NOTES.

456. *Aromatic Reactivity. Part IV.* The 2- and the 3-Position of Thiophen in Protodesilylation.*

By F. B. Deans and C. Eaborn.

The 2-position of thiophen is known to be very reactive towards electrophilic substitution, but no quantitative data on the reactivity are available. The 3-position is considerably less reactive, and it is known that detritiation by aqueous sulphuric acid takes place 955 ± 140 times as readily at the 2-position.[1] Molecular-orbital calculations suggest that the 3-position should be about as reactive as a single position of benzene and the 2-position considerably more reactive.[2]

It has been established that the rate of acid cleavage of the aryl–silicon bond in a substituted phenyltrimethylsilane (protodesilylation) provides an excellent measure of reactivity at the aromatic carbon of the bond,[3,4] and we have now used the cleavage to measure the reactivity of the 2- and the 3-position of thiophen. We find that in acetic acid containing aqueous sulphuric acid at 50·18°, 2-thienyltrimethylsilane is cleaved 43·5 times as fast as the 3-isomer, which in turn is cleaved 6·4 times as fast as *p*-tolyltrimethylsilane. Since the last compound is cleaved 18 times as fast as phenyltrimethylsilane,[3] the 2- and the 3-thienyl compounds are 5000 and 115 times as reactive as the phenyl compound. We conclude with confidence that, while the 3-position of thiophen is considerably less reactive than the 2-position, it is nevertheless markedly more reactive than a single position of benzene. It is of intere t that the reactivity of the 3-thienyl compound is about half that of *p*-hydroxyphenyltrimethylsilane.[3]

The results here presented are consistent with the relative reactivites observed for thiophen in detritiation if a linear free-energy relation is assumed between substituent effects in detritiation and in desilylation. The *p*-methyl group activates about 240 times in detritiation by aqueous sulphuric acid,[5] and about 18 times in desilylation by aqueous sulphuric acid in acetic acid,[3] and the ratio of the logarithms (to base 10) of these values is 1·90. 2-Thienyltrimethylsilane is 43·5 times as reactive as the 3-isomer, and thus the logarithm of the ratio of the reactivites of the 2- and the 3-position of thiophen in detritiation should be 1·90 × log 43·5, *i.e.*, 3·1. In view of the extrapolations involved this represents good agreement with the experimental figure [1] of 2·98 ± 0·06.

* Part III, preceding paper.

[1] Halvarson and Melander, *Arkiv Kemi*, 1955, **8**, 29.
[2] Melander, *ibid.*, 1955, **8**, 361; Heer, *J. Amer. Chem. Soc.*, 1954, **76**, 4802.
[3] Deans and Eaborn, *J.*, 1959, 2299.
[4] Eaborn, *J.*, 1953, 3148, and 1956, 4858; Benkeser and Krysiak, *J. Amer. Chem. Soc.*, 1954, **76**, 6353; Benkeser, Hickner, and Hoke, *ibid.*, 1958, **80**, 2279; Benkeser, Hickner, Hoke, and Thomas, *ibid.*, p. 5289.
[5] Eaborn and Taylor, unpublished work.

Experimental.—Thienyltrimethylsilanes. 2-Thienyltrimethylsilane, b. p. 165·5°, n_D^{20} 1·4996, was prepared from 2-thienyl-lithium and trimethylchlorosilane in ether.

A little ethyl bromide was added to magnesium turnings (22 g.) and ether (150 ml.). When reaction had started a mixture of 3-bromothiophen (24 g.), ethyl bromide (82 g.), and ether (450 ml.) was added slowly with stirring, and addition was followed by 40 hours' refluxing.[6] Trimethylchlorosilane (100 g.) was added at such a rate as to maintain boiling, and the mixture was then boiled for 3 hr. Water and then dilute acid were added until two clear layers separated. The ether layer was washed and dried (Na_2SO_4), and fractionation gave *3-thienyltrimethylsilane* (12 g.), b. p. 168°, n_D^{20} 1·4993 (Found: C, 53·7; H, 7·6. $C_7H_{12}SSi$ requires C, 53·8; H, 7·8%).

Rate studies. The method has been described.[3]

Wavelengths of 252 and 253 mμ were used for the 3-isomer and 255 mμ for the 2-isomer. Good first-order kinetics were observed.

The Table shows the first-order rate constants, k_1, at 50·18° and the activation energies (accurate to ±1 kcal./mole), E_a, and $\log_{10} A$ factors determined from measurements at two temperatures only.

Compound	H_2SO_4 * (M)	k_1 (min.$^{-1}$)	E_a (kcal./mole)	$\log_{10} A$
p-Me·C_6H_4·$SiMe_3$	5·65	0·0656	21·4	13·3
3-C_4H_3·$SiMe_3$	5·65	0·419	19·0	12·5
3-C_4H_3·$SiMe_3$	1·15	0·00786	22·2	12·9
2-C_4H_3·$SiMe_3$	1·15	0·342	19·5	12·7

* Concn. of acid, 3 vol. of which were added to 4 vol. of a solution of the organosilane in acetic acid containing 0·73 wt.-% of water (see ref. 3).

THE UNIVERSITY, LEICESTER. [*Received, February 13th*, 1959.]

[6] Gronowitz, *Arkiv Kemi*, 1954, **7**, 267.

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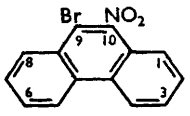
457. *The Nitration of 9-Bromophenanthrene.*

By R. S. W. BRAITHWAITE and P. F. HOLT.

THE only bromomononitrophenanthrene described in the literature, 9-bromo-10-nitrophenanthrene (I), was prepared by nitrating 9-bromophenanthrene in benzene with dinitrogen tetroxide [1,2] or in hot acetic acid with nitric acid.[3-6] The yields are low and 3-nitro-9 : 10-phenanthraquinone is also formed.[4,5] Whilst attempting to improve the method, we investigated the mechanism by which the phenanthraquinone is formed.



(I)

Although insoluble, 9-bromophenanthrene slowly turns yellow in cold nitric acid (*d* 1·42). After some hours, treatment of the solid with acetone yields a residue from which a second bromomononitrophenanthrene, m. p. 192°, and a small quantity of the 9-bromo-10-nitro-compound can be separated. On evaporation, the mother-liquor gives a mixture from which both these two and a third bromomononitrophenanthrene, m. p. 153°, have been isolated, the last in small yield.

Oxidation of the second bromonitrophenanthrene with chromium trioxide yields 3-nitro-9 : 10-phenanthraquinone, proving that the nitro-group is in either the 3- or the 6-position. Reduction with zinc and hydrochloric acid gives 3-amino-9-bromophenanthrene, the orientation of which has been established.[7] Therefore, the compound is 9-bromo-3-nitrophenanthrene.

Hot fuming nitric acid in acetic acid oxidized it to 3-nitro-9 : 10-phenanthraquinone.

[1] Schmidt and Kämpf, *Ber.*, 1902, **35**, 3121.
[2] Schmidt and Ladner, *Ber.*, 1904, **37**, 3573.
[3] Anschütz, *Ber.*, 1878, **11**, 1217.
[4] Werner, *Annalen*, 1902, **321**, 334.
[5] Austin, *J.*, 1908, **93**, 1760.
[6] Callow and Gulland, *J.*, 1929, 2424.
[7] Schultz, Goldberg, Ordas, and Carsch, *J. Org. Chem.*, 1946, **11**, 307.

The formation of this phenanthraquinone during the nitration of 9-bromophenanthrene in hot solution probably therefore involves the production and subsequent oxidation of 9-bromo-3-nitrophenanthrene, the 10-nitro-group preventing the oxidation of the 9 : 10-bridge in the isomer (I).

Chromium trioxide oxidises the third bromomononitrophenanthrene to a mononitrophenanthraquinone not identical with the known 2-, 3-, or 4-nitrophenanthraquinone, and which is therefore 1-nitrophenanthraquinone; the bromonitrophenanthrene must be either the 9-bromo-1-nitro- or the 9-bromo-8-nitro-compound.

Experimental.—Nitration of 9-bromophenanthrene. Finely powdered 9-bromophenanthrene (20 g.) was added during 30 min. to nitric acid (*d* 1·42; 200 ml.) at 18°. After 10 hr. the solid was filtered off, washed with water, boiled with acetone (100 ml.), cooled, filtered off, and again boiled with acetone (100 ml.) and cooled. The residue (10 g.) was crystallised from acetic acid. The first crop formed yellow needles of *9-bromo-3-nitrophenanthrene* (7·4 g.), m. p. 189—191°, raised on recrystallisation to 192° (Found: C, 55·7; H, 2·7; N, 4·7; Br, 26·0. $C_{14}H_8O_2NBr$ requires C, 55·7; H, 2·7; N, 4·6; Br, 26·5%). The second crop, on recrystallisation, gave pale yellow needles of 9-bromo-10-nitrophenanthrene (I) (1·3 g.), m. p. 202—205°, which did not depress the m. p. of an authentic specimen.

The acetone mother-liquors, on concentration at room temperature, deposited a solid (2·6 g.). Fractional crystallization from acetic acid gave the 9-bromo-10-nitro-compound (I) (0·35 g.), and *9-bromo-(1 or 8)-nitrophenanthrene* (III) (44 mg.), yellow needles, m. p. 153°; mixed with (I), m. p. 135—140°; mixed with (II), m. p. 132—150° (Found: C, 55·6; H, 3·0; N, 5·0. $C_{14}H_8O_2NBr$ requires C, 55·7; H, 2·7; N, 4·6%).

Oxidation of 9-bromo-3-nitrophenanthrene. Chromium trioxide (0·2 g.) was added in portions to 9-bromo-3-nitrophenanthrene (0·1 g.) in acetic acid (30 ml.) at 90°. After 2 hr. the mixture was poured into water, and the precipitate was separated and recrystallized from acetic acid, giving 3-nitro-9 : 10-phenanthraquinone (39 mg.), m. p. 279—280° (lit.,[1] m. p. 279—280°); oxime, m. p. 237—238° (lit.,[1] m. p. 240°).

Reduction of 9-bromo-3-nitrophenanthrene. To 9-bromo-3-nitrophenanthrene (0·3 g.) in boiling ethanol (80 ml.) were added hydrochloric acid (*d* 1·18; 10 ml.) and then zinc dust (0·2 g.). After refluxing, the filtered solution when concentrated gave *3-amino-9-bromophenanthrene hydrochloride* (0·35 g.), white needles, m. p. 258° (decomp.) (Found: C, 54·2; H, 4·2. $C_{14}H_{11}NBrCl$ requires C, 54·4; H, 3·6%), converted by ethanolic sodium hydroxide into 3-amino-9-bromophenanthrene, white needles (from aqueous ethanol), m. p. 113° (lit.,[7] m. p. 112·5—113°) (Found: C, 60·9; H, 3·6; N, 5·0; Br, 30·0. Calc. for $C_{14}H_{10}NBr$: C, 61·8; H, 3·7; N, 5·2; Br, 29·4%) (Schultz *et al.*[7] gave N, 5·37%); acetyl derivative, m. p. 221° (lit.,[7] m. p. 220·5—221·5°).

Oxidation of 9-bromo-3-nitrophenanthrene with nitric acid. Nitric acid (*d* 1·5; 3 ml.) was added dropwise to 9-bromo-3-nitrophenanthrene (2 g.) in acetic acid (9 ml.) and acetic anhydride (4·5 ml.) at 90°. After 20 min., the liquid on cooling yielded a precipitate which, when recrystallized from toluene, was identified as 3-nitro-9 : 10-phenanthraquinone (0·16 g.), m. p. 271—278°, mixed m. p. 278—279°.

Oxidation of 9-bromo-(1 or 8)-nitrophenanthrene. Chromium trioxide (25 mg.) in acetic acid (10 ml.) was added in portions to the bromonitrophenanthrene (19 mg.) in acetic acid (10 ml.) at 90°. After 2·5 hr. the mixture was diluted with water (30 ml.) and filtered. The orange precipitate, recrystallized from aqueous acetic acid, gave *1-nitrophenanthraquinone* (5 mg.) as orange prisms, decomposing slowly above about 240° to give a purple sublimate, and finally melting at 270° (Found: C, 64·5; H, 2·72. $C_{14}H_7O_4N$ requires C, 66·2; H, 2·77%). This material depressed the m. p.s of authentic 2-nitrophenanthraquinone and authentic 3-nitrophenanthraquinone. 4-Nitrophenanthraquinone has m. p. 180°.[8] The new phenanthraquinone dissolves in sulphuric acid to give a greenish-brown solution.

The authors are indebted to the Department of Scientific and Industrial Research for a Maintenance Allowance to one of them (R. S. W. B.), to Miss M. L. Booker for technical assistance, and to one of the Referees for helpful advice.

College of Science and Technology, Manchester.
University of Reading. [*Received, September 5th*, 1958.]

[8] Schmidt and Kampf, *Ber.*, 1903, **36**, 3734.

458. *An Aporphine Alkaloid, Nuciferine, from Asiatic Lotus Cultivated in Hong Kong.*

By H. R. Arthur and H. T. Cheung.

Asiatic lotus (*Nelumbo nucifera* Gaertn.) is an endemic species which occurs widely in the Colony of Hong Kong. It is found also in regions from India to Australia, is eaten, and is used in folk-medicine. Leaves, of Hong Kong origin, afforded us a 0·02% yield of an alkaloid, whose hydrochloride was more soluble in chloroform than in cold dilute hydrochloric acid or water, thus providing a simple method of isolation. Analysis and determination of the molecular weight indicated that the alkaloid, which we have named nuciferine, has the formula $C_{16}H_{12}(OMe)_2(\geq NMe)$; it has a blue fluorescence in the solid state or in solution and, after irradiation with ultraviolet light, a yellow phosphorescence. The physical constants of nuciferine and of its derivatives corresponded with those of (—)-5 : 6-dimethoxyaporphine (dimethylnor-roemerine),[1] and identity was confirmed by a mixed melting point and comparison of the infrared spectrum with that of a sample prepared from roemerine by Cooke and Haynes.[2]

An alkaloid, nelumbine (no m. p. or formula given), from the seed and cotyledons of lotus,[3] may or may not be the same as nuciferine.

Amino-acids and other alkaloids have been reported to occur in other (Japanese) species of the Nymphaeaceae.[4] Several Nymphaeaceae alkaloids of unknown constitution are recorded by Henry.[5]

Experimental.—Analyses are by Dr. Zimmermann, Melbourne. Fresh leaves (6 kg.) of *Nelumbo nucifera*, collected in September, were extracted with cold ethanol (14 l.) for 4 days. The solvent was removed from the green extract under reduced pressure. The black residue was distributed between chloroform (3 l.) and 5% aqueous ammonia (1 l.). The chloroform layer was washed with water and shaken several times with 2N-hydrochloric acid. [From the acid extract (4 l.) a brown basic oil was obtained; this did not yield nuciferine.] The residue obtained on removal of the chloroform under reduced pressure was triturated with warm water (2 l.). The aqueous solution was basified with ammonia and then extracted with chloroform (2 l.), from which, on distillation, the crude base (1·2 g.) was obtained. Recrystallisation from ethanol gave *nuciferine*, m. p. 165·5° (Kofler), $[\alpha]_D^{22}$ −157·5° (*c* 1·06 in ethanol) (Found: C, 77·7; H, 7·1; N, 4·7; OMe, 20·8; NMe, 4·6%; *M*, 279. $C_{19}H_{21}O_2N$ requires C, 77·3; H, 7·2; N, 4·7; 2OMe, 21·0; NMe, 5·1%; *M*, 295).

Dry hydrogen chloride was passed into a solution of nuciferine (0·5 g.) in dry ether. The white gel formed was collected. Crystallisation from ether–methanol gave needles of *nuciferine hydrochloride*, m. p. 241° (vac.) (Found: C, 68·8; H, 6·6. $C_{19}H_{21}O_2N$,HCl requires C, 68·8; H, 6·7%). Nuciferine (0·25 g.) was warmed with methyl iodide (20 ml.) for a few minutes; removal of the methyl iodide left *nuciferine methiodide* which crystallised from ethanol as needles, m. p. 177—178° (Kofler) (Found: C, 54·3; H, 5·7; N, 2·6. $C_{19}H_{21}O_2N$,MeI requires C, 54·9; H, 5·5; N, 3·2%) (Yunusov *et al.*[1] give m. p. 164—167°).

The colour reactions of nuciferine were as those published for synthetic (±)-5 : 6-dimethoxyaporphine,[6] except that with Fröhde's reagent the blue colour became brown.

The authors thank Mr. R. G. Cooke (University of Melbourne) for the sample of (—)-5 : 6-dimethoxyaporphine, and for determination of infrared spectra; Mr. H. C. Tang (Government Herbarium, Hong Kong) for identification of plant material; Smith, Kline & French Laboratories, Philadelphia, and the Research Grants Committee of the University of Hong Kong, for grants-in-aid.

University of Hong Kong, Hong Kong. [*Received, November 24th*, 1958.]

[1] Yunusov, Konovalova, and Orekhov, *Bull. Soc. chim. France*, 1940, **7**, 70; *J. Gen. Chem., U.S.S.R.*, 1939, **9**, 1868.
[2] Cooke and Haynes, *Austral. J. Chem.*, 1954, **7**, 99.
[3] Greshoff and Boorsma, *Mededeel. s'Lands Plantent.*, 1899, **31**, 125.
[4] Ukai, Arata, Ohashi, and Seto, *Ann. Report Fac. Pharm., Kanazawa Univ.*, 1953, **3**, 8.
[5] Henry, "The Plant Alkaloids," J. & A. Churchill Ltd., London, 4th edn., 1949, p. 758.
[6] Gulland and Haworth, *J.*, 1928, 590; Callow, Gulland, and Haworth, *J.*, 1929, 670.

459. *The Alcoholysis of Aromatic Acid Chlorides.*

By E. R. A. Peeling.

Recent investigations of the kinetics of the hydrolysis and alcoholysis of benzoyl and substituted benzoyl chlorides have not led to completely concordant conclusions. Hudson and his co-workers [1,2] have suggested that aromatic acid chlorides may be hydrolysed by either the S_N1 or the S_N2 mechanism, and Bunton and Lewis [3] have suggested a two-stage process. We now present some results which we believe support the mechanisms proposed by Bunton and Lewis.

The rates of ethyl alcoholysis in initially neutral solution of the acyl halides studied are shown in Table 1, and the rates in the presence of added alkali in Table 2. The relative

Table 1. *First-order rate coefficients (k_1 in sec.$^{-1}$) of the alcoholysis of* X·C_6H_4·COCl *in "* 80% *" alcoholic acetone at* −10·75°.

X	H	*p*-NO_2	*p*-Me	2 : 4 : 6-Me_3
10^6k_1	4·97	212	2·25	521

Table 2. *Second-order rate coefficients (k_2 in sec.$^{-1}$ mole^{-1} l.) of reaction between* X·C_6H_4·COCl (0·03M) *and* OEt^- (0·02M) *in "* 80% *" alcoholic acetone at* −10·75°.

X	H	*p*-NO_2	2 : 4 : 6-Me_3
k_2	>3	>3	0·34

rates of alcoholysis of the four acyl halides are qualitatively similar to the relative rates in aqueous solvents. In the presence of alkali the rates are much increased (Table 2). The rate of the solvolytic reaction is so much less than that of the reaction with alkali that the solvolytic reaction may be neglected.

These results are similar to those of Bunton and Lewis,[3] who calculated an increase of nearly 1000-fold in the rate of hydrolysis of 2 : 4 : 6-trimethylbenzoyl chloride in 95% aqueous dioxan in the presence of 1M-alkali. Brown and Hudson,[2] on the other hand, found no increase in the rate of hydrolysis on the addition of 0·001M-alkali. It seems possible that in this case the potassium nitrate used to eliminate junction potentials in the titration cell prevents the alkali dissolving in the solvent to give a homogeneous solution.

An alternative explanation * is that the increase of rate of the neutral solvolysis and the reduction of the rate of nucleophilic attack by hydroxide ions caused by the addition of potassium nitrate result in no apparent alkaline catalysis.

The increase in rate of alcoholysis caused by the addition of alkali and the effect of added salts, shown in Table 3, rule out the possibility that even 2 : 4 : 6-trimethylbenzoyl chloride reacts by an S_N1-like mechanism and support the findings and conclusions of Bunton and Lewis.[3]

Table 3. *First-order rate coefficients (10^4 k_1; k_1 in sec.$^{-1}$) of the alcoholysis of* p-*nitro- and* 2 : 4 : 6-*trimethyl-benzoyl chloride in "* 80% *" alcoholic acetone at* −10·75° *in the presence of* 0·1M-LiCl *and* 0·1M-LiBr.

Halide	No salt added	0·1M-LiCl	0·1M-LiBr
p-NO_2·C_6H_4·COCl	2·12	3·42	5·96
2 : 4 : 6-$Me_3C_6H_2$·COCl	5·21	5·20	9·46

Experimental.—Materials. Acetone was purified by the method of Conant and Kirner.[4] Ethyl alcohol was dried by the method of Lund and Bjerrum.[5] Ethyl-alcoholic acetone ("80%")

* The author is grateful to a Referee for this suggestion.

[1] Hudson and Wardill, *J.*, 1950, 1729; *J.*, 1950, 1731; Archer and Hudson, *J.*, 1950, 3259; Brown and Hudson, *J.*, 1953, 883; Archer, Hudson, and Wardill, *J.*, 1953, 888.
[2] Brown and Hudson, *J.*, 1953, 3352.
[3] Bunton and Lewis, *Chem. and Ind.*, 1956, 180.
[4] Conant and Kirner, *J. Amer. Chem. Soc.*, 1924, **46**, 246.
[5] Lund and Bjerrum, *Ber.*, 1931, **64**, 210.

was prepared by mixing 8 vol. of acetone with 2 vol. of dry ethyl alcohol. Sufficient solvent was prepared to carry out all the kinetic measurements on the same batch.

Benzoyl chloride, distilled at atmospheric pressure and protected from moisture, had b. p. 198°. *p*-Nitrobenzoyl chloride, recrystallised from dry light petroleum (b. p. 60—80°), had m. p. 75°. *p*-Toluoyl chloride, prepared from *p*-toluic acid by thionyl chloride and purified by distillation at reduced pressure, had b. p. 118°/20 mm. 2 : 4 : 6-Trimethylbenzoyl chloride was prepared from mesitylene by bromination, conversion of the product into the acid *via* the Grignard reagent by means of carbon dioxide, and treatment of the acid with thionyl chloride. The chloride was purified by distillation under reduced pressure, and then had b. p. 120°/20 mm. Lithium chloride and bromide were heated at 180° for 3 hr. and cooled over P_2O_5.

Rate measurements. These were carried out by the sampling method. For each run ~0·03 mol. of acyl halide was added to solvent (70 ml.) at −10·75°. Samples (5 ml.) were run into acetone (70 ml.) cooled to ~−50° to stop the reaction and were titrated with ~0·03N-potassium hydroxide, lacmoid being used as indicator. For runs in the presence of alkali, the required amount of sodium was dissolved in cold solvent before addition of the acyl halide, and the reaction followed by titration with 0·01N-hydrochloric acid. The following is a typical run with 0·0218M-2 : 4 : 6-trimethylbenzoyl chloride: samples (5 ml.) were titrated with 0·0276N-potassium hydroxide:

Time (sec.)	0	217	372	623	918	1235	1552	2500	∞
Titre (ml.)	0·00	0·44	0·72	1·08	1·46	1·86	2·18	2·86	3·94
10^4k_1 (sec.$^{-1}$)	—	5·4	5·4	5·2	5·1	5·2	5·2	5·2	—

The formula $k_2 = 2{\cdot}303[\log_{10} b(a - x)/a(b - x)]/t(a - b)$ was used to calculate the second-order rate coefficient of the run on 2 : 4 : 6-trimethylbenzoyl chloride in the presence of alkali; a and b are the molarities of the alkali and acyl halide, respectively. The rates of the reactions of benzoyl and *p*-nitrobenzoyl chlorides in alkaline solution were too fast to be measured, and the rates given in Table 2 assume the half-life period of the reaction with alkali of average concentration 0·02M to be <10 sec.

The author thanks Professor E. D. Hughes, F.R.S., for much helpful advice.

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460. *A Molecular-orbital Calculation of the Ultraviolet Absorption Spectra of* 1 : 5- *and* 1 : 8-*Naphthyridine.*

By T. E. PEACOCK.

VARIOUS methods of calculating the electronic absorption spectra of heterocyclic molecules have been compared.[1,2] One of these, employing SCF (self-consistent field) molecular orbitals of the parent hydrocarbon, was found particularly satisfactory under certain well-defined conditions: in other cases it was necessary to incorporate self-consistency in the substituted system. The two types of SCF calculation are here applied to interpret the spectral shifts which accompany di-nitrogen substitution in naphthalene to give naphthyridines.

Spectra of 1 : 5- *and* 1 : 8-*Naphthyridine.*—Naphthalene (numbered as in I), which has the symmetry D_{2h}, is converted into naphthyridine by the substitution of two C–H groups by nitrogen atoms. The ultraviolet spectrum of naphthalene, calculated by use of SCF molecular orbitals, has already been discussed.[2] The energies of its two highest occupied and two lowest unoccupied SCF molecular orbitals are indicated in the Figure, along with symmetry symbols.

The 1 : 8-naphthyridine molecule has the reduced symmetry C_{2v}. The ground state function Φ_0 and the functions of the excited configurations $\Phi(A \longrightarrow A')$, $\Phi(B \longrightarrow B')$, $\Phi(A \longrightarrow B')$, $\Phi(B \longrightarrow A')$ are grouped according to symmetry under C_{2v} as follows,

[1] McWeeny, *Proc. Phys. Soc.*, 1957, *A*, **70**, 593.
[2] Peacock, *Proc. Phys. Soc.*, 1957, *A*, **70**, 654.

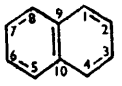
where $\Phi(A \longrightarrow A')$, for instance, is the singlet function in which the configuration is $(A)^1(A')^1$ instead of $(A)^2$:

A.....	Φ_0	$\Phi(A \longrightarrow B')$	$\Phi(B \longrightarrow A')$
B.....	—	$\Phi(A \longrightarrow A')$	$\Phi(B \longrightarrow B')$

Since there are excited functions of the same symmetry as the ground state function, mixing will be allowed and should be adequate to describe the perturbing effecting of the substituents without the necessity for revising the basic orbitals.[1]

Energies and symmetries of the naphthalene SCF molecular orbitals. β is the resonance integral for the C–C *bond in benzene.*

B' ———— $-1{\cdot}12\beta$ (B_2)
A' ———— $-0{\cdot}92\beta$ (B_3)
- - - - - - - -
A ———— $0{\cdot}92\beta$ (B_1)
B ———— $1{\cdot}12\beta$ (A)



(I)

The symmetry of the 1 : 5-naphthyridine molecule is C_{2h}. The ground state function Φ_0 and the excited state functions are grouped according to symmetry as follows:

A_u	Φ_0				
B_g	$\Phi(A \longrightarrow A')$	$\Phi(B \longrightarrow B')$	$\Phi(A \longrightarrow B')$	$\Phi(B \longrightarrow A')$	

Here the effects of the nitrogen atoms on the ground state cannot be described by the limited configuration interaction because this is symmetry-forbidden: to describe the perturbed molecule we must introduce orbitals appropriate to the substituted molecule, *i.e.*, SCF molecular orbitals for 1 : 5-naphthyridine. These can be obtained by an iterative method, starting from the solution for the hydrocarbon.[3]

The general interpretation of the so-called α, *p*, β, and β' bands of an alternant hydrocarbon [4,5] and its heterocyclic derivatives [2,6,7] in terms of the mixing of the configurational functions discussed above, is now well known. The electron-interaction integrals and parameters were given the same numerical values as in previous work.[2,6] Our calculated transition energies for the naphthyridines are given in the Table, with those for naphthalene.[2]

State and symmetry	Transition energy (predicted) ($\bar{\nu}$)	Observed band ($\bar{\nu}$)	State and symmetry	Transition energy (predicted) ($\bar{\nu}$)	Observed band ($\bar{\nu}$)	State and symmetry	Transition energy (predicted) ($\bar{\nu}$)	Observed band ($\bar{\nu}$)
Naphthalene			1 : 5-Naphthyridine *			1 : 8-Naphthyridine *		
$\alpha(B_3)$	35,900	32,300	$\alpha(B_g)$	36,300	32,450	$\alpha(B)$	36,150	32,450
$p(B_2)$	36,600	36,500	$p(B_g)$	37,100	37,450	$p(A)$	37,100	37,450
$\beta(B_3)$	51,000	45,200	$\beta(B_g)$	53,050	>47,600	$\beta(B)$	53,950	>45,200
$\beta'(B_2)$	53,700	59,700	$\beta'(B_g)$	53,050		$\beta'(A)$	54,150	

* The experimental values for these two molecules were personally communicated by Dr. S. F. Mason, University of Exeter.

All the theoretical values above are absolute and no attempt has been made to fit the observed data by revising parameter values or otherwise.

Discussion.—α *Band.* Theory predicts the band to move 400 $\bar{\nu}$ for 1 : 5-naphthyridine and 250 $\bar{\nu}$ for 1 : 8-naphthyridine: experimentally the band moves 150 $\bar{\nu}$. Although the agreement between the calculated and observed energies is only fair, on an absolute scale, it is most significant that the theoretical shifts are of the correct order of magnitude and in the right direction. It is predicted that substitution will increase the intensity of the band,[2,4] as observed.

[3] McWeeny, *Proc. Roy. Soc.*, 1956, *A*, **237**, 355.
[4] Dewar and Longuet-Higgins, *Proc. Phys. Soc.*, 1954, *A*, **67**, 795.
[5] Pople, *Proc. Phys. Soc.*, 1955, *A*, **68**, 81.
[6] McWeeny and Peacock, *Proc. Phys. Soc.*, 1957, *A*, **70**, 41.
[7] Peacock, *Nature*, 1957, **179**, 684.

p Band. On substitution this band moves to higher energies by 950 $\bar{\nu}$ in both cases. It is predicted to move 500 $\bar{\nu}$ this way in both systems. Because of the uncertainty in determining the centre of this band we may say that agreement between theory and experiment is again fair. An increase in the intensity of the band in both substituted systems is observed, again agreeing with theory.

β *and* β′ *Bands.* Experimentally the positions of these bands are uncertain. According to Mason they are certainly higher than 47,600 $\bar{\nu}$ in 1 : 5-naphthyridine and higher than 45,200 $\bar{\nu}$ in 1 : 8-naphthyridine. Our predictions of about 53,000 $\bar{\nu}$ in each case seems to support this. Both bands will be decreased in intensity [2,4] but as the bands are so close a single broad intense band should result in both substituted molecules. Mason has confirmed the presence of a single intense band in 1 : 8-naphthyridine.

I thank Dr. R. McWeeny for his interest, Dr. S. F. Mason for allowing me to quote unpublished results, and the Ramsay Memorial Fellowships Trust for a Fellowship.

UNIVERSITY COLLEGE OF NORTH STAFFORDSHIRE, KEELE. [*Received, December 8th,* 1958.]

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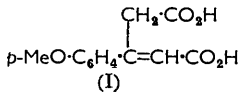
461. N-*Hydroxy-imides. Part III.*[1] β-p-*Methoxyphenylglutaconimides.*

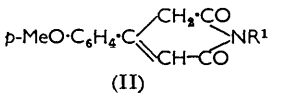
By D. E. AMES and T. F. GREY.

(With spectroscopic data by MISS E. M. TANNER.)

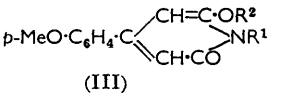
THE preparation of the *N*-benzyloxy- and *N*-hydroxy-imides of some dibasic acids has been described.[1,2] We have now prepared some derivatives of β-*p*-methoxyphenylglutaconic acid (I), which is readily obtained by condensation of anisole with acetonedicarboxylic acid.[3] Condensation of the acid (I) with benzyloxyamine in boiling xylene yielded the *N*-benzyloxy-imide (II; $R^1 = O{\cdot}CH_2Ph$), tautomeric with the pyridone (III; $R^1 = O{\cdot}CH_2Ph$, $R^2 = H$). The latter was debenzylated to the *N*-hydroxy-imide or pyridone (II; $R^1 = OH$ or III; $R^1 = OH$, $R^2 = H$) which was methylated to 1 : 6-dimethoxy-4-*p*-methoxyphenylpyrid-2-one (III; $R^1 = OMe$, $R^2 = Me$).



(I)



(II)



(III)

Methylation of the *N*-benzyloxy-imide (II; $R^1 = O{\cdot}CH_2Ph$) afforded 1-benzyloxy-6-methoxy-4-*p*-methoxyphenylpyrid-2-one (III; $R^1 = O{\cdot}CH_2Ph$, $R^2 = Me$) which, on catalytic debenzylation, gave 1-hydroxy-6-methoxy-4-*p*-methoxyphenylpyrid-2-one (III; $R^1 = OH$, $R^2 = Me$).

The isomeric 6-hydroxy-1-methoxy-4-*p*-methoxyphenylpyrid-2-one (III; $R^1 = OMe$, $R^2 = H$) was obtained from *O*-methylhydroxylamine and β-*p*-methoxyphenylglutaconic anhydride (attempts to use the glutaconic acid failed).

Spectroscopic Data (By MISS E. M. TANNER).—Structures (II) and (III) are readily differentiated spectroscopically (see Table). In infrared spectra of compounds (II) there are two carbonyl bands typical of the group ·CO·NR·CO·, while compounds (III) show amide carbonyl absorption near 1660 $cm.^{-1}$. Most of the pyridones (II) show weak hydroxyl bands in spectra of chloroform solutions which are not present in spectra in

[1] Part II, *J.*, 1955, 3518.
[2] Ames and Grey, *J.*, 1955, 631.
[3] Limaye and Bhave, *J. Indian Chem. Soc.*, 1931, **8**, 137.

Compound	pK_a' [a]	Infrared spectrum [c] OH	C=O	Ultraviolet spectrum 0·1N-HCl $\lambda_{max.}$	ε	0·1N-NaOH $\lambda_{max.}$	ε
(II; R¹ = OH)	4·63 [b]	3232 [d]	1726, 1675	223	13,200	258	9,600
				318	15,650	328	5,610
(II; R¹ = OMe)	3·89	3504 [e] w	1726, 1684	223	13,050	260	21,000
				319	17,750	336	9,300
(II; R¹ = O·CH₂Ph)	5·77 [b]	3536 [e] w	1729, 1691	235	7,240	248	21,100
				293	6,300	337	8,650
(II; R¹ = Me)	5·57	—	1712, 1661	220	15,600	260	23,300
				312	18,800	340	8,600
(II; R¹ = CH₂Ph)	decomp.	—	1703, 1660	—	—	263	24,730
						344	8,360
(II; R¹ = Ph)	5·43 [b]	3536 [e] w	1715, 1665	225 sh	14,300	263	24,400
				312	19,790	325	5,740
(III; R¹ = OH = R² = Me)	7·13	3378	1650	285	19,200	285	19,550
(III; R¹ = OMe, R² = Me)	>11		1661	222	15,930		
				228	19,500	288	19,500
(III; R¹ = O·CH₂Ph, R² = Me)	>11		1658	289	21,400	288	21,900

[a] In 50% ethanol. [b] In 66% ethanol. [c] cm.$^{-1}$; measured in chloroform. [d] Measured in Nujol. [e] No band in corresponding Nujol spectrum. w, weak band. sh, shoulder. Infrared spectra were recorded with a Grubb-Parsons DP1/S3A spectrometer and ultraviolet spectra with a Unicam S.P. 500 spectrophotometer.

Nujol; this indicates that the compounds are tautomeric in solution and is confirmed by their behaviour as acids of medium strength, pK_a' 4—6, and their ultraviolet spectra which differ in acid and alkaline solution. The pyridones (III) are not titratable as acids (except III; R¹ = OH, R² = H) and their ultraviolet spectra are unchanged by change of pH.

Experimental.—Preparation of imides from β-p-*methoxyphenylglutaconic acid.* (i). Ethanolic methylamine (50 c.c.; 33%) was added gradually to the glutaconic acid [3] (15 g.). The solution was then distilled slowly so that the bath temperature reached 200° after 1 hr. After the residue had been heated at 190—200° for a further 1 hr., the residual gum was triturated with ether. Recrystallisation from ethanol yielded needles of β-p-*methoxyphenyl*-N-*methylglutaconimide* (2·5 g.), m. p. 197—199° (Found: C, 67·9; H, 5·7; N, 5·9. $C_{13}H_{13}O_3N$ requires C, 67·5; H, 5·7; N, 6·0%).

(ii). A mixture of the glutaconic acid (10 g.), benzylamine (5 g.), and xylene (100 c.c.) was refluxed through a Dean and Stark phase separator until no more water could be collected (2 hr.). After removal of xylene (30 c.c.) by distillation, the hot solution was filtered. N-*Benzyl*-β-p-*methoxyphenylglutaconimide*, which separated on cooling, formed pale yellow prisms (3·3 g.) (from ethanol), m. p. 150—152° (Found: C, 74·0; H, 5·8; N, 4·7. $C_{19}H_{17}O_3N$ requires C, 74·3; H, 5·6; N, 4·6%).

(iii). *O*-Benzylhydroxylamine (31 g.) and the glutaconic acid (56 g.) were condensed in xylene (900 c.c.) as in the previous example. The *imide* (4·3 g.) separated from 2-methoxyethanol as hexagonal plates, m. p. 214—125° (Found: C, 70·4; H, 5·4; N, 4·3. $C_{19}H_{17}O_4N$ requires C, 70·6; H, 5·3; N, 4·3%).

N-*Hydroxy*-β-p-*methoxyphenylglutaconimide*. The benzyloxy-compound (28 g.) was hydrogenated in ethanol (400 c.c.) over palladised charcoal (3 g.; 10%). Absorption ceased when 1 mole of hydrogen had been taken up and the mixture was then filtered at the b. p. On cooling the *imide* (11 g.) separated; recrystallisation from 2-methoxyethanol gave prisms, m. p. 216—217° (Found: C, 62·0; H, 5·2; N, 5·6. $C_{12}H_{11}O_4N$ requires C, 61·8; H, 4·8; N, 6·0%).

1 : 6-*Dimethoxy*-4-p-*methoxyphenylpyrid*-2-*one*. Ethereal diazomethane (from 25 g. of methylnitrosourea) was added to a suspension of the dihydroxy-pyridone (1·4 g.) in methanol (200 c.c.), and the mixture was set aside overnight. After addition of acetic acid (1 c.c.), the solution was evaporated to dryness under reduced pressure. Recrystallisation of the residue from ethyl acetate–light petroleum (b. p. 60—80°) furnished the *pyridone* as prismatic needles, m. p. 129—130° (Found: C, 64·2; H, 5·8; N, 5·1; MeO, 35·7. $C_{14}H_{15}O_4N$ requires C, 64·4; H, 5·8; N, 5·4; MeO, 35·6%).

1-*Benzyloxy*-6-*methoxy*-4-p-*methoxyphenylpyrid*-2-*one*. The *N*-benzyloxy-imide (5 g.) was suspended in methanol (100 c.c.) and treated with ethereal diazomethane (from 20 g. of methylnitrosourea). After 20 min. all the solid had dissolved, and acetic acid was added to destroy

excess of diazomethane. Evaporation of the solvent, trituration of the residue, and crystallisation from ethyl acetate gave the *pyridone* (3·8 g.), m. p. 142—143° (Found: C, 70·7; H, 5·4; N, 4·2. $C_{20}H_{19}O_4N$ requires C, 71·2; H, 5·7; N, 4·2%).

1-*Hydroxy*-6-*methoxy*-4-p-*methoxyphenylpyrid*-2-*one*. A suspension of the benzyloxy-compound (10 g.) in ethanol (250 c.c.) was hydrogenated in the presence of 10% palladised charcoal (2 g.). Absorption ceased after about one mole of hydrogen had been taken up. The solution was filtered at the b. p., and on cooling the filtrate deposited the *pyridone* (6·3 g.), m. p. 194—196° (after crystallisation from ethanol) (Found: C, 62·8; H, 5·3; N, 5·8; OMe, 24·5. $C_{13}H_{13}O_4N$ requires C, 63·2; H, 5·3; N, 5·7; OMe, 25·1%). An alcoholic solution with ferric chloride had an intense red coloration.

O-*Methylacetoxime*. Acetoxime (108 g.) was added to a hot solution of sodium butoxide [from sodium (36 g.) in butanol (750 c.c.)], and methyl iodide (210 g.) was then added with occasional shaking at such a rate that the mixture refluxed gently. After being kept overnight the mixture was distilled. The fraction, b. p. 65—80°, was left over calcium chloride for 2 days and then refractionated to give the ether (b. p. 70—73°) (40 g.).

N-*Methoxy*-β-p-*methoxyphenylglutaconimide*. *O*-Methylhydroxylamine hydrochloride (7·5 g., obtained by hydrolysis of *O*-methylacetoxime [4]) was added to an ice-cold mixture of ether (100 c.c.) and potassium hydroxide solution (20 g. in 20 c.c. of water). The mixture was shaken vigorously for 5 min., and the organic layer decanted, the aqueous layer being washed with more ether (2 × 50 c.c.). The combined ethereal layers were dried (KOH) and added to a suspension of β-*p*-methoxyphenylglutaconic anhydride [3] (11 g.) in xylene (100 c.c.) and methanol (50 c.c.). After 30 min. the solution was distilled slowly (bath at 100° after 1 hr.). Xylene (200 c.c.) was added and distillation was resumed (a total of 250 c.c. of distillate was collected). On cooling crystals separated, and repeated recrystallisation from methanol gave the *imide* as needles, m. p. 163—166° (Found: C, 63·2; H, 5·4; N, 5·6; OMe, 24·9. $C_{13}H_{13}O_4N$ requires C, 63·2; H, 5·3; N, 5·7; OMe, 25·1%).

The authors are grateful to Dr. R. E. Bowman for discussion and to Mr. F. Oliver for microanalyses.

PARKE, DAVIS & COMPANY, HOUNSLOW, MIDDLESEX. [*Received, January 2nd*, 1959.]

[4] Dunstan and Goulding, *J.*, 1901, **79**, 630.

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462. *Ultraviolet Spectra and Periodate Oxidation of Monosaccharide Phenylhydrazones.*

By J. J. O'DONNELL and ELIZABETH PERCIVAL.

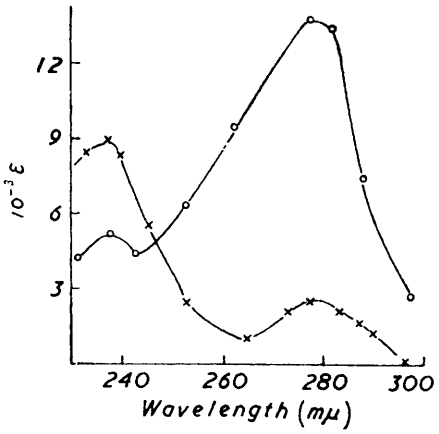
IN work on the repeated Barry degradation of laminarin and cladophoran [1] it became apparent that the periodate ion attacked the nitrogen-containing residues present in the degraded polysaccharides, the nitrogen content being reduced on subsequent oxidation. To obtain information on the nature of these nitrogen-containing residues and quantitative values for the amount of periodate reduced by these groups in the degraded polysaccharide the ultraviolet absorption spectra of, and the action of periodate on, sugar phenylhydrazones have been studied. It was expected that the uptake of periodate by such compounds might be related to that of the degraded polymers.

The ultraviolet spectra of sugar osazones [2] and of the Barry degradation fragments of monomethyl-sugars [3] have already been examined. The spectra of the sugar phenylhydrazones exhibited qualitative and quantitative similarities, but these could not be related to the spectra of the degraded polysaccharides. When the solutions were kept the phenylhydrazone spectra changed to a non-characteristic curve, in keeping with the tendency of these compounds to decompose in solution.

Oxidation of sugar osazones [4] by sodium periodate resulted in rapid consumption of

[1] O'Donnell and Percival, *J.*, 1959, 1739.
[2] Barry, McCormick, and Mitchell, *J.*, 1955, 222.
[3] Mitchell, *Proc. Roy. Irish Acad.*, 1958, **59**, 43.
[4] Chargaff and Magasanik, *J. Amer. Chem. Soc.*, 1947, **69**, 1459; Courtois, Wickstrom, and Le Dizet, *Bull. Soc. chim. France*, 1952, 1006.

the theoretical amount of periodate, and precipitation of mesoxaldehyde 1 : 2-bisphenylhydrazone; this was followed by a slow irregular reduction which was attributed to interaction of the periodate ion with the insoluble mesoxaldehyde derivative. A similar reaction takes place with the phenylhydrazones, and orange-red crystals believed to be glyoxal monophenylhydrazone are deposited. The initial rapid consumption of periodate was complete within an hour and corresponded to the number of glycol groups. This was followed by a further uptake of 1·6—2·8 mol. during 3 days. These results, together with the earlier results on periodate oxidation of osazones, demonstrate clearly that the periodate ion attacks, not only the glycol groups, but also the nitrogenous group in the



Ultraviolet absorption of (○) *monosaccharide phenylhydrazones and* (×) *the Skraup form of glucose phenylhydrazone.*

degraded polymers. Since oxidation of degraded nitrogen-containing polysaccharides is usually allowed to proceed for several days the extent of this attack is considerable and any quantitative conclusions based on it must be viewed with caution.

In this work it was found that, whereas the β-form of glucose phenylhydrazone had adsorption characteristics similar to those of the other sugar phenylhydrazones, the Skraup isomer [4] of glucose phenylhydrazone gave a different spectrum (see Figure) which was qualitatively similar to that of phenylhydrazine. This agrees with the results of Mester and Major [5] who postulated, on the basis of the formation of a crystalline formazan, that glucose β-phenylhydrazone (like mannose phenylhydrazone) had an acyclic structure. In contrast, Skraup's glucose phenylhydrazone did not yield a formazan and was therefore considered to have a cyclic structure.

Experimental.—The phenylhydrazones of mannose, ribose, arabinose, galactose, and glucose (β-form and Skraup form), prepared by the standard method,[6] were isolated as white crystalline solids and recrystallised to constant m. p. The absorption of each phenylhydrazone (10 mg./l.) in 1 : 1 aqueous ethanol was measured in a Unicam S.P. 500 spectrophotometer in the range 222—230 mμ. The value of ε at 277 mμ for each sugar was constant (±10%) at 13,700. A second less well-defined peak at 235—240 mμ was also present. The Skraup isomer had a negligible absorption at 277 mμ but at 237 mμ had ε 8900 (cf. phenylhydrazine which also has a maximum absorption at this wavelength). Degraded laminarin and degraded cladophoran (142 mg./l.) showed weak absorption peaks at 383—385 and 360—362 mμ respectively.

Periodate oxidation. Samples (100 mg.) were dissolved in water (5 ml.) (mannose phenylhydrazone gave a suspension), and 0·197M-sodium periodate solution) (15 ml.) was added. The reaction was followed by withdrawal of samples at intervals, and the amount of periodate reduced was measured.[7] The quantity of periodate (3 or 4 mols.) required to cleave the glycol groups present in each hydrazone was consumed within 1 hr. and this was accompanied by the precipitation of orange-red crystals. As oxidation proceeded these crystals gradually redissolved

[5] Mester and Major, *J. Amer. Chem. Soc.*, 1955, **77**, 4297.
[6] Butler and Cretcher, *J. Amer. Chem. Soc.*, 1929, **51**, 3161; Fischer, *Ber.*, 1887, **20**, 824.
[7] Fleury and Lange, *Compt. rend.*, 1932, **195**, 1395.

and a tar resulted; this had no distinguishing feature in its ultraviolet spectrum. The periodate consumptions (mole/mole) were:

Period of oxidn.	galactose	Phenylhydrazones of: glucose β-isomer	glucose Skraup isomer	arabinose	ribose
30 min.	4·05	3·90	3·95	3·06	3·16
72 hr.	6·30	6·20	6·80	4·60	4·90

The orange-red crystals consumed 1 mole of periodate per mole (calculated as glyoxal monophenylhydrazone) during 30 min. and 2·6 moles per mole during 48 hr.

If the oxidation was stopped after 30 min. by addition of ethylene glycol and sodium hydrogen carbonate the crystalline material could be separated (80% yield calculated as glyoxal monophenylhydrazone). After one recrystallisation from alcohol this had m. p. 85° (decomp.) (Found: N, 18·4. Calc. for $C_8H_8ON_2$: N, 18·9%).

One of us (J. J. O'D.) thanks the Institute of Seaweed Research for a maintenance grant.

CHEMISTRY DEPARTMENT, UNIVERSITY OF EDINBURGH. [*Received, January 9th,* 1959.]

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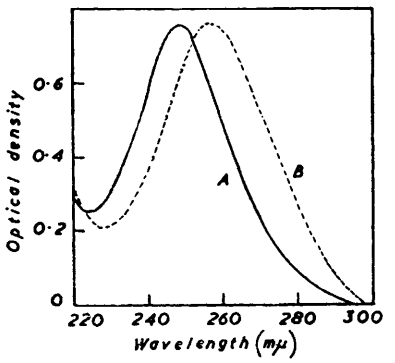
463. *The Ionization Constant of* p-*Iodobenzoic Acid at* 25°.

By R. A. ROBINSON and K. P. ANG.

THE ionization constants of many substituted benzoic acids have been determined, notably by Dippy and his colleagues,[1] but, although Kuhn and Wassermann [2] found pK 5·00 for *p*-iodobenzoic acid in 50% methanol at 20°, no measurements seem to have been made



Absorption spectra of 1·3 × 10^{-5}N-p-*iodobenzoic acid:* 4 *cm. cells.*
(*A*) *Alkaline solution.*
(*B*) *Acid solution.*

for aqueous solutions. This may be due to the low solubility of the acid in water and the method of ultraviolet spectrophotometry [3] therefore commends itself.

p-Iodobenzoic acid from Koch Laboratories was twice sublimed *in vacuo* at 100° (m. p. 271—272°) and optical density measurements were made with solutions 1·76 × 10^{-5}N with respect to the acid, 4 cm. cells being used in a Uvispek instrument. The temperature was maintained at 25° ± 0·5° in an air-conditioned room. The Figure shows the absorption spectra in solutions of pH 0 and pH 12. It will be seen that there is no wavelength at which the absorption is negligible in one solution and appreciable in the other; this diminishes the accuracy of the method but at a wavelength of 270 mμ there is sufficient difference between absorption in acid and in alkaline solution to make the method applicable. Two sets of buffers were used. The first consisted of formic acid partially neutralized with sodium hydroxide. If K_R is the ionization constant of formic acid, then:

$$pK_R = pH - \log \frac{Salt}{Acid} - \log \gamma_F \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

[1] Bray, Dippy, Hughes, and Laxton, *J.*, 1957, 2405.
[2] Kuhn and Wassermann, *Helv. Chim. Acta*, 1928, **11**, 31.
[3] Robinson and Biggs, *Trans. Faraday Soc.*, 1955, **51**, 901; Biggs, *J.*, 1956, 2485.

where pH = $-\log \gamma_H m_H$, γ_F is the activity coefficient of the formate ion, and the ratio salt : acid is corrected for the appreciable ionization of formic acid.

If K is the ionization constant of *p*-iodobenzoic acid, then:

$$pK = pH - \log \frac{D_1 - D}{D - D_2} - \log \gamma_B \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where D_1, D_2, and D are the optical densities in solutions of pH 0 and 12 and in the formate buffer respectively, and γ_B is the activity coefficient of the iodobenzoate ion. Then:

$$pK = pK_R + \log \frac{\text{Salt}}{\text{Acid}} - \log \frac{D_1 - D}{D - D_2} \quad . \quad . \quad . \quad . \quad . \quad (3)$$

if γ_F can be equated to γ_B. It is known [4] that $pK_R = 3{\cdot}754$ at 25°.

The second set consisted of partially neutralized succinic acid with the addition of sodium chloride, *i.e.*, either *x*M-succinic acid + 0·5*x*M-sodium hydrogen succinate + *x*M-sodium chloride or a buffer with half this amount of sodium chloride. In either case, sufficient data are available [5] to afford the log (salt/acid) term in equation (3).

The tabulated results were obtained.

p-*Iodobenzoic acid*, $1{\cdot}76 \times 10^{-5}$N. Wavelength, 270 mμ, 4 cm. cells. Temp., 25°.
D_1 (in M-HCl) 0·760. D_2 (in 0·01M-NaOH) 0·311.

Molality of $H{\cdot}CO_2H$	D	log (Salt/Acid)	log $(D_1 - D)/(D - D_2)$	pK
	Formic acid, *x*M.	Sodium formate, 1·923*x*M.		
0·001733	0·491	0·321	0·175	3·900
0·003466	0·497	0·304	0·150	3·908
0·006932	0·502	0·295	0·130	3·919
	Formic acid, *x*M.	Sodium formate, 1·504*x*M.		
0·001989	0·520	0·222	0·060	3·916
0·003978	0·525	0·201	0·041	3·914
0·007956	0·533	0·190	0·029	3·915
	Formic acid, *x*M.	Sodium formate, *x*M.		
0·002533	0·565	0·059	−0·115	3·928
0·005066	0·572	0·033	−0·142	3·929
0·01013	0·574	0·018	−0·150	3·922

Molality of succinic acid	D	log (Salt/Acid)	log $(D_1 - D)/(D - D_2)$	pK
Succinic acid, *x*M.	Sodium hydrogen succinate, 0·5*x*M.		Sodium chloride, *x*M.	
0·02	0·550	−0·315	−0·056	3·948
0·03	0·549	−0·321	−0·052	3·938
0·04	0·551	−0·326	−0·060	3·941
0·05	0·551	−0·328	−0·060	3·939
Succinic acid, *x*M.	Sodium hydrogen succinate, 0·5*x*M.		Sodium chloride, 0·5*x*M.	
0·02	0·545	−0·318	−0·037	3·926
0·03	0·549	−0·332	−0·052	3·937
0·04	0·550	−0·324	−0·056	3·939
0·05	0·551	−0·327	−0·059	3·939

The average value of pK is 3·927 with a standard deviation of 0·010. The succinate give higher pK's than the formate buffers, and a further study on an acid more suited to the method is needed to see if the difference is real. For the present, we report the best value of pK as 3·93. The Hammett σ parameter is therefore 0·27, compared with 0·276 derived by Hammett [6] from measurement on the alkaline hydrolysis of ethyl benzoates in 88% ethanol at 30°.

UNIVERSITY OF MALAYA, SINGAPORE. [*Received, January 19th*, 1959.]

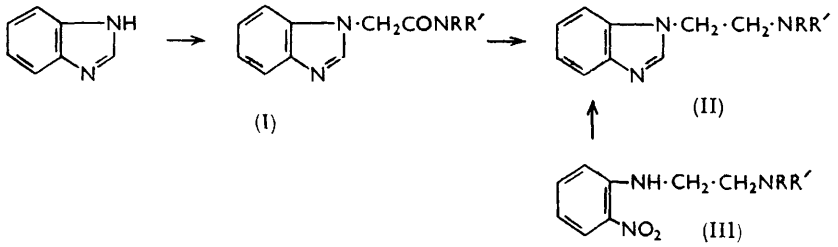
[4] Harned and Embree, *J. Amer. Chem. Soc.*, 1934, **56**, 1042.
[5] Pinching and Bates, *J. Res. Nat. Bur. Stand.*, 1950, **45**, 444.
[6] Hammett, " Physical Organic Chemistry," McGraw-Hill, New York, 1940, p. 188.

464. N-*Alkyl*-2-1′-*benzimidazolylethylamines.*

By S. Bell, R. Foster, and (Miss) W. E. B. Soutar.

Certain *N*-alkyl-2-1′-benzimidazolylethylamines have been prepared in order to discover whether they resemble or antagonise serotonin in its pharmacological action.

2-1′-Benzimidazolyl-*N*-methylethylamine (II; R = H, R′ = Me) has been prepared from the corresponding unsubstituted compound (II; R = R′ = H) by formylation and subsequent reduction with lithium aluminium hydride, but the overall yield starting from



o-chloronitrobenzene is low. The same product has, however, been obtained in high yield by reducing the condensation product (I; R = H, R′ = Me) of benzimidazole and α-chloro-*N*-methylacetamide This method has been applied to the preparation of the *NN*-dimethyl and *NN*-diethyl derivatives. The latter compound has also been prepared from *NN*-diethyl-*N′*-*o*-nitrophenylethylenediamine (III; R = R′ = Et) by reduction and cyclisation.

Experimental.—2-1′-*Benzimidazolyl*-N-*methylethylamine.* (*a*) 2-1′-Benzimidazolylethylamine [1] (3·5 g.), 98—100% formic acid (10 ml.), and toluene (40 ml.) were slowly distilled on a steam-bath. After 6 hr. the residual formic acid and toluene were evaporated *in vacuo*, water (2 ml.) was added, the mixture basified with solid potassium hydrogen carbonate and extracted with chloroform. The dried (Na_2SO_4) solution gave, on evaporation, a brownish-oil which slowly solidified. 2-1′-*Benzimidazolyl*-N-*formylethylamine* was obtained after two recrystallisations from ethyl acetate as needles (15%), m. p. 148·5° (Found: C, 63·6; H, 5·9; N, 22·2. $C_{10}H_{11}ON_3$ requires C, 63·5; H, 5·8; N, 22·2%). The formyl compound (0·9 g.) was added slowly to a suspension of lithium aluminium hydride (1 g.) in tetrahydrofuran and then refluxed with stirring for 4 hr., the excess of hydride decomposed with water, and the product extracted with benzene. Evaporation gave an oil, soluble in water from which 2-1′-*benziminazolyl*-N-*methylethylamine dipicrate* was precipitated. Two crystallisations from water gave red needles (70%), decomp. *ca.* 170° (Found: C, 42·1; H, 3·2. $C_{10}H_{13}N_3,2C_6H_3O_7N_3$ requires C, 41·7; H, 3·0%).

(*b*) Benzimidazole (17·3 g.) was dissolved in ethanol (300 ml.) in which sodium (3·4 g.) had been dissolved. α-Chloro-*N*-methylacetamide [2] (16 g.) in ethanol (100 ml.) was slowly added, and the mixture refluxed for 4 hr. Sodium chloride was removed by filtration, and ethanol by evaporation. The residual oil solidified rapidly and was twice crystallised from ethyl methyl ketone to give 2-1′-*benzimidazolyl*-N-*methylacetamide* as needles (90%), m. p. 172° (Found: C, 63·7; H, 5·8. $C_{10}H_{11}ON_3$ requires C, 63·5; H, 5·9%). This compound (13·5 g.), lithium aluminium hydride (6 g.), and tetrahydrofuran (300 ml.) were refluxed for 6 hr. The excess of hydride was decomposed with tetrahydrofuran, and the combined extracts were dried ($NaSO_4$). On evaporation 2-1′-benzimidazolyl-*N*-methylethylamine was obtained as a colourless oil (95%) which rapidly became brown in the air. The infrared spectra of the dipicrates of the two products were identical.

2-1′-*Benzimidazolyl*-NN-*dimethylethylamine.* Similarly prepared from α-chloro-*NN*-dimethylacetamide,[2] 2-1′-*benzimidazolyl*-NN-*dimethylacetamide* was twice recrystallised from ethyl methyl ketone as plates, m. p. 139° (Found: C, 65·7; H, 6·9. $C_{11}H_{13}ON_3$ requires C, 65·0; H, 6·4%). 2-1′-*Benzimidazolyl*-NN-*dimethylethylamine dipicrate* recrystallised (twice) from water, forming yellow needles (60%), decomp. *ca.* 212° (Found: C, 42·3; H, 3·5. $C_{11}H_{15}N_3,2C_6H_3O_7N_3$ requires C, 42·7; H, 3·2%).

[1] Mamalis, Petrow, and Sturgeon, *J.*, 1950, 1600.
[2] Jacobs and Heidelberger, *J. Biol. Chem.*, 1915, **21**, 147.

2-1′-*Benzimidazolyl*-NN-*diethylethylamine*. (*a*) Similarly prepared from α-chloro-*NN*-diethylacetamide,[2] **2-1′-*benzimidazolyl*-NN-*diethylacetamide*** was recrystallised four times from water, forming needles (50%), m. p. 124° (Found: C, 68·4; H, 7·0; N, 17·5. $C_{13}H_{17}ON_3$ requires C, 67·5; H, 7·0; N, 18·2%). **2-1′-*Benzimidazolyl*-NN-*diethylethylamine dipicrate*** was recrystallised twice from water, forming yellow needles (60%), m. p. 220° (decomp.) (Found: C, 44·5; H, 3·7. $C_{13}H_{19}N_3,2C_6H_3O_7N_3$ requires C, 44·4; H, 3·7%).

(*b*) *NN*-Diethyl-*N′*-*o*-nitrophenylethylenediamine (10 g.) was catalytically reduced in alcohol (100 ml.) over Raney nickel at 5 atm. for 1 hr. The crude oily *N*-(2-diethylaminoethyl)-*o*-phenylenediamine obtained (95%) was refluxed for 40 min. with 4N-hydrochloric acid (100 ml.) and 87% formic acid (20 ml.). The product, basified with concentrated aqueous ammonia, was extracted four times with chloroform. On evaporation 2-1′-benzimidazolyl-*NN*-diethylethylamine was obtained as a brown oil from which the dipicrate, recrystallised thrice from water, was obtained as yellow needles (45%), m. p. and mixed m. p. 220—221° (decomp.) (identical infrared spectra).

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465. *The Reaction between 4-Nitrosoacetamidodiphenyl and Toluene. A Correction.*

By D. I. DAVIES, D. H. HEY, C. W. REES, and F. C. SAUNDERS.

IN an earlier communication it was reported by France, Heilbron, and Hey [1] that a mixture of 2-, 3-, and 4-methyl-*p*-terphenyl was formed in the reaction between 4-nitrosoacetamidodiphenyl and toluene. The constitutions assigned to the 2- and the 4-methyl derivative were established by independent syntheses. The third compound was regarded as 3-methyl-*p*-terphenyl by elimination. A repetition of this experiment has confirmed that the three isomers are formed, but the compound previously described as 3-methyl-*p*-terphenyl was in fact 4-acetamidodiphenyl. The 3-methyl-*p*-terphenyl now isolated agrees in properties with the compound prepared by Gilman and Weipert [2] by the reaction of 4-diphenylyllithium with 3-methylcyclohexanone followed by dehydration and dehydrogenation.

An attempt to prepare 4-nitrosoacetamidodiphenyl by the method of France, Heilbron, and Hey,[3] using nitrosyl chloride prepared by Bachmann and Hoffman's method,[4] gave a product which melted sharply at 116—117° and was shown unexpectedly to be an approximately equimolar mixture of 4-acetamido-3-nitrodiphenyl and 4-acetamido-3-chlorodiphenyl. When this preparation was repeated with pure redistilled nitrosyl chloride, 4-nitrosoacetamidodiphenyl was obtained which on reaction with benzene gave *p*-terphenyl and 4-acetamidodiphenyl. The use of nitrosyl chloride prepared by Bachmann and Hoffman's method without redistillation gave nitrosoacetanilide in the normal manner from acetanilide.

Experimental.—Reaction of 4-nitrosoacetamidodiphenyl with toluene. 4-Nitrosoacetamidodiphenyl was prepared from 4-acetamidodiphenyl and nitrous fumes, as described by France, Heilbron, and Hey.[5] A solution of the nitroso-compound (10 g.) in toluene (500 g.) was set aside at room temperature for 48 hr. It darkened and nitrogen was evolved. The reaction was completed by heating the solution on a boiling-water bath for 4 hr. The excess of the solvent was removed by distillation and the dark residue was boiled under reflux for 12 hr. with concentrated hydrochloric acid (100 ml.) and ethanol (100 ml.). The ethanol was then removed by distillation and the residue was extracted with hot benzene (4 × 100 ml.). The benzene

[1] France, Heilbron, and Hey, *J.*, 1939, 1283.
[2] Gilman and Weipert, *J. Org. Chem.*, 1957, **22**, 446.
[3] France, Heilbron, and Hey, *J.*, 1940, 369.
[4] Organic Reactions, Vol. II, John Wiley & Sons, Inc., New York, 1944, p. 251.
[5] France, Heilbron, and Hey, *J.*, 1938, 1364.

solution was filtered from some 4-aminodiphenyl hydrochloride and washed successively with concentrated hydrochloric acid, water, aqueous sodium hydroxide, and water. After having been dried ($CaCl_2$) the benzene was removed by distillation and the residue was distilled at 0·1 mm. to give two fractions: (*a*) bath-temp. 100—200°, b. p. *ca.* 70°/0·1 mm., a white solid (0·86 g.), which after crystallisation from light petroleum (b. p. 60—80°) had m. p. 65°, with an infrared spectrum (Nujol mull) practically identical with that of diphenyl; (*b*) bath-temp. 200—300°, b. p. *ca.* 130—170°/0·1 mm., a yellowish-brown semi-solid material (3·2 g.). Material (*b*) was shown to be mainly a mixture of 2- and 4-methyl-*p*-terphenyl by comparison of its infrared spectrum in cyclohexane solution with those of authentic specimens of 2- and 4-methyl-*p*-terphenyl. The whole fraction was dissolved in hot ethanol (100 ml.) and fractionally crystallised to give materials: (i) m. p. 180—190° (0·05 g.); (ii) m. p. 170—185° (0·03 g.); (iii) m. p. 130—160° (0·10 g.). The mother-liquor was then heated to the b. p. and water was added so that the solute was just not precipitated from the solution. From the cooled solution the following fractions were collected: (iv) m. p. 70° (0·60 g.); (v) m. p. 80—82° (0·30 g.); (vi) m. p. 84—86° (0·22 g.); (vii) m. p. >350° (0·04 g.). There was a residue of non-crystallisable oil. Fractions (i), (ii), and (iii) were combined and recrystallised from ethanol (charcoal) to constant m. p. 207—208°, which was not depressed on admixture with authentic 4-methyl-*p*-terphenyl. The infrared spectra of the two specimens were identical over the 2—15 μ range. Fraction (iv) in ethanol (25 ml.) was cooled to −5°, a yellow crystalline solid (0·05 g.) then separating (m. p. 110—115°). Several recrystallisations from methanol (charcoal) raised the m. p. to 125—126° (Found: C, 93·4; H, 6·65. Calc. for $C_{19}H_{16}$: C, 93·4; H, 6·6%), which was not depressed on admixture with a specimen of 3-methyl-*p*-terphenyl kindly provided by Professor H. Gilman. The infrared spectrum was consistent with this structure. Fractions (v) and (vi) were combined and recrystallisation from ethanol (charcoal) gave plates, m. p. 88—89°, which was not depressed on admixture with an authentic specimen of 2-methyl-*p*-terphenyl.

The infrared spectra of the above three methyl-*p*-terphenyls in Nujol mulls were measured over the range 2—15 μ. The main bands were as follows: 2-methyl-*p*-terphenyl 845·2(m), 761·8(s), 756·0(s), 736·9(w), 727·2(w), and 701·8(m) $cm.^{-1}$; 3-methyl-*p*-terphenyl 838·0(m), 813·0(m), 787·4(m), 760·7(s), 721·9(m) and 691·1(m) $cm.^{-1}$; 4-methyl-*p*-terphenyl 856·0(w), 817·8(s), 766·5(s), 730·9(m), 696·9(m) $cm.^{-1}$.

Reactions of 4-acetamidodiphenyl with nitrosyl chloride. When 4-acetamidodiphenyl was treated with nitrosyl chloride in glacial acetic acid–acetic anhydride in the presence of potassium acetate and phosphoric oxide, as described by France, Heilbron, and Hey,[3] a product was obtained which crystallised from light petroleum (b. p. 100—120°) in yellow needles, m. p. 116—117° (Found: C, 67·0, 66·5; H, 4·8, 5·0; N, 9·7, 9·5; Cl, 6·3, 5·7%). The nitrosyl chloride was prepared as described by Bachmann and Hoffman.[4] Fractional crystallisation of 1·0 g. from ethanol gave 4-acetamido-3-nitrodiphenyl in yellow needles, m. p. 134° (0·58 g.), while the mother-liquors gave 4-acetamido-3-chlorodiphenyl (0·19 g.), which separated from light petroleun (b. p. 80—100°) in needles, m. p. 147°. Separation was also effected by chromatography on alumina from benzene solution (0·5 g. gave 0·27 g. of 4-acetamido-3-nitrodiphenyl and 0·20 g. of 4-acetamido-3-chlorodiphenyl). 4-Acetamido-3-nitrodiphenyl was identified by hydrolysis to 4-amino-3-nitrodiphenyl, m. p. 171°, and subsequent benzoylation to give 4-benzamido-3-nitrodiphenyl, m. p. 150°, and reduction to 3,4-diaminodiphenyl, m. p. 100°. 4-Acetamido-3-chlorodiphenyl was identified by hydrolysis to 4-amino-3-chlorodiphenyl, m. p. 67°, and nitration to give 4-acetamido-3-chloro-4′-nitrodiphenyl, m. p. 220°. A mixture of 4-acetamido-3-nitrodiphenyl (55%) and 4-acetamido-3-chlorodiphenyl (45%) melts at 117—119° and requires C, 66·8; H, 4·8; N, 8·6; Cl, 6·4%.

Reaction of 4-acetamidodiphenyl with redistilled nitrosyl chloride, by the general procedure of France, Heilbron, and Hey,[3] gave 4-nitrosoacetamidodiphenyl as a yellow solid, m. p. 85° (decomp.). The nitroso-compound (2 g.), kept in benzene (100 ml.) for 46 hr., gave *p*-terphenyl (0·79 g.; m. p. and mixed m. p. 212°) and 4-acetamidodiphenyl (0·36 g.; m. p. and mixed m. p. 173°).

The authors are indebted to Professor H. Gilman for having drawn their attention to the earlier erroneous statements concerning 3-methyl-*p*-terphenyl, and for his assistance in clearing up the discrepancy.

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