phenylhydroxylamine did form, not dimethyl indole-2,3-dicarboxylate, but the monomethyl ester, a compound already reported.[4] The same reaction, using N-(*p*)-tolylhydroxylamine gave the corresponding monomethyl 5-methylindole-2,3-dicarboxylate, which was characterized by methylation to the dimethyl ester.

Although the expected reaction could be made to occur, it was found that dimethyl acetylenedicarboxylate and N-phenylhydroxylamine also formed two adducts, one of which was readily converted to tetramethyl 1-phenylpyrrole-2,3,4,5-tetracarboxylate. This reaction was found to be a general one for arylhydroxylamines and should serve usefully for preparing 1-arylpyrrole derivatives, compounds not easy to prepare in good yields by other routes.

One mole of dimethyl acetylenedicarboxylate and one mole of N-phenylhydroxylamine in ether at low temperature gave an adduct A which had a 1:1 mole ratio of the two reagents. This adduct was not stable for long periods, even at room temperature but decomposed to its original components. Because of this, adduct A would appear to be a loose molecular complex of the two constituents in which no new primary valence bonds have been established. Adduct A with another mole of dimethyl acetylenedicarboxylate or even refluxing alone in methanol gave in good yields adduct B described below.

When two moles of dimethyl acetylenedicarboxylate and one mole of N-phenylhydroxylamine were refluxed together in any one of several solvents, a second adduct designated B was formed in good yields together with an orange colored oil. Adduct B was found by analysis to contain its constituents in the 1:2 ratio used in its preparation. It was a stable compound with no tendency to revert to its constituents. Although an alkoxyl determination showed four methoxyl groups to be present, a neutralization equivalent gave the equivalent weight at one-third the molecular weight rather than one-fourth. The same experience with the saponification of tetramethyl 1-phenylpyrrole-2,3,4,5-tetracarboxylate was proved to be due not to the failure of one ester group to hydrolyze but to the neutralization *p*H of the fourth carboxyl group being higher than the *p*H at which phenolphthalein changes. Adduct B would not form an acetyl, phenylhydrazone, *p*-nitrophenylhydrazone or methiodide derivative.

The adduct B could have one of the three structures (and their tautomers) given below depending on the method of addition of the N-phenylhydroxylamine to the two molecules of dimethyl acetylenedicarboxylate.



In an attempt to elucidate the structure of adduct B, dimethyl oxaloacetate, dimethyl oxalobromoacetate and aniline were condensed by a method analogous to Hantzsch's pyrrole synthesis.[5] The reactions using Korschun's[6,7] sequence of bond formation is

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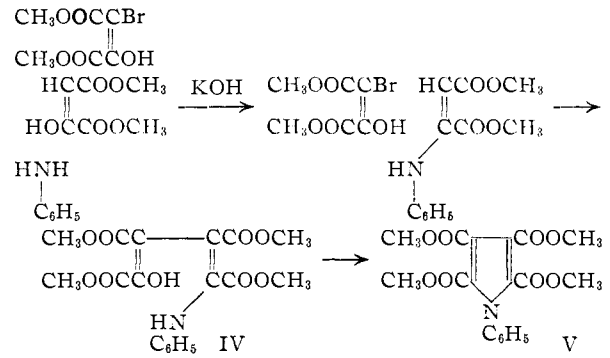
(3) E. H. Huntress and W. M. Hearon, THIS JOURNAL, **63**, 2762 (1941).

(4) O. Diels and J. Reese, *Ann.*, **511**, 168 (1934).

(5) A. Hantzsch, *Ber.*, **23**, 1474 (1890).

(6) C. Hollins, "Synthesis of Nitrogen Ring Compounds," Ernest Benn Ltd., London, 1924, p. 38.

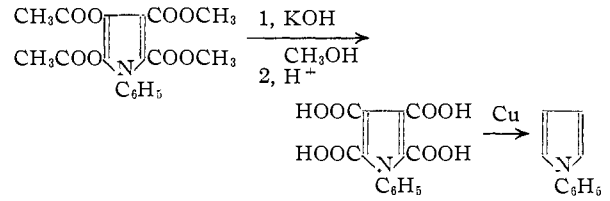
(7) G. Korschun, *Ber.*, **38**, 1125 (1905).



The product from this synthesis, obtained in 14% yield, was found to be identical in all respects with that made from N-phenylhydroxylamine.

The exact structure of adduct B is not firmly established; however the authors prefer structure (a) above based on the Hantzsch synthesis. This structure does not explain though, the lack of hydroxyl and carbonyl derivatives.

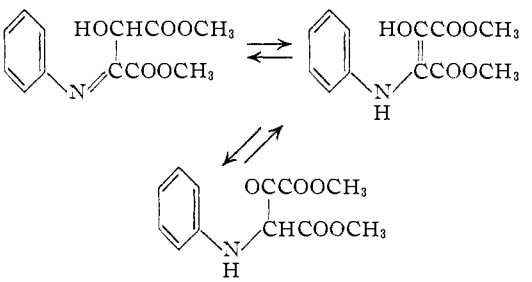
This pyrrole derivative has not previously been reported but its identity was proved by analysis and degradation to 1-phenylpyrrole thus



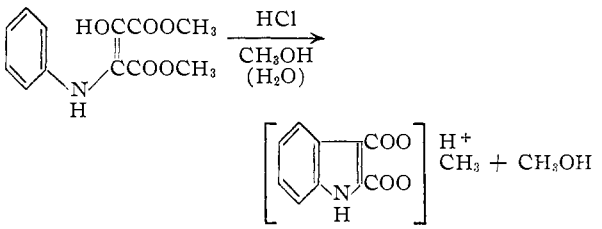
Tetramethyl 1-(*p*)-tolylpyrrole-2,3,4,5-tetracarboxylate made from N-(*p*)-tolylhydroxylamine was also degraded to 1-(*p*)-tolylpyrrole.

The generality of this 1-arylpyrrole synthesis was shown by reaction of *o*-chlorophenyl-, *p*-chlorophenyl-, *m*-tolyl-, *p*-tolyl-, 2,4,6-trimethylphenyl-, *p*-nitrophenyl- and *p*-carboxymethylphenylhydroxylamines with dimethyl acetylenedicarboxylate to form the corresponding pyrrole derivatives.

The orange oil occurring during the preparation of adduct B is probably



It is readily converted in good yields to the monomethyl ester of indole-2,3-dicarboxylic acid[6] by warming with methanolic hydrogen chloride.



The above may be a general reaction but in the present study only the corresponding 5-methylindole derivative was prepared.

Experimental

N-Arylhydroxylamines.—N-Phenyl-,[8,9,10] N-(*m*)-tolyl-,[11] N-(*p*)-tolyl-,[12] N-2,4,6-trimethylphenyl-,[11] N-(*o*)-chlorophenyl-,[13] N-(*p*)-chlorophenyl-[14] and N-(*p*-)-nitrophenylhydroxylamines[15] were prepared by published procedures.

N-(*p*-)-Carboxymethylphenylhydroxylamine.—A stirred mixture of 10 g. of methyl *p*-nitrobenzoate, 5 g. of ammonium chloride, 100 ml. of methanol and 10 ml. of water was treated with small portions of zinc dust (15 g. total) over a period of 15 minutes. The precipitated zinc oxide was removed by filtration and the filtrate diluted with 200 ml. of ice-water. The precipitate of yellow flakes was collected and extracted with 150 ml. of hot benzene. On cooling the extracts, 7.0 g. (75%) of yellowish crystals precipitated, m.p. 120.9–121.9°. For analysis, a sample was recrystallized four times from hot benzene and dried at 5 mm. and room temperature for three hours.

Anal. Calcd. for C_8H_9NO: C, 57.48; H, 5.43; N, 8.38. Found: C, 57.88; H, 5.48; N, 8.60.

Adduct A.—To 9.0 g. of dimethyl acetylenedicarboxylate in 30 ml. of anhydrous ether was added 7.0 g. of N-phenylhydroxylamine while maintaining the temperature below 10°. After 70 hours at 5°, the mixture was filtered and the precipitate washed with 20 ml. of anhydrous, cold ether. Dried in air at room temperature, the colorless crystals weighed 10.4 g. (65% of theory), m.p. 85.6–86.1°. For analysis, a sample was recrystallized twice from 6:1 ether–methanol and dried at 30 mm. and room temperature, m.p. 86.1–86.6°.

Anal. Calcd. for $C_{13}H_{13}NO_5$: C, 57.36; H, 5.21; N, 5.58. Found: C, 57.46; H, 5.44; N, 5.55.

Adduct B. A. From Adduct A.—A 3.5-g. portion of adduct A was dissolved in 25 ml. of boiling methanol and set in a refrigerator (5°) overnight. The crystalline precipitate was collected by filtration from the yellow solution, recrystallized from methanol, and dried giving 1.2 g. (44% of theory), m.p. 152.8–153.3°. For analysis, a sample was recrystallized three times from 1:1 methanol–water, m.p. 154.4–154.9°. A cryoscopic molecular weight determination in benzene gave 453 (calcd. 393). The saponification equivalent found was 123.5, 124.0 and 124.0 in three determinations (calcd. for three ester groups, 131.1; for four ester groups, 98.3).

Anal. Calcd. for $C_{18}H_{19}NO_9$: C, 54.96; H, 4.87; N, 3.56; OCH_3, 31.53. Found: C, 55.06; H, 4.97; N, 3.57; OCH_3, 31.40.

B. From Adduct A and Dimethyl Acetylenedicarboxylate.—A mixture of 1.0 g. of adduct A and 0.6 g. of dimethyl acetylenedicarboxylate was refluxed in 10 ml. of benzene for three hours. The benzene was then removed by air evaporation, 3 ml. of anhydrous ether added and the viscous oil stirred. Colorless crystals formed which were recrystallized from 1:1 methanol–water giving 0.8 g. (50%), m.p. 153.0–153.5°. A mixture with adduct B prepared from adduct A alone melted at the same temperature.

C. From N-Phenylhydroxylamine and Dimethyl Acetylenedicarboxylate.—In a 500-ml. erlenmeyer flask equipped with a reflux condenser was placed 71 g. of dimethyl acetylenedicarboxylate and 50 ml. of benzene. The solution was heated to boiling on a water-bath, and a solution of 27.2 g. of freshly prepared N-phenylhydroxylamine was gradually added over a period of 15 minutes. After the exothermic reaction had ceased, the orange solution was refluxed for 30 minutes, concentrated to 100 ml., and set aside overnight. The precipitate was filtered off, washed with 50 ml. of ether to remove the orange oil, and dried. The washings were

(8) "Organic Syntheses," Coll. Vol. I, 1st ed., 1932, p. 435.
(9) *Ibid.*, 2nd ed., 1941, p. 445.
(10) *Ibid.*, Vol. IV, 1925, p. 57.
(11) E. Bamberger and A. Rising, *Ber.*, **33**, 3626 (1900).
(12) E. Bamberger, *ibid.*, **28**, 245 (1895).
(13) E. Müller and W. Kreutzmann, *Ann.*, **495**, 143 (1932).
(14) M. D. Farrow and C. K. Ingold, *J. Chem. Soc.*, **125**, 2550 (1924).
(15) A. Reissert, *Ber.*, **30**, 1045 (1897).

TABLE I

ADDUCTS

Arylhydroxylamine	Wt., g.	Solvent, ml.	Dimethyl acetylenedicarboxylate, g.	Recryst. from	Wt. of adduct, g.	Yield, %	M.p., °C.
m-Methyl	2.0	Benzene, 10	4.6	Methanol	2.3	35	160.5–160.9
p-Methyl	2.0	Benzene, 10	4.6	Methanol	3.4	51.5	174.6–175.1
2,4,6-Trimethyl	2.0	Benzene, 5	3.8	Dil. MeOH	1.15	20	203.8–204.8
o-Chloro	2.0	Toluene, 10	4.0	Methanol	2.4	40	177.0–177.5
p-Chloro	2.0	Benzene, 10	4.0	1:1 MeOH–water	1.7	28	189.4–189.9
p-Nitro	0.80	Benzene, 5	2.0	Methanol	1.4	61	185.3–185.8
p-Carboxymethyl	3.0	Benzene, 10	5.1	Methanol	4.3	53	195.9–196.5

TABLE II

ANALYSES

Adduct	Empirical formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	Chlorine, % Calcd.	Chlorine, % Found
m-Methyl	$C_{19}H_{21}NO_9$	56.01	55.65	5.20	5.17	3.44	3.52		
p-Methyl	$C_{19}H_{21}NO_9$	56.01	55.86	5.20	5.08	3.44	3.54		
2,4,6-Trimethyl	$C_{21}H_{25}NO_9$	57.92	57.91	5.79	5.94	3.22	2.97		
o-Chloro	$C_{18}H_{18}NO_9Cl$	50.53	50.21	4.24	4.37	3.28	3.34	8.29	8.19
p-Chloro	$C_{18}H_{18}NO_9Cl$	50.53	50.64	4.24	4.36	3.28	3.10	8.29	7.99
p-Nitro	$C_{18}H_{18}N_2O_{11}$	49.32	49.12	4.14	4.11	6.39	6.65		
p-Carboxymethyl	$C_{20}H_{21}NO_{11}$	53.21	52.95	4.69	4.73	3.11	3.22		

combined with the filtrate, the solvent distilled, and the residue, a viscous orange oil, set aside for another crop. The yield of colorless crystals was 36.3 g. (37%), m.p. 152.6–153.2°. A mixed m.p. determination with previously prepared adduct B showed no depression.

D. From Aniline, Dimethyl Oxalobromoacetate and Dimethyl Oxaloacetate.—In a 200-ml. flask were placed 3.0 g. of dimethyl oxalobromoacetate, 2.0 g. of dimethyl oxaloacetate, 1.2 g. of aniline, 6.5 ml. of 2 *N* KOH in methanol, 20 ml. of methanol and 20 ml. of water. The mixture was refluxed one hour, acidified with 1.0 g. of glacial acetic acid, and refluxed again for 15 minutes. The cooled solution was diluted with 100 ml. of water and extracted with three 100-ml. portions of ether. The combined ethereal extracts were washed with 100 ml. of 1 *N* hydrochloric acid and then 100 ml. of water. After distillation of the ether, the residual orange oil was left overnight and deposited a small amount of colorless crystals. The mixture was agitated with 10 ml. of ether and the crystals filtered off. The yield was 0.5 g. (11%) when recrystallized from 1:1 methanol–water, m.p. 154.4–154.9°. There was no depression of the m.p. when the product was mixed with adduct B prepared by any of the above methods.

Anal. Calcd. for $C_{18}H_{19}NO_9$: C, 54.96; H, 4.87; N, 3.56. Found: C, 54.73; H, 4.94; N, 3.86.

Adducts from Two Moles of Dimethyl Acetylenedicarboxylate and Arylhydroxylamines.—All these adducts were prepared by treating two moles of dimethyl acetylenedicarboxylate in a suitable neutral solvent with small portions of one mole of the arylhydroxylamine, warming the mixture for 30 minutes and allowing it to stand at least overnight. The crystals which had formed were washed with ether, dried, and recrystallized from a suitable solvent. Experimental data are given in Table I, and analyses in Table II.

Effect of Solvent on Forming Adduct B.—Six samples of N-(*p*)-tolylhydroxylamine (4.0 g.) and dimethyl acetylenedicarboxylate (9.25 g.) reacted in six different solvents and the products were isolated in the procedure described above. The yields were: for toluene, 34%; methanol, 19; ligroin, 35; chloroform, 37; xylene, 28; and benzene, 39.

Tetramethyl 1-Phenylpyrrole-2,3,4,5-tetracarboxylate. A. With Sulfuric Acid.—A 6.4-g. portion of adduct B was dissolved in 25 ml. of cold, concentrated sulfuric acid with the evolution of a small amount of heat to give a clear, colorless solution. On pouring this solution into 100 ml. of cold water, a colorless crystalline precipitate formed which was filtered, dissolved in the mininum amount of 1:1 methanol–water and allowed to crystallize slowly. The long, thin, colorless crystals were collected by filtration and dried giving 6.1 g. (99%), m.p. 116.3–116.8°. For analysis, a sample was twice recrystallized from 1:1 methanol–water. A cryoscopic molecular weight determination in benzene gave a value of 433 (calcd. 375). The average saponification equivalent found in five determinations was 124.3 (calcd. for three ester groups, 125.1; for four ester groups, 93.8).

Anal. Calcd. for $C_{18}H_{17}NO_8$: C, 57.60; H, 4.57; N, 3.73; OCH_3, 33.08. Found: C, 57.65; H, 4.65; N, 3.88; OCH_3, 33.05.

B. **With Methanolic Ammonia.**—A 5.0-g. portion of adduct B was dissolved in boiling methanol. The solution was cooled to room temperature and saturated with gaseous ammonia. After standing at room temperature for 50 hours, the solution was concentrated to one-third volume and allowed to cool to room temperature. The precipitate (2.6 g.) of long, colorless needles was collected by filtration, the filtrate diluted with an equal volume of water and the additional precipitate (2.1 g.) filtered off, total yield 4.7 g. (quantitative), m.p. 116.3–117.3°. A mixture with tetramethyl 1-phenylpyrrole-2,3,4,5-tetracarboxylate made with sulfuric acid melted at the same temperature.

C. With Methanolic Hydrogen Chloride.—A solution of 2.0 g. adduct B in 60 ml. of 1% hydrogen chloride in methanol was refluxed for two hours. The clear, hot solution was diluted with hot water and allowed to cool slowly. The precipitate of long, colorless needles was filtered off and dried; yield 1.9 g. (quantitative), m.p. 116.3–117.3° showing no depression when mixed with tetramethyl 1-phenylpyrrole-2,3,4,5-tetracarboxylate made with sulfuric acid.

D. Unsuccessful Attempts.—Attempted removal of water from adduct B by azeotropic distillation of benzene gave only the unchanged adduct in 90% yield. Refluxing of adduct B for an hour with acetic anhydride gave the unchanged adduct with 80% recovery.

Tetramethyl 1-Arylpyrrole-2,3,4,5-tetracarboxylate.—These were all prepared exactly like the 1-phenyl derivative. Data are given in Table III and analyses in Table IV.

TABLE III

TETRAMETHYL 1-ARYLPYRROLE-2,3,4,5-TETRACARBOXYLATES[a]

Aryl group	Adduct, g.	H_2SO_4, ml.	Product, g.	Yield, %	M.p., °C.
m-Tolyl	0.9	10	0.8	86	136.9–137.3
p-Tolyl	1.7	10	1.4	86	121.6–122.1
2,4,6-Trimethyl	1.0	10	0.7	75	119.6–120.0
o-Chloro	0.5	5	..	..	102.5–103.2
p-Chloro	1.0	10	..	..	106.5–107.0
p-Nitro	0.7	10	..	..	137.6–138.0
p-Carboxymethyl	1.3	10	1.1	90	165.5–166.0

[a] All recrystallized from methanol–water.

TABLE IV

ANALYSES

Aryl group	Empirical formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	Chlorine, % Calcd.	Chlorine, % Found
m-Methyl	$C_{19}H_{19}NO_8$	58.61	58.27	4.92	5.03	3.60	3.33		
p-Methyl	$C_{19}H_{19}NO_8$	58.61	58.55	4.92	4.82	3.60	3.55		
2,4,6-Trimethyl	$C_{21}H_{23}NO_8$	60.42	60.43	5.55	5.52	3.36	3.57		
o-Chloro	$C_{18}H_{16}NO_8Cl$	52.75	52.86	3.93	4.13	3.43	3.57	8.65	8.63
p-Chloro	$C_{18}H_{16}NO_8Cl$	52.75	52.83	3.93	3.95	3.43	3.30	8.65	8.24
p-Nitro	$C_{18}H_{16}N_2O_{10}$	51.43	51.46	3.83	3.85	6.67	7.00		
p-Carboxymethyl	$C_{20}H_{19}NO_{10}$	55.43	55.16	4.42	4.44	3.23	3.28		

The *p*-nitro derivative was also prepared by direct nitration of tetramethyl 1-phenylpyrrole-2,3,4,5-tetracarboxylate (2.0 g.) with a mixture of concentrated sulfuric acid (6.0 g.) and concentrated nitric acid (5.0 g.) at room temperature for three hours. The crude yield was 1.4 g. (63% of theory) and from methanol gave m.p. 136.5–137.0°. The m.p. of a mixture with the *p*-nitro derivative made from the adduct of N-(*p*)-nitrophenylhydroxylamine and dimethyl acetylenedicarboxylate was 136.8–137.5°.

Anal. Calcd. for $C_{18}H_{16}N_2O_{10}$: C, 51.43; H, 3.83; N, 6.67. Found: C, 51.66; H, 3.79; N, 6.76.

Monopotassium Trihydrogen 1-Phenylpyrrole-2,3,4,5-tetracarboxylate Monohydrate.—In a 250-ml. erlenmeyer flask were refluxed for 30 minutes, 7.0 g. of adduct B and 100 ml. of 2 *N* alcoholic potassium hydroxide. Within a few minutes, a colorless precipitate formed which became heavy by the end of the refluxing period. The mixture was cooled and the white precipitate (8.6 g.) of the tetrapotassium salt sucked off and dissolved in 25 ml. of water. On the addition of 56 ml. of 1 *N* sulfuric acid, a crystalline precipitate began forming. After standing overnight, the mixture was filtered and the precipitate was recrystallized from 80 ml. of hot water giving 6.0 g. (86%). For analysis, a sample was recrystallized three times from hot water and dried at 55° for 36 hours. The product did not melt but decomposed above 200°. Saponification equivalent found was 186.4 (calcd. for two hydrogen equivalents, 187.6; for three hydrogen equivalents, 125.1).

Anal. Calcd. for $C_{14}H_{10}NO_8K$: C, 44.80; H, 2.69; N, 3.73; K, 10.42. Found: C, 37.50,[16] H, 2.96; N, 3.98; K, 10.14.

1-Phenylpyrrole-2,3,4,5-tetracarboxylic Acid Monohydrate.—A 2.3-g. portion of the monopotassium salt of 1-phenylpyrrole-2,3,4,5-tetracarboxylic acid was covered with 30 ml. of concd. hydrochloric acid and the mixture stirred occasionally for four hours. The crystals were filtered off, dissolved in 20 ml. of water, and reprecipitated by saturating the solution with gaseous hydrogen chloride. The yield of strongly acidic, colorless needles (melting with decomposition above 200°) was 1.9 g. (92%). A neutralization equivalent for the monohydrate was found to be 111.5, corresponding to three carboxyl groups (calcd. 112.4). For analysis, a sample was dried at 55° for 36 hours.

Anal. Calcd. for $C_{14}H_{11}NO_9$: C, 49.86; H, 3.29; N, 4.15. Found: C, 49.68; H, 3.32; N, 4.30.

Remethylation of 1-Phenylpyrrole-2,3,4,5-tetracarboxylic Acid Monohydrate.—A 0.50-g. portion of the acid in 30 ml. of diethyl ether treated with diazomethane gave from 1:1 methanol–water 0.55 g. (98%), m.p. 115.8–116.0°. A mixture with tetramethyl 1-phenylpyrrole-2,3,4,5-tetracarboxylate prepared from adduct B melted at the same temperature.

Anal. Calcd. for $C_{18}H_{17}NO_8$: C, 57.60; H, 4.54; N, 3.74. Found: C, 57.50; H, 4.60; N, 3.79.

1-Phenylpyrrole.—A 1.9-g. portion of 1-phenylpyrrole-2,3,4,5-tetracarboxylic acid in a small test-tube was heated by a glycerol bath to 210°. The acid melted and turned brown. The evolution of carbon dioxide was shown by the precipitation of barium carbonate from baryta water. The delivery tube was connected to a water aspirator and the temperature raised to 230°. Crystals of 1-phenylpyrrole were collected in the cooler portion of the delivery tube; m.p. 57.5–58.0°, reported m.p. 58°,[17a] 60–61°.[17b]

Tetrapotassium 1-(*p*)-Tolylpyrrole-2,3,4,5-tetracarboxylate.—Saponification of 11.2 g. of tetramethyl 1-(*p*)-tolylpyrrole-2,3,4,5-tetracarboxylate with 100 ml. of 2 *N* methanolic potassium hydroxide at 60–80° for two hours gave a colorless, crystalline precipitate which was sucked off, washed with methanol, and dried; yield 13.7 g. (98%). For analysis, a sample was washed twice with methanol and dried at 100° for 60 hours.

Anal. Calcd. for $C_{18}H_{17}NO_8K_4$: K, 32.20. Found: K, 31.48, 31.71.

Monopotassium Trihydrogen 1-(*p*)-Tolylpyrrole-2,3,4,5-tetracarboxylate Monohydrate.—A 15.7-g. portion of the tetrapotassium salt was dissolved in 100 ml. of water and treated with 10 ml. of 8.11 *N* hydrochloric acid. The precipitate of fine, colorless needles was filtered, and dried at 72° for 100 hours, yielding 8.1 g. (83%).

1-(*p*)-Tolylpyrrole.—A 7.1-g. sample of monopotassium trihydrogen 1-(*p*)-tolylpyrrole-2,3,4,5-tetracarboxylate was intimately mixed with 5 g. of copper powder, the mixture placed in a test-tube, and arrangements made to bubble any escaping gas through a saturated solution of barium hydroxide. The tube was then heated in a metal-bath to 250–310°. At this temperature, a crystalline sublimate was collected and resublimed for analysis; m.p. 81.4–82.1°, recorded m.p. 79.0–79.5,[18] 82°.[19] A copious precipitate of barium carbonate was formed.

Anal. Calcd. for $C_{11}H_{11}N$: C, 84.04; H, 7.05; N, 8.90. Found: C, 83.30; H, 7.07; N, 8.76.

A sample of 1-(*p*)-tolylpyrrole was prepared by a known method[19] and it was found to melt at 81.2–81.7°. A mixture with the material obtained by decarboxylation melted at 80.6–81.5°, establishing their identity.

Potentiometric Titration of Monopotassium Trihydrogen 1-Phenylpyrrole-2,3,4,5-Tetracarboxylate Monohydrate.—A sample of the monopotassium salt (0.1498 g., 0.0004 mole) was put in 150 ml. of distilled water and titrated with 0.04382 *N* sodium hydroxide solution. Simultaneous readings were made of *p*H (Beckman *p*H meter) and of volume. The inflection points occurred at 9.10, 17.95 and 27.25 ml. corresponding, respectively, to neutralization equivalents of 375.7, 190.4 and 125.4; calcd. for one, two and three carboxyls: 375.3, 197.6 and 125.1.

Monomethyl Ester of Indole-2,3-dicarboxylate.—The filtrate and ethereal washings from the preparation of adduct B using 22.7 g. of dimethyl acetylenedicarboxylate and 8.8 g. of N-phenylhydroxylamine in 25 ml. of toluene were combined, acidified with 20 ml. of concd. hydrochloric acid, and reduced to half-volume by distillation on a water-bath. A crystalline precipitate began forming in 15 minutes. After standing overnight, the mixture was filtered and the precipitate dried at 55° for two hours. The filtrate was further acidified with 10 ml. of concd. hydrochloric acid and two more crops of crystalline precipitate collected; total yield 8.0 g. (46%). The product was recrystallized from dioxane to give colorless needles, m.p. 254.3–255.1° (recorded 256°[6]).

Anal. Calcd. for $C_{11}H_9NO_4$: C, 60.27; H, 4.14; N, 6.39; neut. equiv., 219.2. Found: C, 60.59; H, 4.34; N, 6.48; neut. equiv., 218.6.

A small sample of the product with diazomethane gave the dimethyl ester, m.p. 112.0–112.5°, which did not depress the melting point of an authentic sample prepared from hydrazobenzene and dimethyl acetylenedicarboxylate.[6]

Monomethyl 5-Methylindole-2,3-dicarboxylate.—To a

(16) The potassium prevented complete burning of the carbon.

(17) (a) F. F. Blicke and J. L. Powers, THIS JOURNAL, **66**, 304 (1924); (b) H. Adkins and H. L. Coonradt, *ibid.*, **63**, 1567 (1941).

(18) J. K. Jurjew, *Ber.*, **69**, 1945 (1936).

(19) A. Pictet, *ibid.*, **37**, 2795 (1904).

solution of 9.25 g. of dimethyl acetylenedicarboxylate in 20 ml. of toluene was added in small portions 4.0 g. of N-(*p*)-tolylhydroxylamine. After the mixture had stood overnight, the precipitate of adduct was filtered off, washed with two 20-ml. portions of ether, and dried. The combined filtrate and washings were treated with 20 ml. of concd. hydrochloric acid in 50 ml. of methanol. The volume of the solution was reduced to half by distillation. After standing overnight, the precipitate of colorless crystals was removed by filtration and dried at 55° for two hours; m.p. 246–247°, yield 2.7 g. (36%).

Anal. Calcd. for $C_{12}H_{11}NO_4$: neut. equiv., 233.2. Found: neut. equiv., 231.0.

Dimethyl 5-Methylindole-2,3-dicarboxylate.—A 1.0-g. portion of the monomethyl ester was treated in 20 ml. of ether with diazomethane giving 1.0 g. (93%) from 5:1 methanol–water; m.p. 130.3–130.8°. For analysis a sample was dried at 100° for two hours.

Anal. Calcd. for $C_{13}H_{13}NO_4$: C, 63.15; H, 5.30; N, 5.67. Found: C, 63.26; H, 5.38; N, 6.04.

CAMBRIDGE, MASSACHUSETTS

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, TULANE UNIVERSITY]

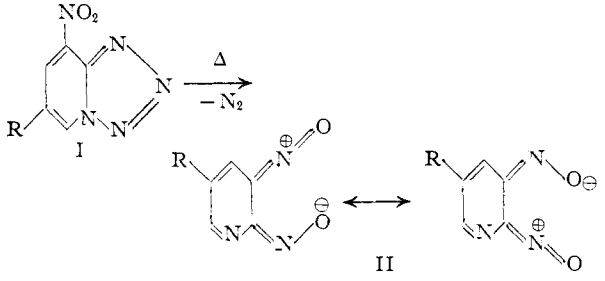
2,3-ψ-Dinitrosopyridines[1]

BY J. H. BOYER AND W. SCHOEN

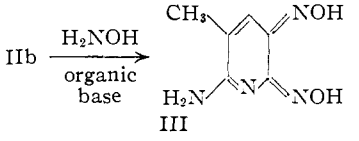
RECEIVED SEPTEMBER 12, 1955

Pyrolysis of appropriate derivatives of 8-nitropyridotetrazole brought about the formation of 5-methyl-, 5-carboxy- and 5-carbomethoxy-2,3-ψ-dinitrosopyridine. Hydroxylamine in diethylamine or in triethanolamine reduced ψ-*o*-dinitrosobenzene to a dioxime (presumably *amphi*) of *o*-benzquinone. Similar treatment of 5-methyl-2,3-ψ-dinitrosopyridine brought about reduction together with amination. The product appeared to be a dioxime of 3-aza-4-amino-5-methyl-*o*-benzquinone. Amination by hydroxylamine in aqueous alkali occurred at the 6-position for 2-amino-3-nitropyridine and 2-amino-3-nitro-5-methylpyridine but failed to occur with certain other derivatives of pyridine.

In the reported synthesis for ψ-2,3-dinitrosopyridine (IIa),[2] an essential step required the nitration of 2-amino or 2-hydroxypyridine at the 3-position. Undesirable alternate mononitration at the 5-position was eliminated in the present work with 2-hydroxy-5-carboxypyridine, the corresponding methyl ester and with 2-amino-5-methylpyridine. Usual procedures were employed to transform the nitration products into the corresponding derivatives of 8-nitropyridotetrazole (I). Interaction between the nitro group and a tetrazole nitrogen upon pyrolysis of each compound occurred with the formation of a 5-substituted-2,3-ψ-dinitrosopyridine (II).



a, R = H; b, R = CH_3; c, R = CO_2H; d, R = CO_2CH_3



Homocyclic aromatic ψ-*o*-dinitroso compounds have been reduced smoothly to dioximes by alkaline hydroxylamine.[3] Sensitivity of the nitroso compounds to alkaline degradation, however, has limited the usefulness of this reaction. A fairly rapid decomposition of ψ-1,2-dinitroso-3,5-dinitrobenzene, and apparently no reduction, occurred in both sodium and ammonium hydroxide which also contained hydroxylamine. In contrast, reduction to 1,2-diamino-3,5-dinitrobenzene occurred readily in hydroiodic acid. Presumably alkaline degradation also accounted for the difficulty in obtaining a reduction product from similar treatment of ψ-2,3-dinitroso-5-methylpyridine (IIb).

The use of hydroxylamine in diethylamine or in triethanolamine was then found successful in reducing pseudonitroso groups. The dioxime of *o*-benzoquinone was obtained in this manner from ψ-*o*-dinitrosobenzene. Surprisingly, amination of the pyridine ring took place as well as reduction of the nitroso groups when ψ-2,3-dinitroso-5-methylpyridine was treated with hydroxylamine and an organic base. This unexpected facility in aminating a pyridine derivative was also observed in similar experiments with both 2-amino-3-nitropyridine and 2-amino-3-nitro-5-methylpyridine in aqueous alkali and hydroxylamine. In the former case the known 2,6-diamino-3-nitropyridine was obtained and, by analogy, the formation of 2,6-diamino-3-nitro-5-methylpyridine in the latter example was assumed. Attempts to aminate 2-hydroxy-3-nitropyridine, 2-amino-5-methylpyridine, pyridine and 3-methylisoquinoline with alkaline hydroxylamine were unsuccessful. In agreement with these reactions the above reduction–amination product was assigned the structure of the dioxime of 3-aza-4-amino-5-methyl-*o*-benzquinone (III). Configuration of the dioxime was not determined, but was assumed to be one of the two possible *amphi* forms.

Experimental[4]

Coumalic acid[5] was esterified with methanol in sulfuric

(1) Grants from the Research Corporation and the American Cyanamid Co. made this investigation possible and are gratefully acknowledged.

(2) Previously named pyrido-2,3-furoxane; see J. H. Boyer, D. I. McCane, W. J. McCarville and A. T. Tweedie, THIS JOURNAL, **75**, 5298 (1953), and J. H. Boyer, R. F. Reinisch, M. J. Danzig, G. A. Stoner and F. Sahhar, *ibid.*, **77**, 5688 (1955).

(3) T. Zincke and P. Schwarz, *Ann.*, **307**, 28 (1899).

(4) Analyses by Micro-tech Laboratories, Skokie, Ill. Infrared spectra were obtained through the courtesy of the Perkin-Elmer Corporation, New Orleans. Melting points are corrected unless otherwise specified; boiling points, uncorrected.

(5) R. H. Wiley and N. R. Smith, *Org. Syntheses*, **31**, 23 (1951).