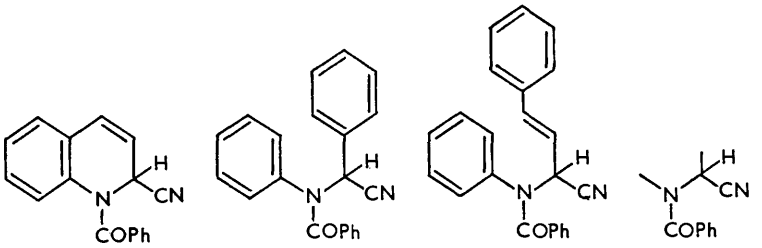
369. *Some Experiments towards the Elucidation of the Reissert Reaction.*

By R. F. Collins and T. Henshall.

During experiments on the reaction mechanism of the acid hydrolysis of the Reissert complex,[1] 1-benzoyl-2-cyano-1 : 2-dihydroquinoline (I), the effect of anhydrous hydrochloric acid was investigated. Other workers [2,3] have shown that this reaction in various solvents gives a red oily precipitate which reacts further with water to yield benzaldehyde and quinaldamide. However, the reaction in chloroform and ethanol rapidly gives a yellow crystalline precipitate, believed to be the ethyl imidate dihydrochloride derived from 2-cyanoquinoline, together with benzaldehyde. The former product was hygroscopic and it was not possible to obtain a good analysis but it was readily converted into 2-amidinoquinoline hydrochloride by ethanolic ammonia. However, 2-cyanoquinoline under identical conditions merely gave its insoluble hydrochloride, with no further reaction.

Other workers,[4] using slightly different conditions and a longer reaction period, have claimed that 2-cyanoquinoline does form the imidic ester and ultimately the amidine. The amidine hydrochloride so obtained was described as a very hygroscopic solid for which no analysis was given. A picrate was formed which had nearly the same properties as the picrate prepared from the amidine hydrochloride in present work, and a supporting analysis was given. It appears that pure 2-amidinoquinoline hydrochloride is better prepared from the Reissert complex (I) than from 2-cyanoquinoline.

McEwen and Cobb [5] recently described the direct action of hydrochloric acid on the Reissert complex (I) in the presence of 95% ethanol and obtained ethyl quinaldate, quinaldamide, and quinaldic acid, together with benzaldehyde, but, presumably because the reagents were not anhydrous, they did not isolate any imidic ester which might have been formed initially. The conditions employed to isolate the products would almost certainly have decomposed the imidic ester to quinaldic ester or quinaldic acid.



(I) (II) (III) (IV)

We have prepared the formally analogous compounds (II) and (III) : neither yields significant quantities of benzaldehyde on acid hydrolysis. Since the completion of this work Elliott [6] has shown that *N*-benzoyl-*N*-phenylglycine nitrile yields benzoic acid on treatment with acid. From these results we infer that the complete (although partially reduced) quinoline nucleus, as in (I), is necessary, in addition to the other essential structural feature (IV), for the production of benzaldehyde.

1-Benzoyl-2-cyano-1 : 2 : 3 : 4-tetrahydroquinoline [7] contains the structure (IV), but not the 3 : 4-double bond; its acid hydrolysis yields 1 : 2 : 3 : 4-tetrahydroquinoline-2-carboxylic acid and benzoic acid but no benzaldehyde. Thus the formation of

[1] Reissert, *Ber.*, 1905, **38**, 1603.
[2] Kaufmann and Dandliker, *Ber.*, 1913, **46**, 2924.
[3] McEwen, Kindall, Hazlett, and Glazier, *J. Amer. Chem. Soc.*, 1951, **73**, 4591.
[4] Coates, Cook, Heilbron, and Lewis, *J.*, 1943, 420.
[5] McEwen and Cobb, *J. Amer. Chem. Soc.*, 1955, **77**, 5042.
[6] Elliott, *ibid.*, p. 4408.
[7] Collins, *ibid.*, p. 4921.

benzaldehyde from compound (I), in contrast to the normal acid hydrolysis of the amide and the cyano-group, must depend on the 3 : 4-double bond which would transmit any electronic disturbance at the amide group through the benzene ring to the 2-carbon atom with possible activation of the hydrogen atom at this position. It is also possible for the reverse effect to occur since we have shown that compound (I) is readily attacked at the cyano-group (more rapidly than 2-cyanoquinoline), probably forming an imidic ester salt which might effect an electronic shift *via* the 3 : 4-double bond and the benzene ring to the amide group. The presence of the 3 : 4-double bond in the compound (I) also leads to a fully aromatic ring, after the benzaldehyde is formed, and probably provides the necessary energy for the reaction to proceed.

Experimental.—*2-Amidinoquinoline hydrochloride.* 1-Benzoyl-2-cyano-1 : 2-dihydroquinoline (15·7 g.) in dry chloroform (230 mol.) and dry ethanol (4 ml.) was saturated at 0° with dry hydrogen chloride. A thick yellow precipitate was formed and after 1 week (a much shorter period can be used) at room temperature the yellow solid was collected, rapidly washed with dry ether, and placed immediately in a vacuum-desiccator. There was a strong odour of benzaldehyde during this operation. The product was analysed without further purification, owing to its hygroscopic nature, and was assumed to be crude ethyl quinoline-2-carboxyimidoate dihydrochloride (Found : C, 49·3; H, 5·75; N, 10·0; Cl, 25·9. Calc. for $C_{12}H_{12}ON_2,2HCl$: C, 52·8; H, 5·1; N, 10·25; Cl, 26·0%) containing a little excess of hydrochloric acid and water (from the atmosphere), which was not lost on drying before analysis. Approximately half of this material was treated with saturated ethanolic ammonia at 55—60° for 5 hr. The yellow product (6·7 g.) was soluble in ethanol and was precipitated therefrom by ether. Repetition of this process freed the amidine hydrochloride from ammonium chloride. The crude product was then recrystallised from ethanol and acetone, to yield pure *2-amidinoquinoline hydrochloride* (1·5 g.), m. p. 238° (Found : C, 58·0; H, 4·85; N, 20·3. $C_{10}H_9N_3,HCl$ requires C, 57·8; H, 4·8; N, 20·2%). The picrate, m. p. 263—264° (Found : N, 21·2. Calc. for $C_{16}H_{12}O_7N_6$: N, 21·0%) [Coates *et al.*[4] give m. p. 258—259° (decomp.)], was formed from the hydrochloride and was recrystallised from acetone.

The original chloroform filtrate, from the imidic ester, was concentrated and the residue steam-distilled. Extraction of the distillate with ether afforded benzaldehyde (5 g.).

α-Benzanilidophenylacetonitrile (II). α-Anilinophenylacetonitrile [8] (10 g.) in dry pyridine (30 ml.) was treated dropwise with benzoyl chloride (6·8 ml.) at <25°. Next day the mixture was poured on ice and extracted with ether, and the extract was washed with dilute hydrochloric acid, water, and dilute sodium hydroxide, and was dried ($MgSO_4$). Evaporation under reduced pressure afforded a viscous oil, which was extracted repeatedly with light petroleum (b. p. 60—80°). Evaporation under reduced pressure and trituration of the residue with light petroleum (b. p. 40—60°) gave a solid (10·7 g.), m. p. 78—81°. Recrystallisation from methanol yielded the pure *amido-nitrile* (9 g.), m. p. 87—88° (Found : C, 80·5; H, 4·95; N, 9·0. $C_{21}H_{16}ON_2$ requires C, 80·7; H, 5·1; N, 9·0%).

2-Benzanilido-4-phenylbut-3-enonitrile (III). 2-Anilino-4-phenylbut-3-enonitrile [9] (10 g.) in pyridine (30 ml.) was treated dropwise with benzoyl chloride (6·5 ml.) at <25° and worked up as above. The ethereal solution of the product was concentrated *in vacuo* and afforded a red viscous oil. Approx. 2 g. of this oil were chromatographed over alumina in benzene, with ether, followed by ether–ethanol for elution. After several months crystals appeared in one of the residues obtained by evaporation of aliquot parts of the eluate. After the addition of some ether, the crystals (0·3 g.; m. p. 94—98°) were collected and recrystallised from methanol to yield *2-benzanilido-4-phenylbut-3-enonitrile* (0·2 g.), m. p. 97—98° (Found : C, 81·8; H, 5·5; N, 8·2. $C_{23}H_{18}ON_2$ requires C, 81·6; H, 5·3; N, 8·3%).

The bulk of the original solution was then treated with methanol, seeded, and kept at 0° overnight. The crystalline product was collected and recrystallised from methanol to yield the pure product (2·3 g.), m. p. 96—97°.

The filtrate from the separation of the crude product was stored for several days and a crystalline solid slowly appeared. It was collected and recrystallised from methanol and yielded a second *product* (3·1 g.), m. p. 115—117° (Found : C, 81·8; H, 5·6; N, 8·25%). The m. p. was depressed to 86—90° on admixture with the first product and to 98—105° on admixture with the anilinonitrile (m. p. 127—128°). The products are thus probably *cis–trans*-isomers.

[8] Tiemann and Piest, *Ber.*, 1882, **15**, 2029.
[9] Von Miller, Plöchl, and Jungmann, *Ber.*, 1892, **25**, 2052.

Hydrolysis of the nitrile (II). The nitrile (1 g.) was refluxed for 1·5 hr. with concentrated hydrochloric acid (10 ml.) and water (10 ml.). Steam-distillation and extraction of the basified distillate with ether gave a negligible quantity of benzaldehyde (2 : 4-dinitrophenylhydrazone, m. p. 237—238°). The alkaline aqueous steam-distillate was acidified but no benzoic acid was isolated, presumably because of the volume of water present. The residue in the flask, after the steam-distillation, was filtered off, dissolved in dilute sodium hydroxide, filtered, and acidified with acetic acid, and the product (0·45 g.), m. p. 157—158°, was collected. It recrystallised from aqueous ethanol and then from benzene, giving α-anilinophenylacetic acid (0·35 g.), m. p. 172—173° (Found : C, 74·6; H, 6·1; N, 6·25. Calc. for $C_{14}H_{13}O_2N$: C, 74·0; H, 5·7; N, 6·2%). McKenzie and Bate [10] give m. p. 174—175°. The original acid filtrate from the latter product gave a positive diazo-reaction, indicating the presence of a trace of primary aromatic amine.

Hydrolysis of the nitrile (III). The nitrile (0·5 g.) was refluxed with concentrated hydrochloric acid (5 ml.) and water (5 ml.) for 1·5 hr. Benzaldehyde could not be detected either by its odour or by treatment of the hydrolysate with 2 : 4-dinitrophenylhydrazine. Each isomer gave the same result.

One of the authors (R. F. C.) thanks May & Baker Ltd., for general laboratory facilities. The semimicroanalyses were carried out by Mr. S. Bance, B.Sc., A.R.I.C., of May and Baker Ltd.

Department of Chemistry, Sir John Cass College,
Jewry Street, Aldgate, London, E.C.3. [*Received, October 21st*, 1955.]

[10] McKenzie and Bate, *J.*, 1915, **107**, 1682.

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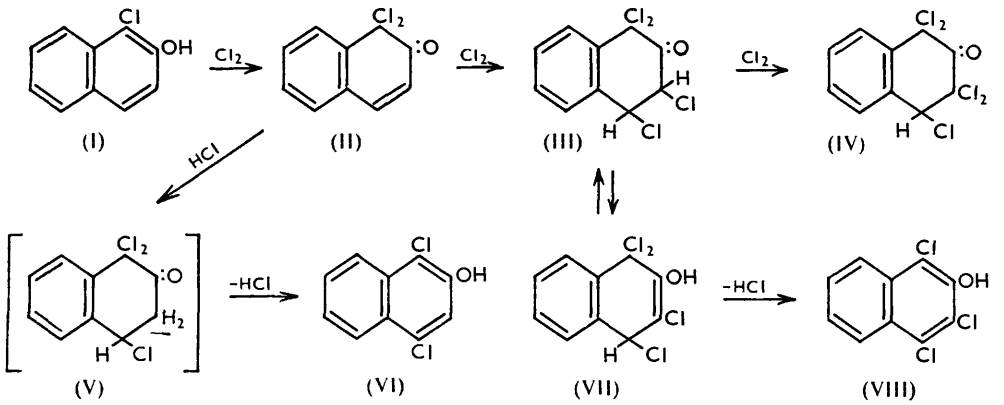
370. *Secondary Mechanisms in the Halogenation of Phenols and Aromatic Sulphonamides.*

By P. W. Robertson.

None of the mechanisms proposed hitherto accounts satisfactorily for all the complex products of halogenation of phenols or aromatic sulphonamides,[1] and the present note suggests an alternative. These reactions involve nucleophilic halogen addition (the kinetics of which have recently been investigated [2]) as well as addition and subsequent elimination of hydrogen halide.

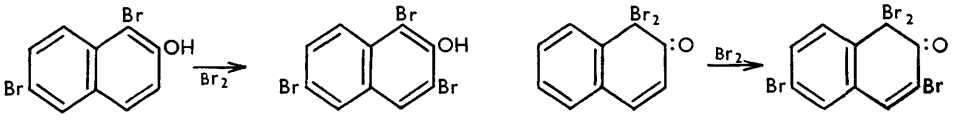


Chlorination of β-naphthol yields the products [3] shown in the annexed scheme. Electrophilic substitution gives first 1-chloro-2-naphthol (I), which by addition of chlorine

[1] Bell and Mulholland, *J.*, 1949, 2020; Bell, *J.*, 1953, 3035; 1955, 2376; Bell and Gibson, *J.*, 1954, 4635; 1955, 24.
[2] de la Mare and Robertson, *J.*, 1945, 888; Rothbaum, Ting, and Robertson, *J.*, 1948, 980.
[3] Zincke, *Ber.*, 1888, **21**, 3378; James and Woodcock, *J.*, 1951, 1931.

and elimination of hydrogen halide yields the dichloro-compound (II). This αβ-unsaturated ketone undergoes acid-catalysed nucleophilic addition of chlorine, the reactive agent being HCl_3 and the product the tetrachloro-oxotetralin (III). Further chlorination then gives the pentachloro-ketone (IV) or, if no more than 3 mols. of chlorine are used, the tetrachloro-ketone changes, *via* the enol (VII), into the trichlorophenol (VIII). 1 : 4-Dichloro-2-naphthol (VI) is produced in practice by bubbling chlorine into the reaction mixture, two mols. of chlorine being consumed: it cannot be formed by electrophilic substitution which, as shown, for example, by nitration, would yield a 1 : 6-disubstituted product; its formation is prevented by addition of sodium acetate to the acetic acid solvent, in which it acts as a base, so it follows that hydrogen chloride is required and reaction *via* the intermediate (V) (which is not isolated) can be assumed. The dichloronaphthol is however not obtained when an excess of chlorine is used, for addition of chlorine, to give the product (III), is more rapid than that of hydrogen halide.

Bromination of β-naphthol[4] takes a different course. The 1 : 6-dibromo-compound (IX), the normal disubstitution product, when further brominated in acetic acid, yields the

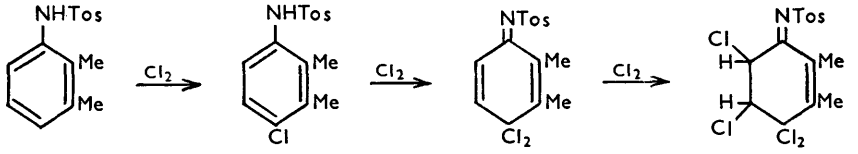


(IX) (X) (XI) (XII)

tribromonaphthol (X), probably by acid-catalysed addition of bromine to the keto-form with subsequent elimination of hydrogen bromide: in this case there is no 4-substitution because the equilibrium $-CX_2{\cdot}CO^- + HX \rightleftharpoons -CHX{\cdot}CO- + X_2$ lies more to the right when X = Br than when X = Cl. However, in presence of sodium acetate dibromination leads to the ketone (XI), which by nucleophilic addition (involving Br_3^- ions, which may react rapidly even in the absence of H^+) followed by elimination of hydrogen halide (favoured by sodium acetate) affords the tetrabromo-ketone (XII).

In the analogous bromination of arenesulphonyl-2-naphthylamides in pyridine, Bell[1] obtained the 1 : 3-dibromo-derivative as end-product. Here, " positive " bromine cannot be the reagent, for this would merely react at the 1 : 6-positions. Reaction with Br_3^- ions probably proceeds by way of the *N*-arenesulphonyl-1 : 1 : 3-tribromo-1 : 2-dihydro-2-naphthylimine [analogous to (XII)] which passes into the *N*-arenesulphonyl-1 : 3-dibromonaphthylamine during the working up (by the action of hydrochloric acid).

The behaviour of certain sulphonamide derivatives is illustrated for 2 : 3-xylidine (XIII) ⟶ (XVI). In the intermediate (XV) the deactivating C=N·Tos and CCl_2 groups



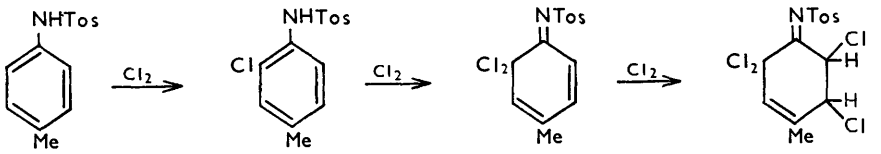
(XIII) (XIV) (XV) (XVI)

(Tos = $ArSO_2$)

should cause the electrophilic addition of chlorine to be very slow. The alternative, nucleophilic addition of chlorine may be expected to be fast, and should therefore, be the mechanism that is in operation. The isolation of the addition product (XVI) confirms this view, since methyl groups are known to reduce the rate of nucleophilic addition (*e.g.*, acrylic acid > α-methylacrylic acid, benzoquinone > 2 : 6-dimethylbenzoquinone).[2]

[4] Franzen, *J. prakt. Chem.*, 1922, **103**, 352; Fries, *Annalen*, 1930, **484**, 245.

Chlorination of a *p*-toluidine derivative (XVII) occurs by the steps (XVII—XX). In the last step, acid-catalysed 1 : 2-nucleophilic addition (by means of HCl_3) should be fast,



(XVII) (XVIII) (XIX) (XX)

and 1 : 2-electrophilic addition should be slow [as for the acid, $CHPh{:}CH{\cdot}CH{:}C(CO_2H)_2$].[5] Here again the nature of the product indicates that a nucleophilic addition process is a secondary mechanism in the halogenation.

32, Dorset Square, London, N.W.1. [*Received, November 8th*, 1955.]

[5] Evans, Watson, and Robertson, *J.*, 1950, 1624.

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371. *Heterocyclic N-Oxides. Oxides of Some Diphenylpyrazine Derivatives and of 3-Nitro- and 7-Nitro-quinoline.*

By Justus K. Landquist.

During an investigation of the chemotherapeutic properties of quinoxaline di-*N*-oxides a search was made for other heterocyclic *N*-oxides with similar antibacterial or antiprotozoal activity. Some of the closely related pyrazine *N*-oxides have already been described.[1] Certain nitroquinoline *N*-oxides bear a formal resemblance to quinoxaline 1 : 4-dioxide, and the *N*-oxides of 4-, 5-, 6-, and 8-nitroquinoline have been described.[2] 3-Nitro- and 7-nitro-quinoline *N*-oxides were made by oxidation of the corresponding nitroquinolines with monoperphthalic acid.

2 : 3-Diphenylpyrazine on oxidation with peracetic acid gave mono- and di-*N*-oxides, but 2 : 6-diphenylpyrazine gave only a monoxide, probably 2 : 6-diphenylpyrazine 4-oxide. 5 : 6-Dihydro-2 : 3-diphenylpyrazine was treated with peracetic acid in the expectation that dehydrogenation and *N*-oxidation would occur, but the product appeared to be a di-*N*-oxide of the dihydro-compound. 2 : 3-Diphenylpyrazine 1-oxide reacted with phosphoryl chloride, giving 5-chloro-2 : 3-diphenylpyrazine. Like 2- and 3-chloro-5 : 6-benzoquinoxaline [3] this compound was unreactive towards arylamines, but the chlorine was replaced by piperidine.

Oxidation of quinazoline with peracetic acid gave 4-hydroxyquinazoline. It is probable that some compounds described in the literature as *N*-oxides are in fact *C*-hydroxy-compounds; such compounds may usually be distinguished from *N*-oxides by their high melting points (2-hydroxy-5 : 6-diphenylpyrazine [4] and 2-hydroxy-3 : 5-diphenylpyrazine [5] melt at 243—244° and 270—272°, respectively), their solubility in aqueous sodium hydroxide, and their sparing solubility in organic solvents.

Experimental.—*3-Nitroquinoline N-oxide.* 3-Nitroquinoline (8·7 g.) in dry dioxan (60 c.c.) was added during 10 min. to an ice-cold 0·5N-solution of monoperphthalic acid in ether (125 c.c.). After 3 days the solvent was evaporated under reduced pressure and the residue was stirred for 30 min. with 5% ammonia solution (90 c.c.). Unchanged 3-nitroquinoline (4·5 g.) was filtered off and washed with water, and the aqueous filtrate was extracted with chloroform (3 × 80 c.c.). Evaporation of the dried (Na_2SO_4) extract and repeated crystallisation of the residue (1·2 g.)

[1] Newbold and Spring, *J.*, 1947, 1183.
[2] Ochiai, Ishikawa, and Zai-Ren, *J. Pharm. Soc. Japan*, 1943, **63**, 280; Gouley, Moersch, and Mosher, *J. Amer. Chem. Soc.*, 1947, **69**, 303; Bachman and Cooper, *J. Org. Chem.*, 1944, **9**, 302.
[3] Landquist, *J.*, 1953, 2816.
[4] Karmas and Spoerri, *J. Amer. Chem. Soc.*, 1952, **74**, 1580.
[5] Dunn, Elvidge, Newbold, Ramsay, Spring, and Sweeny, *J.*, 1949, 2707.

from ethanol yielded 3-*nitroquinoline* N-*oxide* (0·5 g.) as yellow crystals, m. p. 192—193° (Found : C, 56·8; H, 3·3; N, 14·4. $C_9H_6O_3N_2$ requires C, 56·8; H, 3·15; N, 14·7%). The same *N*-oxide was obtained by oxidation with 1·2M-peracetic acid at 50° overnight.

7-*Nitroquinoline* N-*oxide*. 7-Nitroquinoline (5·0 g.) in dioxan (50 c.c.) was added to a 25% excess of monoperphthalic acid in ether at 0—5° and the mixture set aside for 5 days at room temperature. The bulk of the solvent was then evaporated under reduced pressure (bath temp. 50°) and the residue was stirred for 30 min. with 5% ammonia solution (60 c.c.). The solid (4·5 g.) was filtered off and washed with water, and extraction of the filtrate with chloroform afforded a further 0·8 g. Crystallisation from benzene and then from methanol gave 7-*nitroquinoline* N-*oxide* (1·6 g.), yellow crystals, m. p. 174—175° (Found : C, 57·2; H, 3·5; N, 14·6%).

Oxidation of 2 : 3-*Diphenylpyrazine*. 2 : 3-Diphenylpyrazine (5·8 g.) and 1·2M = peracetic acid (80 c.c.) were heated overnight at 50°, cooled, and diluted with water to 350 c.c.; 2 : 3-*diphenylpyrazine* 1-*oxide* (2·9 g.) was removed by filtration and washed with water. It crystallised from light petroleum (b. p. 100—120°) in needles, m. p. 171—172° (Found : C, 76·6; H, 4·8; N, 10·95. $C_{16}H_{12}ON_2$ requires C, 77·4; H, 4·8; N, 11·3%). The aqueous filtrate was cooled in ice and made just alkaline (Brilliant yellow) with sodium hydroxide, and the precipitated 2 : 3-*diphenylpyrazine* 1 : 4-*dioxide* (2·0 g.) was collected and washed with water. Extraction of the mother liquors with chloroform afforded 1 g. of impure material. The product crystallised from ethanol in platelets, m. p. 262° (decomp.) (Found : C, 72·4; H, 4·55; N, 10·7. $C_{16}H_{12}O_2N_2$ requires C, 72·6; H, 4·55; N, 10·6%).

By using similar oxidation conditions the following were prepared : 5 : 6-*dihydro*-2 : 3-*diphenylpyrazine* 1 : 4-*dioxide*, needles, m. p. 244°, from 2-ethoxyethanol (Found : C, 71·9; H, 6·2; N, 11·0. $C_{16}H_{14}O_2N_2$ requires C, 72·1; H, 5·25; N, 10·5%), and 2 : 6-*diphenylpyrazine* 4(?)-*oxide*, needles, m. p. 200—201°, from ethanol (Found : C, 77·3; H, 4·85; N, 11·4. $C_{16}H_{12}ON_2$ requires C, 77·4; H, 4·8; N, 11·3%).

2-*Chloro*-5 : 6-*diphenylpyrazine*. 2 : 3-Diphenylpyrazine 1-oxide (1·6 g.) and phosphoryl chloride (6 c.c.) were boiled under reflux for 20 min. and then poured on ice (100 g.), and the mixture was made alkaline with potassium hydroxide. The precipitated oil solidified slowly and the crude solid (1·7 g.; m. p. 123—124°) was washed with water, dried, and crystallised from ethanol. 2-Chloro-5 : 6-diphenylpyrazine was obtained as prisms, m. p. 125—126°, from *cyclo*hexane (Found : C, 72·2; H, 4·2; N, 10·6. Calc. for $C_{16}H_{11}N_2Cl$: C, 72·0; H, 4·1; N, 10·5%). Karmas and Spoerri [4] found m. p. 126—127°.

5 : 6-*Diphenyl*-2-*piperidino-pyrazine*. 2-Chloro-5 : 6-diphenylpyrazine (2·6 g.) and piperidine (9 c.c.) were boiled under reflux for 1·5 hr. and poured into water. The precipitate hardened when rubbed, and was crystallised from ethanol, giving 5 : 6-*diphenyl*-2-*piperidinopyrazine* (2·4 g.) m. p. 127—129° (Found : C, 79·9; H, 6·5; N, 13·3. $C_{21}H_{21}N_3$ requires C, 80·0; H, 6·7; N, 13·3%).

IMPERIAL CHEMICAL (PHARMACEUTICALS) LIMITED,
HEXAGON HOUSE, BLACKLEY, MANCHESTER, 9.

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372. *A Simple Approximation to the Resonance Energies of Aromatic Molecules.*

By A. L. GREEN.

ALTHOUGH many approximate formulæ, both empirical [1] and based on perturbation treatments of more rigorous quantum-mechanical methods,[2] have been given for the calculation of resonance energies, the simple dependence of the resonance energies of aromatic molecules containing only six-membered rings on the number of bonds in the molecule, *i.e.*, $E_{res.} = kn$, has not been reported. If $k = \beta/3$, then the energy is given in terms of the molecular-orbital resonance integral β. The slightly greater resonance energies of angular molecules compared with those of their linear isomers can be corrected by addition of $m\beta/10$, where

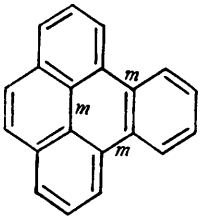
[1] (*a*) Brown, *Trans. Faraday Soc.*, 1950, **46**, 1013; (*b*) Carter, *ibid.*, 1949, **45**, 597; (*c*) Wheland, "The Theory of Resonance," John Wiley and Sons, New York, 1944, p. 79.

[2] (*a*) Wheland, *J. Chem. Phys.*, 1935, **3**, 230; (*b*) Daudel and Vroelant, *Bull. Soc. chim. France*, 1949, **16**, 217; (*c*) Dewar, *J. Amer. Chem. Soc.*, 1952, **74**, 3345; (*d*) Dewar and Petitt, *J.*, 1954, 1617.

m is the number of bonds contained in one benzene ring in the molecule and linking two others, giving the complete formula :

$$E_{\text{res.}} = (n/3 + m/10)\beta \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

The calculation is illustrated below for 4 : 5-benzopyrene :



$n = 24$, $m = 3$, $E_{\text{res.}} = 8{\cdot}30\beta$.

In Table 1 the resonance energies calculated for a number of aromatic molecules are compared with those obtained by the complete molecular-orbital method by Wheland's method,[1c,2a] in which the resonance energy is directly proportional to the number of single bonds in any " Kekulé " representation of the aromatic system, and by Daudel and Vroelant's method[2b] in which the total π-electron energy is an additive function of the number of bonds. Wheland's method does not allow for the variation in resonance energy of isomers and could be improved by some factor such as our " m " term.

TABLE 1. *Resonance energies (in units of β) calculated by various approximate formulæ compared with accurate molecular-orbital values.*

Compound *	Accurate †	This note	Wheland ‡	Daudel and Vroelant ‡
Benzene	2·00 [a]	2·00	1·82	1·80
Naphthalene	3·68 [a]	3·67	3·64	3·52
Anthracene	5·31 [a]	5·33	5·46	5·24
Phenanthrene	5·45 [a]	5·43	5·46	5·33
Pyrene	6·51 [b]	6·43	6·67	6·54
Naphthacene	6·93 [b]	7·00	7·27	6·94
Benzanthracene	7·10 [b]	7·10	7·27	7·05
Chrysene	7·19 [b]	7·20	7·27	7·14
Triphenylene	7·27 [b]	7·30	7·27	7·21
Perylene	8·25 [c]	8·20	8·50	8·40
4 : 5-Benzopyrene	8·34 [d]	8·30	8·50	8·40
Pentacene	8·54 [c]	8·67	9·10	8·65
Pentaphene	8·76 [c]	8·77	9·10	8·78
1 : 2-5 : 6-Dibenzanthracene	8·88 [c]	8·87	9·10	8·85
Picene	8·94 [c]	8·97	9·10	8·95
2 : 3-6 : 7-Dibenzopyrene	9·95 [d]	9·97	10·31	10·07
2 : 3-4 : 5-Dibenzopyrene	10·03 [d]	10·07	10·31	10·22
Hexacene	10·16 [a]	10·33	10·92	10·41
2 : 3-8 : 9-Dibenzochrysene	10·48 [d]	10·53	10·92	10·59
Coronene	10·57 [e]	10·60	10·92	10·84
Tetrabenzonaphthalene	10·80 [f]	10·93	10·92	10·90
Tetrabenzanthracene	12·55 [f]	12·60	12·73	12·61
Chalcacene	12·84 [g]	12·83	13·34	13·32

* The numbering is that of the " Ring Index."

† Accurate values are taken from : (*a*) Brown, *Trans. Faraday Soc.*, 1950, **46**, 1013; (*b*) Berthier, Coulson, Greenwood, and Pullman, *Compt. rend.*, 1948, **226**, 1906; (*c*) Baldock, Berthier, and Pullman, *ibid.*, 1949, **228**, 931; (*d*) Chalvet and Peltier, *ibid.*, 1955, **240**, 1709; (*e*) Moffitt and Coulson, *Proc. Phys. Soc.*, 1948, **60**, *A*, 309; (*f*) Herraez Zarza, *Anales Fis. Quím.*, 1955, **51**, *B*, 305; (*g*) Coulson, Bradburn, and Rushbrooke, *Proc. Roy. Soc. Edinburgh*, 1946, **62**, *A*, 336.

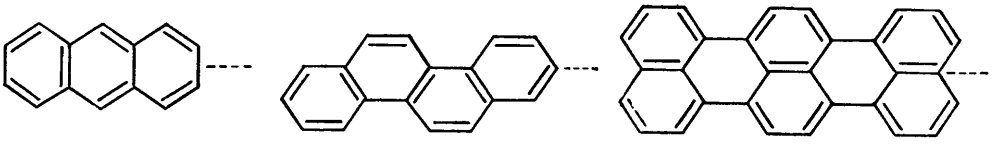
‡ These approximations are derived from valence-bond theory and give results in terms of the valence-bond exchange integral, α. These have been multiplied by 1·82 to give comparable resonance energies in terms of the molecular-orbital resonance integral, β.

Coulson and his co-workers[3,4] have studied large condensed aromatic systems. Their numerical results indicate that the resonance energies depend simply on the number of

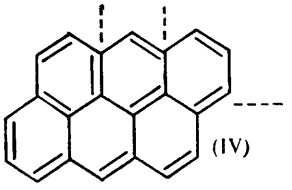
[3] Coulson, Bradburn, and Rushbrooke, *Proc. Roy. Soc. Edinburgh*, 1946, **62**, *A*, 336.
[4] Coulson and Rushbrooke, *ibid.*, p. 350.

bonds but vary with the shape of the molecule. In our formula this variation is corrected by m. Coulson and Rushbrooke [4] give the resonance energies per atom of several infinitely large structures; for these structures they can be easily calculated by the present formula and some results are given in Table 2.

TABLE 2. *Resonance energies (in units of β) per atom of "infinite" condensed aromatic systems.*



(I) (II) (III)



(IV)

Structure	Accurate	Approximate
"Polyacene" (I)	0·403	0·417
"Skewed linear" (II) ...	0·437	0·442
"Polynaphthylene" (III)	0·461	0·463
"Graphite" (IV)	0·576	0·550

The formula is also related to the "annelation" energy formula used by Brown,[1a] who found that, for any aromatic molecule that can be constructed by the fusion of two simpler molecules, the resonance energy is given approximately by:

$$E_{res.} = E_{res.}^{(1)} + E_{res.}^{(2)} + [2{\cdot}15(p_a p_b)^{\frac{1}{2}} - 1{\cdot}73]\beta$$

where $E_{res.}^{(1)}$ and $E_{res.}^{(2)}$ are the separate resonance energies and p_a and p_b are the mobile bond orders of the bonds being fused. If in every case $E_{res.}^{(2)}$ is that of benzene, then

$$E_{res.} = E_{res.}^{(1)} + [0{\cdot}27 + 2{\cdot}15(0{\cdot}67p_b)^{\frac{1}{2}}]\beta \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Aromatic bonds at which fusion can occur are generally of three types, similar to the 2 : 3-, 1 : 2-, and 9 : 10-bonds in phenanthrene with mobile bond orders about 0·61, 0·72, and 0·78, respectively. If these values are substituted in equation (2) the additional resonance energies due to the annelation of a single benzene ring at these three types of bond are: 2 : 3-, 1·64β; 1 :2-, 1·76β; 9 : 10-, 1·83β. Annelation of a benzene ring requires the addition of five bonds to the molecule. If fusion occurs at a 1 : 2-bond one "m" type bond is created, while if at a 9 : 10-bond, there are two. Thus the additional resonance energies are 1·67β, 1·77β, and 1·87β, so that the two formulæ are almost equivalent. However, Brown's formula is not applicable to condensed structures such as pyrene, perylene, or coronene for which the simple formula still gives good agreement.

CHEMICAL DEFENCE EXPERIMENTAL ESTABLISHMENT,
PORTON, WILTS.

[*Received, November 28th*, 1955.]

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373. *Oxanil.*

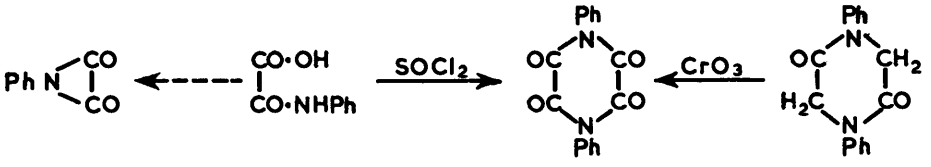
By D. BUCKLEY and H. B. HENBEST.

WARREN and BRIGGS [1] reported that treatment of oxanilic acid (I) with thionyl chloride gave a high-melting compound which they regarded as oxanil (II) on the basis of analytical data and a molecular-weight determination in boiling nitrobenzene. The yield was not stated.

In view of the unique ring structure of the formulation (II), this reaction has been reinvestigated. When a solution of oxanilic acid in purified thionyl chloride was heated

[1] Warren and Briggs, *Ber.*, 1931, **64**, 26.

under reflux for 12 hours and the precipitate crystallised from nitromethane, a 12% yield of a crystalline compound, subliming at 335—340°, was obtained (Warren and Briggs state that their compound had not melted at 320°). The analytical data for this compound



agreed with $C_8H_5O_2N$, and the compound gave aniline on hydrolysis with aqueous alkali and a single band at 1709 cm.$^{-1}$ in the carbonyl region of the infrared spectrum.

The suspicion that this " oxanil " might be the long-known 2 : 3 : 5 : 6-tetraoxo-1 : 4-diphenylpiperazine (III) was confirmed by comparison with authentic material prepared [2] by chromic acid oxidation of the 2 : 5-dioxo-compound (IV). Both (III) and (IV) were converted in high yield into 1 : 4-diphenylpiperazine by reduction with lithium aluminium hydride in boiling dioxan.

The similarity of the method of preparation and of the properties of the high-melting products prepared from oxanilic acid by Warren and Briggs and by the present authors make it reasonably certain that the earlier workers also obtained (III), and that oxanil (II) has yet to be prepared.

Experimental.—(M. p.s were determined on a Kofler block.)

Action of thionyl chloride on oxanilic acid. A mixture of the acid (5 g.; prepared by Tingle and Bates's method [3]) and thionyl chloride (25 c.c.; purified by distillation from quinoline and from linseed oil) was heated under reflux for 15 hr. The cooled suspension was filtered and the solid product crystallised from nitromethane, to give 2 : 3 : 5 : 6-tetraoxo-1 : 4-diphenylpiperazine (0·48 g.), subliming at 335—340° (Found : C, 65·25; H, 3·45; N, 9·65. Calc. for $C_{16}H_{10}O_4N_2$: C, 65·3; H, 3·45; N, 9·5%).

The compound synthesised by Abenius's method [2] also sublimed at 335—340°. Both products gave identical infrared spectra in Nujol suspensions; carbonyl peak at 1709 cm.$^{-1}$. Both products showed $\lambda_{max.}$ 2250 Å and $\lambda_{min.}$ 2160 Å in the ultraviolet region (in saturated dioxan solutions).

1 : 4-*Diphenylpiperazine.* The tetraoxo-compound (0·26 g.) was extracted in a Soxhlet thimble above a solution of lithium aluminium hydride (0·16 g.) in boiling dioxan (100 c.c.). After 4 hr. the compound had dissolved, and the product was isolated with ether. The crude product in benzene solution was filtered through alumina (10 g.) yielding material (0·17 g.), m. p. 166—168°, raised to 169—170° by crystallisation from ether–light petroleum (Found : C, 80·4; H, 7·35; N, 11·65. Calc. for $C_{16}H_{18}N_2$: C, 80·65; H, 7·6; N, 11·75%). Identical results were obtained by reduction of the tetraoxo-compound from either route. Wedekind and Bruch [4] record m. p. 164—165° for this compound.

THE UNIVERSITY, MANCHESTER 13. [*Received, December 9th*, 1955.]

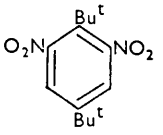
[2] Hausdorfer, *Ber.*, 1889, **22**, 1797; Abenius, *J. prakt. Chem.*, 1908, **41**, 80.
[3] Tingle and Bates, *J. Amer. Chem. Soc.*, 1909, **31**, 1237.
[4] Wedekind and Bruch, *Annalen*, 1929, **471**, 88.

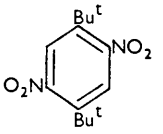
374. *The Dinitration of* p-*Di*-tert.-*butylbenzene.*

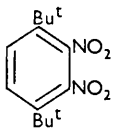
By F. Bell and K. R. Buck.

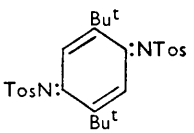
The dinitration of *p*-di-*tert.*-butylbenzene was described by Bauer [1] and Verley [2] but it was left to Boedtker [3] to isolate for the first time a pure dinitro-derivative (m. p. 191°). Carpenter and Easter [4] have recently obtained the same compound, m. p. 193°, in improved yield. Boedtker ascribes to it formula (I) because after reduction with tin and hydrochloric acid the resulting solution gives an intense colour with nitrous acid and, further, oxidation with ferric chloride or chromic acid led to negative results. Crawford and Stewart [5] have emphasized the difficulty which must attend the preparation of a compound in which the *tert.*-butyl group is flanked by two nitro-groups but since the experiments of Carpenter, Easter, and Wood [4,6,7] had provided at least twelve examples of this type of structure there had been little reason to question the correctness of Boedtker's conclusion, lightly founded though it appeared.

On repeating this dinitration we found that the product, which was very complex, contained Boedtker's compound together with an isomer, m. p. 141°. The dipole moment of the compound of m. p. 191° in benzene solution was indistinguishable from zero; that of


(I)


(II)


(III)


(IV)

the compound of m. p. 141° was 2·3 D. It thus appears that Boedtker's compound must be the 2 : 5-dinitro-compound (II) and it may be recalled that Kofod, Kumar, and Sutton [8] found a negligible moment for the dibromo-compound to which they ascribed the analogous constitution. The isomer, for which (I) and (III) are possible formulæ, is regarded as (I) by comparison with the dinitrobenzenes for which the dipole moments are: *ortho* 5·98; *meta* 3·78 D; *para*, zero.[9] Further, structure (III) was rejected on chemical grounds because the compound, m. p. 141°, could be recovered unchanged from boiling piperidine, which Le Fèvre and Turner [10] found to react readily with *o*-dinitro-compounds, and, also, the product of reduction of the compound did not condense with phenanthraquinone as an *o*-diamine would be expected to do. The low dipole moment compared with that of *m*-dinitrobenzene suggests that the nitro-groups are laterally displaced about 12° away from the *tert.*-butyl group or, alternatively, that they have moved out of the plane of the benzene ring, or have suffered both types of displacement.

Additional evidence in favour of structure (II) for Boedtker's compound was obtained by preparing from it a *p*-quinonoid compound, such as he sought but failed to obtain. The dinitro-compound was reduced to the diamine from which was prepared the ditoluene-*p*-sulphonyl derivative. This on oxidation with *N*-bromosuccinimide in pyridine gave an almost quantitative yield of the corresponding ditoluene-*p*-sulphonimido-derivative (IV; Tos = *p*-$C_6H_4Me{\cdot}SO_2$).

1 : 4-Di-*tert.*-butyl-2 : 5-ditoluene-*p*-sulphonamidobenzene, on crystallisation from *o*-dichlorobenzene (nominal), separated with 1 mol. of *p*-dichlorobenzene, which was tenaciously

[1] Bauer, *Ber.*, 1896, **27**, 1608.
[2] Verley, *Bull. Soc. chim. France*, 1898, **19**, 72.
[3] Boedtker, *ibid.*, 1906, **35**, 835.
[4] Carpenter and Easter, *J. Org. Chem.*, 1954, **19**, 77.
[5] Crawford and Stewart, *Nature*, 1952, **170**, 322.
[6] Carpenter and Easter, *J. Org. Chem.*, 1951, **16**, 618; 1954, **19**, 77.
[7] Carpenter, Easter, and Wood, *ibid.*, 1951, **16**, 586.
[8] Kofod, Kumar, and Sutton, *J.*, 1951, 1790.
[9] Partington, "Advanced Treatise on Physical Chemistry," Longmans, London, 1954, Vol. V, p. 499.
[10] Le Fèvre and Turner, *J.*, 1927, 1113; see also Le Fèvre and Le Fèvre, *J.*, 1935, 964.

held. This is a remarkable example of selective action for the percentage of *p*-dichlorobenzene in *o*-dichlorobenzene (B.D.H.) is presumably quite low. Neither *p*-di-*tert.*-butylbenzene nor *p*-ditoluene-*p*-sulphonamidobenzene combined with *p*-dichlorobenzene.

Experimental.—Physical measurements. These were made on dilute solutions in benzene at 20°. Dielectric constants were measured by a heterodyne beat method, and refractive indices with a Pulfrich refractometer. The customary correction (of doubtful validity) of 5% of P_E for P_A was ignored as this would affect only the second decimal place in a moment as high as 2·3 D.

Preparations. *p*-Di-*tert.*-butylbenzene (20 g.) was mononitrated by the method of Carpenter, Easter, and Wood,[7] the crude product further nitrated by Boedtker's method, and the final product recrystallised from acetic acid. The first crops consisted of 1 : 4-di-*tert.*-butyl-2 : 5-dinitrobenzene, m. p. 191° (6 g.). From the later crops there was isolated 1 : 4-*di*-tert.-*butyl*-2 : 6-*dinitrobenzene*, which formed stout needles, m. p. 141° (1 g.) (Found : C, 60·1; H, 6·9. $C_{14}H_{20}O_4N_2$ requires C, 60·0; H, 7·1%). The final mother-liquors yielded pale yellow needles (1·6 g.), m. p. 74—90°, which were not examined further. The result was slightly less favourable when *p*-di-*tert.*-butylbenzene was dinitrated directly by Boedtker's method.

Reduction of 1 : 4-di-*tert.*-butyl-2 : 5-dinitrobenzene by iron powder in boiling ethanol with a little hydrochloric acid for 24 hr. gave a very dark diamine, which could not be obtained pure. With toluene-*p*-sulphonyl chloride in pyridine it gave a *ditoluene*-p-*sulphonyl derivative*, which readily crystallised from commercial *o*-dichlorobenzene in "solvated" needles, m. p. 272° (decomp.) (Found : C, 60·2; H, 5·9. $C_{28}H_{36}O_4N_2S_2,C_6H_4Cl_2$ requires C, 60·4; H, 5·9%). Above 170° the crystals became opaque and pure *p*-dichlorobenzene, m. p. and mixed m. p. 53°, was evolved (Found, after this treatment : C, 63·8; H, 6·7. $C_{28}H_{36}O_4N_2S_2$ requires C, 63·7; H, 6·8%). On addition of *N*-bromosuccinimide to an equal weight of this compound, dissolved in pyridine, a yellow precipitate began to separate. Precipitation was completed by addition of dilute hydrochloric acid, and the product recrystallised from *o*-dichlorobenzene to yield 1 : 4-*di*-tert.-*butyl*-2 : 5-*ditoluene*-p-*sulphonimidobenzene* (IV) in bright yellow prisms, m. p. 258—260° (decomp.) (Found : C, 63·6; H, 6·5. $C_{28}H_{34}O_4N_2S_2$ requires C, 63·9; H, 6·5%).

The authors are indebted to Dr. J. W. Minnis for the microanalyses and to the Carnegie Trust for the Universities of Scotland for a grant.

HERIOT-WATT COLLEGE, EDINBURGH. [*Received, December 12th*, 1955.]

375. *Phenoxyacetic Acid.*

By R. BRETTLE.

THE condensation of phenol and chloroacetic acid in aqueous alkali [1-3] gave poor yields of phenoxyacetic acid. This acid was, however, obtained in excellent yield from the hydrolysis of ethyl phenoxyacetate, which was prepared by the reaction of phenol with ethyl chloroacetate and sodium iodide in acetone, in the presence of potassium carbonate (cf. ref. 4).

The preparation of phenoxyacetone from phenoxyacetic acid by Blaise's general method [5] is also recorded.

Experimental.—Phenoxyacetic acid. Phenol (18·5 g., 1 mol.), ethyl chloroacetate (25 g., 1 mol.), sodium iodide (30 g., 1 mol.), and anhydrous potassium carbonate (28 g.) were refluxed for 12 hr. in dry acetone (100 ml.). The mixture was then stirred into a large volume of water, and the solution extracted with ether. Unchanged phenol (4·4 g.) was removed with aqueous alkali. Distillation then gave ethyl phenoxyacetate (21·8 g., 62%), b. p. 140—144°/24 mm., which was hydrolysed by 10% aqueous potassium hydroxide, affording phenoxyacetic acid (17·0 g., 90%), m. p. 99° (Koelsch [3] records m. p. 98—99°).

Phenoxyacetone. An ice-cold solution of phenoxyacetyl chloride [from thionyl chloride

[1] Mameli, *Gazzetta*, 1926, **56**, 762.
[2] van Alphen, *Rec. Trav. chim.*, 1926, **46**, 148.
[3] Koelsch, *J. Amer. Chem. Soc.*, 1931, **53**, 304.
[4] Mauthner, *J. prakt. Chem.*, 1937, **148**, 95.
[5] Blaise and Piccard, *Ann. Chim. phys.*, 1912, **26**, 274.

and the acid (8 g.) in benzene] in toluene (15 ml.) was gradually added to a vigorously stirred solution of methylzinc iodide [from methyl iodide (21 g.) and zinc–copper couple [6] (18 g.)] in toluene (20 ml.) and ethyl acetate (5 ml.). The mixture was then poured on ice. Phenoxyacetone (2·6 g., 32·5%), b. p. 127—128°/23 mm., was isolated by the usual procedure, and purified through its bisulphite compound.[7] The semicarbazone had m. p. 172° (from ethanol) (Stoemer [8] records m. p. 173°).

DEPARTMENT OF BIOCHEMISTRY, OXFORD UNIVERSITY. [*Received, December 14th*, 1955.]

[6] Howard, *J. Res. Nat. Bur. Stand.*, 1940, **24**, 677.
[7] Stoermer, *Ber.*, 1895, **28**, 1253.
[8] *Idem, Annalen*, 1900, **312**, 273.

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376. *The Preparation of* [^{14}C]*Dimethylamine and* [^{14}C]*Dimethylnitrosamine.*

By (MRS.) A. H. DUTTON and D. F. HEATH.

^{14}C-LABELLED dimethylamine and dimethylnitrosamine were prepared from labelled methyl iodide in high yield on a 0·1 g. scale. Excess of *N*-methyltoluene-*p*-sulphonamide was converted into its dimethyl homologue with methyl iodide in alcoholic potassium hydroxide; the dimethyl was separated from the methyl compound by extraction of the former with benzene from alkaline solution, and was hydrolysed. The dimethylamine released was separated by distillation from 2N-sodium hydroxide and estimated by titration (yield 78% on methyl iodide). The hydrochloride was concentrated to a small volume and converted nearly quantitatively into dimethylnitrosamine with sodium nitrite in glacial acetic acid. The product was separated and concentrated by distillation from 3N-sodium hydroxide, and estimated by the method of Heath and Jarvis.[1]

Trial runs presented two features of interest. First, the dimethyltoluene-*p*-sulphonamide melted at 80·6—81·1°, 6° lower than given by Steinkopf.[2] So we made the compound also from dimethylamine and toluene-*p*-sulphonyl chloride, and obtained a recrystallised product, m. p. 80·4—81·1°. Chaplin and Hunter [3] also give m. p. 80—81°, which therefore appears to be correct. Secondly, neither of the two known methods for hydrolysing sulphonamides is simple. Hinsberg [4] used concentrated hydrochloric acid at 150—160°, Fischer [5] concentrated hydriodic acid and phosphonium iodide at 100°. Dimethylamine is released quantitatively from dimethylsulphonamide by the action of concentrated hydriodic acid alone for 2 hr. at 100°. The method is relatively simple and safe, and should be applicable to the preparation of other amines.

Experimental.—*N*-Methyltoluene-*p*-sulphonamide, prepared by the method of Remsen and Palmer,[6] had m. p. 77·5—78·4°. Reverdin [7] gives m. p. 78—79°.

Labelled NN-*dimethyltoluene*-p-*sulphonamide.* Labelled methyl iodide (0·1 mc in 2·6 mg.), purchased from the Radiochemical Centre, Amersham, Bucks., was diluted with inactive methyl iodide in a vacuum manifold system. The total weight, calculated from the pressure in a bulb, was 247 mg. (1·74 mmoles). This was frozen by liquid nitrogen into a bulb containing methyltoluene-*p*-sulphonamide (370 mg., 2·0 mmoles), potassium hydroxide (130 mg., 2·28 mmoles), and 70% aqueous ethanol (4 ml.). The bulb was sealed under a vacuum and kept at 76° in a carbon tetrachloride vapour bath for 72 hr. The mixture was then transferred to a flask and concentrated. Sodium hydroxide (35 ml.; 3N) was added and the solution extracted with benzene (40 ml.). The benzene layer was washed with 3N-sodium hydroxide (15 ml.) and concentrated to dryness in a heavy-walled tube of 10 ml. capacity (yield, 270 mg., 78% on

[1] Heath and Jarvis, *Analyst*, 1955, **80**, 613.
[2] Steinkopf, *J. prakt. Chem.*, 1927, **117**, 25.
[3] Chaplin and Hunter, *J.*, 1937, 1114.
[4] Hinsberg, *Annalan*, 1891, **265**, 179.
[5] Fischer, *Ber.*, 1915, **48**, 93.
[6] Remsen and Palmer, *Amer. Chem. J.*, 1888, **8**, 241.
[7] Reverdin, *Ber.*, 1909, **42**, 1526.

methyl iodide). The purity of the labelled product was not checked. M. p.s were taken in trial runs, with the results already described.

Dimethylamine. Hydriodic acid (8 ml.; *d* 1·94) was added to the dimethylamide in the bulb, and the bulb was sealed and kept at 100° for 2 hr. in a steam-bath. The contents were then diluted and extracted with benzene to remove by-products. The benzene layer was washed with water, the aqueous layer and washings were treated with sodium hydroxide (12 g. per 100 ml. of solution), and half the solution was distilled into 0·1N-hydrochloric acid (15 ml.). The dimethylamine was estimated by titration after redistillation from sodium hydroxide solution (yield, 100% on dimethyltoluene-*p*-sulphonamide).

Dimethylnitrosamine. The dimethylamine solution was slightly acidified with hydrochloric acid and concentrated to 5 ml., and glacial acetic acid (5 ml.) and sodium nitrite (3 g.) were added and allowed to react for 10 min. at 25°. The product was diluted to 45 ml., sodium hydroxide (7 g.) added, and half the mixture distilled. The distillate contained the dimethylnitrosamine, which was estimated polarographically [1] (yield, 98·8 mg., 99% on dimethylamine, 77% on methyl iodide).

Identification and estimation of products. Dimethylnitrosamine was prepared as a dilute aqueous solution, from which it is not readily separated. The polarographic wave-form agreed with that of samples of known purity. Dimethylamine has been estimated by conversion into dimethylnitrosamine and polarographic estimation of the product.[3] In our experiments the estimation of dimethylnitrosamine constitutes an estimation of dimethylamine, and agrees within experimental error with the yield estimated by titration.

MEDICAL RESEARCH COUNCIL, TOXICOLOGY RESEARCH UNIT, SERUM RESEARCH INSTITUTE, WOODMANSTERNE ROAD, CARSHALTON, SURREY. [*Received, December 15th*, 1955.]

[3] English, *Analyt. Chem.*, 1951, **23**, 344.

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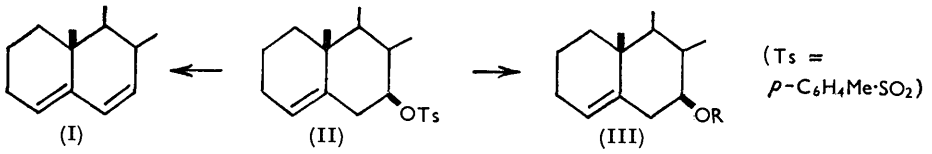
377. *Steroids and Walden Inversion. Part XXXI.* The Solvolysis of Cholest-4-en-7β-yl (ψ-Cholesteryl) Toluene-p-sulphonate.*

By C. W. SHOPPEE, G. H. R. SUMMERS, and R. J. W. WILLIAMS.

METHANOLYSIS of cholest-4-en-7β-yl (ψ-cholesteryl) toluene-*p*-sulphonate (II) in the presence or absence of potassium acetate has been shown [1] to yield cholesta-4 : 6-diene (I) and a methyl ether provisionally regarded as 7β-methoxycholest-4-ene (III; R = Me); the identity of the latter compound has now been confirmed by its demethylation to cholest-4-en-7β-ol (ψ-cholesterol) (III; R = H). Acetolysis of the ester (II) with acetic acid and potassium acetate furnished cholesta-4 : 6-diene (11%) (I) and cholest-4-en-7β-yl acetate (70%) (III; R = Ac); hydrolysis in aqueous acetone in the presence of potassium acetate yielded the diene (14·5%) (I) and the alcohol (78%) (III; R = H). Reduction of the toluenesulphonate (II) with lithium aluminium hydride gave cholest-4-ene (85%) unaccompanied by 5 : 7-*cyclo*cholestane (cf. Karrer and Schmid [2]).



(I) (II) (III)

It thus appears that reactions which convert 3β-substituted Δ^5-steroids into derivatives of 3 : 5-*cyclo*cholestane do not permit the conversion of cholest-4-en-7β-yl toluene-*p*-sulphonate into derivatives of 5 : 7-*cyclo*cholestane even though intervention of the π-electrons of the 4 : 5-double bond does occur to preserve configuration at $C_{(7)}$. The

* Part XXX, *J.*, 1956, 1649.

[1] Cremlyn, Rees, and Shoppee, *J.*, 1954, 3790.
[2] Karrer and Schmid, *Helv. Chim. Acta*, 1949, **32**, 1371.

predominant behaviour is replacement with retention of configuration [S_N1] accompanied by elimination [$E1$],[3,4] insofar as weakly nucleophilic agents are involved.

Experimental.—All rotations are in $CHCl_3$

Cholest-4-en-7β-yl toluene-*p*-sulphonate, m. p. 134—136°, $[\alpha]_D$ +19° (*c* 0·9), was refluxed with methanol and anhydrous potassium acetate (cf. Cremlyn *et al.*[1]). Chromatography of the product yielded cholesta-4 : 6-diene, m. p. 87—90°, $[\alpha]_D$ +9° (*c* 0·82), and an oily methyl ether, $[\alpha]_D$ +71° (*c*, 1·0), $\lambda_{max.}$ 211 mμ (log ε 3·41).

The methyl ether (155 mg.) in acetic acid (15 c.c.) and water (0·7 c.c.) was refluxed with hydrobromic acid (0·7 c.c.; 60%) for 1·5 hr. The dark red solution was diluted with water and extracted with ether. The ethereal extract, after being washed with saturated sodium hydrogen carbonate solution and water, yielded on evaporation a brown oil which was chromatographed on aluminium oxide (6 g.). Elution with pentane, benzene–pentane (1 : 9; 1 : 1), and benzene gave yellow oils, whilst elution with ether and ether–acetone (1 : 1) gave cholest-4-en-7β-ol (17 mg.), m. p. and mixed m. p. 118—121°, $[\alpha]_D$ +80° (*c* 0·7).

*Acetolysis of cholest-4-en-7β-yl toluene-*p*-sulphonate.* This toluene-*p*-sulphonate (500 mg.) and anhydrous potassium acetate (800 mg.) in acetic acid (24 c.c.) were heated at 95° under anhydrous conditions for 4 hr. The acetic acid was evaporated under reduced pressure and the product, a yellow oil (394 mg.), isolated in the usual way and chromatographed on neutralised aluminium oxide (Woelm; activity I; 24 g.); elution with pentane (12 × 20 c.c.) gave cholesta-4 : 6-diene (38 mg.), m. p. 88—89°, $[\alpha]_D$ +9° (*c* 0·3), whilst elution with benzene–pentane (1 : 1) (5 × 20 c.c.) and benzene (3 × 20 c.c.) gave cholest-4-en-7β-yl acetate (276 mg.), m. p. 94—96°, $[\alpha]_D$ +72° (*c* 0·92) (cf. Petersen and Chen [5]).

*Hydrolysis of the toluene-*p*-sulphonate.* The toluene-*p*-sulphonate (500 mg.) in acetone (35 c.c.) and water (9 c.c.) was refluxed with anhydrous potassium acetate (1·4 g.) for 9 hr. The solution was poured into water and the product isolated by means of ether. To ensure absence of acetate the product was refluxed with 5% ethanolic potassium hydroxide (20 c.c.) for 0·5 hr. Extraction with ether and working up in the usual way gave an oil (360 mg.), which was chromatographed on neutral aluminium oxide (Woelm; activity I; 11 g.). Elution with pentane (2 × 50 c.c.) gave cholesta-4 : 6-diene (49·5 mg.), m. p. 90°, $[\alpha]_D$ +4° (*c* 0·5), whilst elution with ether (2 × 50 c.c.) gave cholest-4-en-7β-ol (280 mg.), m. p. 121—124°, $[\alpha]_D$ +81° (*c* 0·82). No other product was isolated.

Reduction with lithium aluminium hydride. The toluene-*p*-sulphonate (500 mg.) in anhydrous ether (50 c.c.) was refluxed with lithium aluminium hydride for 17 hr. Working up in the usual way gave an oil (355 mg.), which was chromatographed on aluminium oxide (11 g.). Elution with pentane gave cholest-4-ene (300 mg.), m. p. and mixed m. p. 74—76°, $[\alpha]_D$ +58° (*c* 0·96); further elution with pentane gave an insignificant amount of material, whilst use of ether gave a trace of oil (7 mg.), and no detectable amount of cholest-4-en-7β-ol.

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[3] Shoppee and Westcott, *J.*, 1955, 1891, and references these cited.
[4] Pierce, Richards, Shoppee, Stephenson, and Summers, *J.*, 1955, 694.
[5] Petersen and Chen, *J. Amer. Chem. Soc.*, 1955, **77**, 2557.