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Preparation of Quinol Imide Acetates. VI. Scope and Limitations

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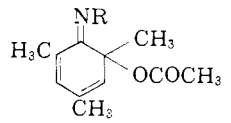
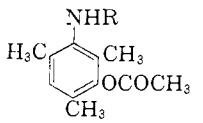
Extension of the syntheses of benzoquinol imide acetates beyond the mesidine series was generally not successful. Variation of the amide portions of the system did not improve the yields in the mesidine series nor enable isolation of products with the other amines studied. A number of rearranged acetates were obtained with other alkyl and aryl anilines. The first pyridine quinol imide acetate was prepared.

In order to determine the practical value of quinol imide acetates as synthetic intermediates in the preparation of highly substituted aromatic systems it was necessary to enlarge upon the scope of previous investigations.[2-6] The benzoquinol sulfonamide acetates investigated thus far were formed in yields of not greater than 50%. A related system might afford better yields and thus provide a more useful synthetic tool.

Since in previous work the mesidine derivative seemed most susceptible to oxidation, initial efforts were directed to that system. Lead tetraacetate oxidation of N-benzoylmesidine yielded a small quantity of the imide acetate I (R = COC_6H_5), but the major portion of the material



I



II

isolated appeared to consist of the rearranged acetate II (R = COC_6H_5). The infrared spectra of these materials enable ready differentiation. The imide acetates are characterized by the lowering of the acetate ester carbonyl absorption to about 1740 cm.$^{-1}$ from the values some 10–20 cm.$^{-1}$ higher exhibited by the vinyl ester of the rearranged acetates, and the absence of absorption in the NH region. In the above case further demonstration of the presence of the imide acetate was obtained by *in situ* addition of hydrogen chloride and thiophenol to form 3-chloro- and 3-phenylmercapto-N-benzoylmesidine.

Compound II (R = COC_6H_5) was synthesized independently from 3-nitromesidine by diazotization and hydrolysis to 3-nitromesitol, followed by acetylation to 2-acetoxy-4-nitromesitylene, reduction to the amine and benzoylation in pyridine. This material was identical with that obtained as the major product from the lead tetraacetate oxidation of N-benzoylmesidine, as well as that obtained as the sole isolable compound when the oxidation reaction mixture was treated with acetic acid. The rearranged acetate was converted readily to hydroxy-N-benzoylmesidine by hydrolysis with 15% aqueous sodium hydroxide.

Chromatography of the oxidation mixture revealed also the presence of benzamide, indicating a rather unique cleavage effected by the lead tetraacetate. In later work it was shown that hydrolytic cleavage of the amide also could take place in the course of treatment by the oxidizing agent.

Examination of the effect of introduction of substituents into the benzoyl group of the amide moiety was undertaken. Lead tetraacetate oxidation of a chloroform solution of N-*p*-ethoxybenzoylmesidine yielded no isolable product. However, the presence of the imide acetate in the oxidation mixture was demonstrated by treatment with hydrogen chloride and isolation of an adduct. A similar oxidation of N-*p*-nitrobenzoylmesidine gave only the rearranged acetate II (R = $COC_6H_4NO_2$-*p*). However, addition of calcium carbonate to this particular reaction mixture as a scavenger for acetic acid enabled isolation of the imide acetate I (R = $COC_6H_4NO_2$-*p*) in 37.4% yield. The imide acetate was converted to the rearranged acetate upon warming with glacial acetic acid.

The utilization of aqueous sodium hydroxide to determine whether the oxidation product was the desired imide acetate or the rearranged acetate proved not to be feasible. Treatment either of an imide acetate or the rearranged acetate with 15% aqueous sodium hydroxide led to a phenol. Thus 2,4,6-trimethyl-*o*-quinolbenzenesulfonimide acetate (I, R = $SO_2C_6H_5$) yielded 57.3% of hydroxy-N-benzenesulfonylmesidine.

Lead tetraacetate oxidation of N-*p*-nitrobenzenesulfonylmesidine also yielded the imide acetate I (R = $SO_2C_6H_4NO_2$-*p*) but in low yield, 34%.

A series of amides with N-benzoyl, N-*p*-nitrobenzoyl and N-*p*-nitrobenzenesulfonyl substituents was oxidized both in chloroform and acetic acid solution and at various temperatures. The structures of the products were not determined unequivocally, but were assigned on the basis of previously recorded observations.[8]

N-(*p*-Nitrobenzoyl)-*p*-toluidine, N-(*p*-nitrobenzenesulfonyl)-*o*-toluidine, N-*p*-nitrobenzoyl-2,6-didimethylaniline, N-benzoyl-2,4-dimethylaniline, N-*p*-nitrobenzoyl-2,4-dimethylaniline, N-*p*-nitrobenzenesulfonyl-2,4-dimethylaniline and N-benzoyl-2-aminobiphenyl upon oxidation in acetic acid yielded not the imide acetates but only the corresponding rearranged acetates. When the reactions were run in chloroform obstinate mixtures resulted from which the only isolable compounds were occasional recovered starting materials.

N-Benzoyl-*p*-toluidine, N-acetyl-*p*-toluidine, N-acetyl-*o*-toluidine, N-benzoyl-*o*-toluidine, N-(*p*-

(1) Abstract of a portion of a thesis submitted by Leslie M. Werbel in partial fulfillment for the degree of Doctor of Philosophy at the University of Illinois, 1957. Minnesota Mining and Manufacturing Fellow, 1952–1953; Allied Chemical Co. Fellow, 1955–1956; Dow Chemical Co. Fellow, 1956–1957.

(2) R. Adams, E. J. Agnello and R. S. Colgrove, THIS JOURNAL, **77**, 5617 (1955).

(3) R. Adams and K. R. Brower, *ibid.*, **78**, 4770 (1956).

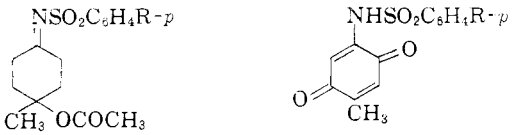
(4) R. Adams and J. E. Dunbar, *ibid.*, **78**, 4774 (1956).

(5) R. Adams and E. L. DeYoung, *ibid.*, **79**, 417 (1957).

(6) R. Adams and K. R. Brower, *ibid.*, **79**, 1950 (1957).

nitrobenzoyl)-*o*-toluidine, N-benzoyl-2,6-dimethylaniline, N-*p*-nitrobenzenesulfonyl-2,6-dimethylaniline, N-*p*-nitrobenzenesulfonyl-4-aminobiphenyl, N-*p*-nitrobenzoyl-2-aminobiphenyl and N-*p*-nitrobenzenesulfonyl-2-aminobiphenyl yielded no isolable oxidation products.

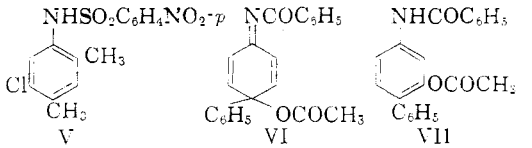
The amide acetates III and the corresponding quinones IV were formed by oxidation of N-(*p*-toluenesulfonyl)- and N-(*p*-nitrobenzenesulfonyl)-*p*-toluidine in acetic acid.[7]



III R = CH_3, NO_2 IV

The quinol imide acetate from N-*p*-nitrobenzenesulfonyl-2,4-dimethylaniline could not be isolated, but *in situ* addition of hydrogen chloride yielded the chloro compound V derived from it.

N-Benzoyl-4-aminobiphenyl was oxidized readily by lead tetraacetate when heated in acetic acid for 16 hours. However, an inseparable mixture of imide acetate VI and rearranged acetate VII was obtained. Evidence for this conclusion was the

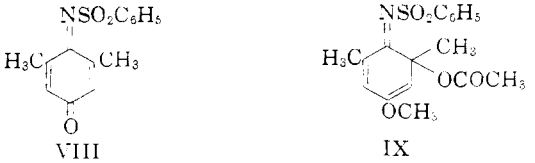


V VI VII

wide melting point range of the product which gave correct analytical values, the presence in the infrared spectrum of NH and acetate ester bands corresponding to the rearranged acetate, the quinol imide acetate carbon–carbon double bond 1627 cm.$^{-1}$ and the ultraviolet spectrum which exhibited absorption at 272 mμ (log 4.34) indicative of a *p*-benzoquinol imide acetate.

N-*p*-Nitrobenzoyl-4-aminobiphenyl proved less susceptible to oxidation, but in acetic acid a small amount of mixture of imide acetate and rearranged acetate similar to VI and VII was formed.

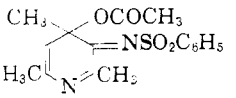
Brower[8] found that treatment of N-benzenesulfonyl-*p*-anisidine in chloroform with lead tetraacetate led to formation of *p*-quinonemonobenzenesulfonimide. In the present studies similar treatment of N-(*p*-toluenesulfonyl)-*o*-anisidine yielded only intractable gums. However, the oxidation of N-benzenesulfonyl-4-methoxy-2,6-dimethylaniline led to a very small amount of solid product which appears to be the quinonemonoimide VIII, rather than the quinol imide acetate IX. An adequate



VIII IX

amount of material for preparation of an analytical sample was not available. The infrared spectrum, however, confirms the loss of the methoxy group and indicates a quinonemonoimide structure. This suggests a preferential attack on a carbon bearing an alkoxy group over that bearing an alkyl group.

Certain members of the pyridine series were studied in the hope of obtaining pyridine analogs of the benzoquinones (azaquinones) *via* the quinol imide acetate procedure. Attempts at oxidation of N-benzenesulfonyl-2-amino-3-methylpyridine and N-benzenesulfonyl-2-amino-5-methylpyridine in both chloroform and acetic acid solution failed. Starting material was recovered and gummy products were formed. However, treatment of N-benzenesulfonyl-3-amino-2,4,6-trimethylpyridine in acetic acid with lead tetraacetate resulted in a product whose infrared spectrum and analytical values are indicative of the desired quinol imide acetate. Structure X or one of its isomeric structures involving the α-methyl groups illustrate the character of the product.



X

In an effort to determine whether stable quinol imide acetates could be formed in a system containing other than alkyl or aryl substituents, N-benzenesulfonyl *p*-chloro-, *p*-nitro- and *p*-cyano-aniline, and N,O-ditosyl-*p*-aminophenol were subjected to the action of lead tetraacetate in both chloroform and acetic acid solution. In all cases only formation of amorphous tarry materials and recovery of starting materials was noted.

Acknowledgment.—The authors are indebted to Mr. J. Nemeth, Mrs. M. Stingl and Miss C. Higham for the microanalyses and to Mr. J. Brader for the infrared spectral determinations.

Experimental

All melting points are corrected.

Preparation of Amides.—The amides utilized in this investigation (with the exception of acetamide) were prepared by treating a solution of the amine in pyridine with an equimolar amount of the acid chloride corresponding to the desired amide. The solution was warmed on the steam-bath for an hour or two, and then poured into iced hydrochloric acid. The solid product was removed by filtration, washed with water and recrystallized from ethanol (see Table I).

The products of the oxidation reactions of the amides which are not described in detail below will be found in Table II.

2,4,6-Trimethyl-*o*-quinolbenzimide Acetate.—To a solution of 2 g. of N-benzoylmesidine in 50 ml. of chloroform was added a solution of 3.7 g. of lead tetraacetate in 25 ml. of chloroform. The mixture was allowed to stand for 24 hours, during which time the initial red color bleached to pale yellow and solid lead salts were deposited from solution. These were removed and the filtrate dried and evaporated to dryness. Trituration of the resultant gum with methanol yielded 0.77 g. of yellow solid, fraction A. The filtrate upon evaporation to dryness and treatment with dilute ethanol after long standing yielded 0.7 g. of an amorphous yellow solid, fraction B. Fraction A upon repeated recrystallization from dilute acetone yielded a small amount of pure imide acetate; white needles, m.p. 123.5–125.5°.

Anal. Calcd. for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71. Found: C, 72.99; H, 6.28; N, 4.70.

The infrared spectrum of fraction B indicated it to consist mainly of the rearranged acetate, acetoxy-N-benzoylmesidine.

(7) R. Adams and C. Plantz, unpublished results.

(8) K. R. Brower, private communication.

TABLE I

Mesidine derivatives Amides	Yield, %	M.p. °C. (lit. m.p.)	Formula	Analyses, % Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
N-Benzoyl	96	204.5–206.5 (204[a])							
N-*p*-Nitrobenzoyl	89	223–224	$C_{16}H_{16}N_2O_3$	67.59	5.67	9.86	67.82	5.69	9.73
N-Acetyl	87.5	216.5–219.5 (216[a])							
N-*p*-Ethoxybenzoyl	94	195–196	$C_{18}H_{21}NO_2$	76.29	7.47	4.94	76.32	7.55	4.99
N-*p*-Nitrobenzenesulfonyl	67	151–152	$C_{15}H_{16}N_2O_4S$	56.23	5.03	8.75	56.44	4.96	8.48
p-Toluidine derivatives									
N-Benzoyl	94	158–160 (158[a])							
N-Acetyl	..	146.5–147.5 (153[b])							
N-*p*-Nitrobenzoyl	89.5	200–202	$C_{14}H_{12}N_2O_3$	65.62	4.72	10.93	65.73	4.64	10.82
N-*p*-Nitrobenzenesulfonyl	61	180.5–183 (179–180[b])							
N-*p*-Toluenesulfonyl	69.5	117.5–119.5 (117[a])							
o-Toluidine derivatives									
N-Benzoyl	85	143–145 (143[a])							
N-*p*-Nitrobenzoyl	85	160–161.5	$C_{14}H_{12}N_2O_3$	65.62	4.72	10.93	65.69	4.73	11.20
N-*p*-Nitrobenzenesulfonyl	59.6	156–158	$C_{13}H_{12}N_2O_4S$	53.41	4.14	9.59	53.46	4.06	9.39
2,4-Dimethylaniline									
N-Benzoyl	96.5	193–194.5 (192[a])							
N-*p*-Nitrobenzoyl	86	173–175	$C_{15}H_{14}N_2O_3$	66.65	5.22	10.37	66.70	5.25	10.53
N-*p*-Nitrobenzenesulfonyl	62	133.5–135.5	$C_{14}H_{14}N_2O_4S$	54.89	4.61	9.11	54.73	4.89	9.09
2,6-Dimethylaniline									
N-Benzoyl	87	161–163 (168[a])							
N-*p*-Nitrobenzoyl	91.6	193–196	$C_{15}H_{14}N_2O_3$	66.65	5.22	10.37	66.49	..	10.43
N-*p*-Nitrobenzenesulfonyl	51.7	181–183	$C_{14}H_{14}N_2O_4S$	54.89	4.61	9.15	54.98	4.43	9.12
4-Aminobiphenyl									
N-Benzoyl	86	232–234 (230[a])							
N-*p*-Nitrobenzoyl	92	275–277[c]	$C_{19}H_{14}N_2O_3$	71.69	4.43	8.80	72.01	4.74	9.04
N-*p*-Nitrobenzenesulfonyl	..[d]	191–192	$C_{18}H_{14}N_2O_4S$	61.00	3.98	7.91	60.90	4.10	8.02
2-Aminobiphenyl									
N-Benzoyl	99.3	87–89 (86[a])							
N-*p*-Nitrobenzoyl	92	158–160	$C_{19}H_{14}N_2O_3$	71.69	4.43	8.80	71.83	4.40	8.91
N-*p*-Nitrobenzenesulfonyl	46.4	152–153	$C_{18}H_{14}N_2O_4S$	61.00	3.98	7.91	61.12	3.82	7.69
N-Benzenesulfonyl-2-amino-5-methylpyridine	68.4	170.5–172	$C_{12}H_{12}N_2O_2S$	58.04	4.87		58.17	4.91	
N-Benzenesulfonyl-2-amino-3-methylpyridine	54.3	152–154	$C_{12}H_{12}N_2O_2S$	58.04	4.87	11.28	58.23	4.70	11.34
N-Benzenesulfonyl-3-amino-2,4,6-trimethyl-pyridine	93.5	124.5 d. (125.5–126.5[e])							
N-Benzoyl-2-methyl-5-nitroaniline	93.5	184–185	$C_{14}H_{12}N_2O_3$	65.61	4.72	10.93	65.98	4.70	10.90
N-Benzenesulfonyl-2-methyl-5-nitroaniline	92.5	175.5–178	$C_{13}H_{12}N_2O_4S$	53.41	4.14	9.59	53.63	4.07	9.53
N-Benzenesulfonyl-*p*-chloroaniline	95	121–123.5 (121[a])							
N-Benzenesulfonyl-*p*-nitroaniline	92.8	138–140.5 (139[a])							
N,O-Di-(*p*-toluenesulfonyl)-*p*-aminophenol	58.6	167–169	$C_{20}H_{19}NO_5S_2$	57.53	4.59	3.36	57.45	4.59	3.52
N-Benzenesulfonyl-*p*-aminobenzonitrile	Quant.	176–178	$C_{13}H_{10}N_2O_2S$	60.45	3.90	10.85	60.63	4.06	10.84
N-Benzenesulfonyl-2,6-dimethyl-4-methoxy-aniline	95.7	134.5–137	$C_{15}H_{17}NO_3S$	61.83	5.88	4.81	61.90	6.05	4.75

[a] R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1948. [b] F. Bell, *J. Chem. Soc.*, 2770 (1928). [c] Recrystallized from glacial acetic acid. [d] The product was contaminated with 4-aminobiphenyl hydrochloride and no accurate yield was obtained. The by-product was separated by fractional crystallization with ethanol and purified from a mixture of ethanol and ether; white solid, m.p. 282°. *Anal.* Calcd. for $C_{12}H_{12}ClN$: C, 70.07; H, 5.88; N, 6.81. Found: C, 70.10; H, 5.76; N, 6.93. [e] J. E. Dunbar, Thesis, Doctor of Philosophy, University of Illinois, 1956. [f] B. C. Saunders and G. H. R. Watson, *Biochem. J.*, 46, 629 (1950).

2-Acetoxy-4-nitromesitylene.—A solution of 1 g. of 3-nitromesitol[9] in 15 ml. of acetic anhydride was heated under reflux for 2.5 hours. The brown solution was poured into iced water. The resultant oil solidified upon standing for a short time and upon filtration yielded 4.7 g. (96%) of product. Recrystallization from dilute ethanol gave pale yellow crystals, m.p. 73–75°.

Anal. Calcd. for $C_{11}H_{13}NO_4$: C, 59.19; H, 5.87; N, 6.28. Found: C, 59.33; H, 5.96; N, 6.19.

3-Acetoxy-N-benzoylmesidine. A.—A solution of 0.52 g. of acetoxynitromesitylene in 10 ml. of ethanol was hydrogenated over Raney nickel at 2000 lb. pressure and 85° for 14 hours. The solution was filtered and evaporated to dryness. The resultant gum was dissolved in pyridine and the calculated amount of benzoyl chloride added. The mix was heated on the steam-bath for one hour and poured into iced hydrochloric acid, yielding 0.2 g. of solid (29%). Recrystallization from dilute ethanol afforded the pure product, m.p. 140–142°. The infrared spectrum of this material was essentially identical with that of fraction B obtained in the oxidation of N-benzoylmesidine.

Anal. Calcd. for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71. Found: C, 72.53; H, 6.35; N, 4.92.

(9) E. Knecht, *Ann.*, **215**, 98 (1882).

B. *In Situ* **Rearrangement of 2,4,6-Trimethyl-*o*-quinolbenzimide Acetate.**—To a solution of 1.9 g. of lead tetraacetate in 20 ml. of chloroform was added a solution of 1 g. of N-benzoylmesidine in 20 ml. of chloroform. The mixture was allowed to stand for 12 hours, filtered, and the solvent removed in a stream of dry air. The residue was heated under reflux for 9 hours with 25 ml. of glacial acetic acid. The acetic acid was removed under vacuum and the resultant oil triturated with ethanol and cooled to yield 0.74 g. (59.5%) of solid product. Recrystallization from dilute ethanol gave pure material, m.p. 136–138°. The melting point of a mixture of this material with an authentic sample prepared by an unequivocal synthesis (A) was not depressed.

Anal. Calcd. for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71. Found: C, 72.76; H, 6.33; N, 4.86.

3-Chloro-N-benzoylmesidine.—To a solution of 1.9 g. of lead tetraacetate in 20 ml. of chloroform was added a solution of 1 g. of N-benzoylmesidine in chloroform. The mixture was allowed to stand overnight, filtered to remove deposited lead salts, and concentrated to one-half the original volume. Dry hydrogen chloride was bubbled into the solution. The color was bleached and the product separated as a white solid. Evaporation to dryness yielded 1 g. of white solid, which was purified by several recrystallizations from dilute ethanol, m.p. 199–200°. A lower melting

TABLE II

PRODUCTS FROM LEAD TETRAACETATE OXIDATIONS

	Amide	Product	Procedure	Yield, %	M.p., °C.	Formula	Analyses, %					
							C	Calcd. H	N	C	Found H	N
1.	N-*p*-Nitrobenzoyl-*p*-toluidine	3′-Acetoxy-4′-methyl-*p*-nitrobenzanilide	HOAc	54.6	189.5–191	$C_{16}H_{14}N_2O_5$	61.14	4.49	8.92	60.92	4.66	9.06
2.	N-*p*-Nitrobenzoyl-2,6-dimethylaniline	3′-Acetoxy-2′,6′-dimethyl-*p*-nitrobenzanilide	HOAc	24.7	171.5–173	$C_{17}H_{16}N_2O_5$	62.19	4.91	8.53	62.45	5.21	8.41
3.	N-Benzoyl-2,4-dimethylaniline	5′-Acetoxy-2′,4′-dimethylbenzanilide	$CHCl_3$	23.9	220.5–223	$C_{17}H_{17}NO_3$	72.06	6.05	4.94	72.24	6.18	5.01
4.	N-*p*-Nitrobenzoyl-2,4-dimethylaniline	5′-Acetoxy-2′,4′-dimethyl-*p*-nitrobenzanilide	$CHCl_3$	12.3	212.5–213.5	$C_{17}H_{16}N_2O_5$	62.19	4.91	8.53	62.21	4.86	8.38
5.	N-*p*-Nitrobenzenesulfonyl-2,4-dimethylaniline	5′-Acetoxy-2′,4′-dimethyl-*p*-nitrobenzenesulfonanilide	HOAc	..	171–173	$C_{16}H_{16}N_2O_6S$	52.74	4.43	7.69	53.08	4.33	7.70
6.	N-*p*-Nitrobenzenesulfonyl-2,4-dimethylaniline	5′-Chloro-2′,4′-dimethyl-*p*-nitrobenzenesulfonanilide	$CHCl_3$ HCl	36	216.5–218.5	$C_{14}H_{13}ClN_2O_4S$	49.34	3.84	8.22	49.48	3.98	8.06
7.	N-Benzoyl-2-aminobiphenyl	5′-Acetoxy-2′-phenylbenzanilide	HOAc	23.1	177–179.5	$C_{21}H_{17}NO_3$	76.11	5.17	4.23	76.45	5.35	4.57
8.	N-Benzenesulfonyl-3-amino-2,4,6-trimethylpyridine	Exact structure not identified (see formula X)	HOAc 15 hr. reflux	35.5[a]	133–138	$C_{18}H_{18}N_2O_4S$	57.47	5.43	8.38	57.75	5.35	8.68
9.	N-*p*-Nitrobenzenesulfonyl-*o*-toluidine	5′-Acetoxy-2′-methyl-*p*-nitrobenzenesulfonanilide	HOAc	16.7	195–197.5	$C_{15}H_{14}N_2O_6S$	51.42	4.03	8.00	51.53	4.19	7.99

[a] Recrystallized from a mixture of benzene and cyclohexane.

solid by-product was probably rearranged acetate as indicated by the infrared spectrum.

Anal. Calcd. for $C_{16}H_{16}ClNO$: C, 70.19; H, 5.89; N, 5.12. Found: C, 70.33; H, 6.16; N, 5.04.

3-Phenylmercapto-N-benzoylmesidine.—To a solution of 1.9 g. of lead tetraacetate in 20 ml. of chloroform was added a solution of 1 g. of N-benzoylmesidine in 20 ml. of chloroform. After 12 hours the mix was filtered and the chloroform removed in a stream of dry air. To the resultant yellow oil was added 0.6 g. of thiophenol in 5 ml. of ethanol. This solution was allowed to stand for 18 hours, concentrated, and the resultant oil recrystallized from dilute ethanol to give a very small amount of solid, m.p. 162–163°.

Anal. Calcd. for $C_{22}H_{21}NOS$: C, 76.04; H, 6.09. Found: C, 76.32; H, 6.04.

3-Hydroxy-N-benzoylmesidine.—A solution of 0.14 g. of 3-acetoxy-N-benzoylmesidine, 5 ml. of ethanol, 5 ml. of water and 5 ml. of 15% aqueous sodium hydroxide was heated under reflux for one hour. The solution was made acidic with hydrochloric acid, and water added to complete precipitation of the product; white solid, 0.07 g. (59%), m.p. 193–194.5°. Recrystallization from dilute ethanol did not change the melting point.

Anal. Calcd. for $C_{16}H_{15}NO_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.27; H, 6.83; N, 5.45.

2,4,6-Trimethyl-*o*-quinol-*p*-nitrobenzimide Acetate.—A suspension of 1 g. of N-*p*-nitrobenzoylmesidine in 25 ml. of chloroform was added to a solution of 1.6 g. of lead tetraacetate in 25 ml. of chloroform. To the stirred mixture was added 0.5 g. of calcium carbonate. After 6 hours the mixture was filtered. Evaporation of the filtrate to dryness yielded 0.45 g. (37.4%) of yellow solid which was purified by recrystallization from ethanol, m.p. 152–153.5°.

Anal. Calcd. for $C_{18}H_{18}N_2O_5$: C, 63.15; H, 5.30; N, 8.18. Found: C, 63.09; H, 5.50; N, 8.08.

3-Acetoxy-N-*p*-nitrobenzoylmesidine.—A solution of 0.58 g. of 2,4,6-trimethyl-*o*-quinol-*p*-nitrobenzimide acetate in 20 ml. of glacial acetic acid was heated under reflux for 3 hours. The solution first turned yellow and then bleached. It was poured into water, yielding 0.5 g. (86.2%) of white solid. Recrystallization from dilute ethanol gave white crystals, m.p. 238–239°.

Anal. Calcd. for $C_{18}H_{18}N_2O_5$: C, 63.15; H, 5.30; N, 8.18. Found: C, 62.85; H, 5.20; N, 8.47.

3-Chloro-N-*p*-ethoxybenzoylmesidine.—A solution of 1 g. of N-*p*-ethoxybenzoylmesidine and 1.66 g. of lead tetraacetate in chloroform was allowed to stand for 24 hours. It then was filtered and dry hydrogen chloride was passed into the filtrate for 20 minutes. The white precipitate of lead chloride was removed and the solution evaporated to dryness. The residue, after recrystallization from dilute ethanol, yielded 0.61 g. of white solid. The pure product was obtained by multiple recrystallizations from ethanol; white plates, m.p. 202.5–204.5°.

Anal. Calcd. for $C_{18}H_{20}ClNO_2$: C, 68.02; H, 6.34; N, 4.41. Found: C, 68.23; H, 6.36; N, 4.48.

2,4,6-Trimethyl-*o*-quinol-*p*-nitrobenzenesulfonimide Acetate.—To a solution of 1 g. of N-*p*-nitrobenzenesulfonylmesidine in chloroform was added 1.4 g. of lead tetraacetate in chloroform. The solution was stirred for 24 hours, filtered and the filtrate evaporated to dryness. The residue was triturated with ethanol and yielded 0.76 g. of yellow powder. Recrystallization from ethanol yielded the pure product; 0.4 g. (34%), yellow plates, m.p. 144–145°.

Anal. Calcd. for $C_{17}H_{18}N_2O_6S$: C, 53.96; H, 4.79; N, 7.40. Found: C, 54.34; H, 5.13; N, 7.30.

3-Acetoxy-N-*p*-nitrobenzenesulfonylmesidine.—A solution of 0.44 g. of 2,4,6-trimethyl-*o*-quinol-*p*-nitrobenzenesulfonimide acetate in 15 ml. of glacial acetic acid was heated under reflux for 3 hours. The solution was poured into water to yield 0.38 g. (86.5%) of tan solid. Recrystallization from dilute ethanol afforded the pure product; yellow needles, m.p. 168.5–171°.

Anal. Calcd. for $C_{17}H_{18}N_2O_6S$: C, 53.96; H, 4.79; N, 7.40. Found: C, 53.98; H, 4.81; N, 7.09.

General Procedure for Lead Tetraacetate Oxidation in Acetic Acid.—To a solution of 1 g. of the amide in a minimum amount of glacial acetic acid was added an equivalent

of lead tetraacetate (calculated on the basis of an assay with iodide and thiosulfate). The mixture usually was heated under reflux for 3 hours, and then cooled and poured into water. The aqueous solution was extracted with ether, and the extracts washed with water and aqueous sodium or potassium carbonate. It was found that the use of 5% aqueous sodium hydroxide as a wash in some cases caused hydrolysis of the acetate esters in the products. The ether extracts were evaporated to dryness and the pure product usually obtained by recrystallization from ethanol.

Reaction of Sodium Hydroxide with 2,4,6-Trimethyl-*o*-quinolbenzenesulfonimide Acetate.—A suspension of 0.5 g. of 2,4,6-trimethyl-*o*-quinolbenzenesulfonimide acetate in 20 ml. of 15% aqueous sodium hydroxide was heated under reflux for 3 hours and allowed to cool and stand overnight. A small amount of solid was removed by filtration and discarded. The filtrate upon acidification with concentrated hydrochloric acid yielded 0.25 g. (57.3%) of pale yellow solid. Recrystallization from dilute ethanol gave pure product, m.p. 180–181.5°.

Anal. Calcd. for $C_{15}H_{17}NO_3S$: C, 61.83; H, 5.88; N, 4.81. Found: C, 61.86; H, 5.93; N, 5.02.

URBANA, ILL.

[CONTRIBUTION FROM THE DEPARTMENT OF ORGANIC CHEMISTRY, HEBREW UNIVERSITY]

1,2-Cyclopentenofluorene. Part II[1]

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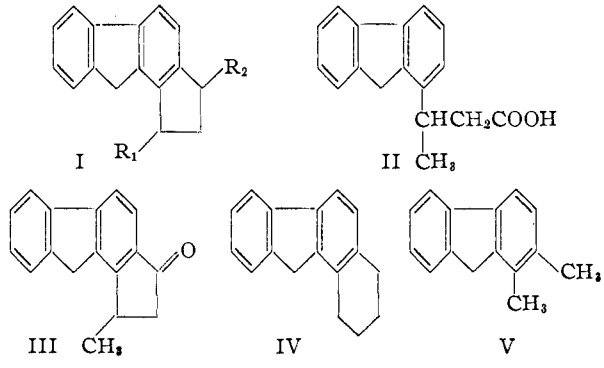
For comparsion with the dehydrogenation products of cevine and jervine, 1'-methyl- and 1',3'-dimethyl-1,2-cyclopentenofluorene, 1,2-cyclohexenofluorene and 1,2-dimethylfluorene have been synthesized. All these substances have very similar spectra. It is not impossible that the dehydrogenation products in question are 1,2-benzofluorene derivatives.

In order to test the current hypothesis that the dehydrogenation of cevine and jervine leads to derivatives of 1,2-cyclopentenofluorene, thus involving the transformation of a six- to a five membered ring, the parent substance (I, $R_1 = R_2 = H$) and its 3'-methyl derivative (I, $R_1 = H$; $R_2 = CH_3$) had been synthesized.[1] The two hydrocarbons resembled in their spectrum closely the above dehydrogenation products, but were not identical with them. In the present communication, the 1'-methyl derivative (I, $R_1 = CH_3$; $R_2 = H$) and the 1',3'-dimethyl compound (I, $R_1 = R_2 = CH_3$) have been prepared. From the chloride



of fluorene-1-carboxylic acid and dimethylcadmium, 1-acetylfluorene has been obtained. Its condensation with ethyl cyanoacetate, followed by hydrolysis, partial decarboxylation and catalytic hydrogenation led to β-(1-fluorenyl)-butyric acid (II); an alternative method consists in the reaction of 1-acetylfluorene with ethyl bromoacetate and zinc, followed by dehydration and catalytic reduction. Cyclization of II gave 3'-keto-1'-methyl-1,2-cyclopentenofluorene (III) which by reduction gave (I, $R_1 = CH_3$, $R_2 = H$) and by reaction with methylmagnesium iodide and subsequent hydrogenation yielded (I, $R_1 = R_2 = CH_3$). The melting points of these two hydrocarbons (71 and 82°, respectively) were not identical with that of any of the compounds isolated from the dehydrogenation products of cevine and jervine.[1] The absorption spectra were very similar to those reported for these dehydrogenation products; this was in accordance with the observations made in our previous communication.[1]

Winkler and Reichstein[2] have suggested that the ultraviolet absorption spectra cannot be expected to differentiate between 1,2-cyclopentenofluorene and other 1,2-alkyl derivatives of fluorene. In order to substantiate this suggestion, 1,2-cyclohexenofluorene (IV) and 1,2-dimethylfluorene (V) have been synthesized; obviously, a compound like IV would not be formed in the dehydrogenation of a polycyclic natural product.

The previously described[1] β-(1-fluorenyl)-propionic acid was converted by an Arndt–Eistert reaction into γ-(1-fluorenyl)-butyric acid (VI) and the latter cyclized to 4'-keto-1,2-cyclohexenofluorene (VII). Reduction by the method of Huang-Minlon gave IV as a well-crystallized substance. For the synthesis of the liquid 1,2-dimethylfluorene (V) a method was applied which recently has been developed in our laboratories[3]: 2,3-dimethylbenzoic acid was prepared from *o*-xylene by a 4-step synthesis (over-all yield, 21%) and its chloride condensed with cyclohexene. (2,3-Dimethylbenzoyl)-cyclohexene (VIII) was then isomerized by means of a mixture of phosphoric and formic acid[4] to 5,5a,6,7,8,8a-hexahydro-2,3-dimethylfluorenone (IX) and the latter dehydrogenated to 2,3-dimethylfluorenone. Reduction by the method of Huang-Minlon gave V.

In Table I, the spectra of the compounds prepared in this study are compared with that of the dehydrogenation product $C_{24}H_{30}$ obtained by Craig

(1) Part I, E. D. Bergmann and R. Ikan, THIS JOURNAL, **78**, 2921 (1956). In this paper, the melting point of 1,2,3,4-tetrahydrofluorene-1-carboxylic acid had been omitted; it is 168°.

(2) R. E. Winkler and T. Reichstein, *Helv. Chim. Acta*, **37**, 721 (1954); *cf.* F. Korte, *Ber.*, **88**, 1527 (1957).

(3) E. D. Bergmann, *Bull. Res. Council Israel*, **6A**, 150 (1955–1956).

(4) E. A. Braude and W. F. Forbes, *J. Chem. Soc.*, 2208 (1953).