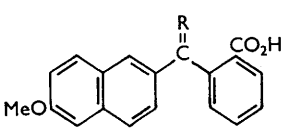
NOTES.

125. *The Synthesis of 3-Methoxybenz*[a]*anthracene and of 2-Methoxynaphthacene.*

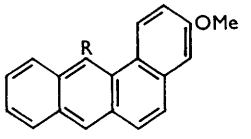
By D. C. C. SMITH.

o-(6-METHOXY-2-NAPHTHOYL)BENZOIC ACID (I) [1] was reduced to *o*-(6-methoxy-2-naphthylmethyl)benzoic acid (II). Cyclisation with zinc chloride in acetic anhydride gave 12-acetoxy-3-methoxybenz[*a*]anthracene (III), which on reduction by zinc and sodium hydroxide gave 3-methoxybenz[*a*]anthracene (IV).

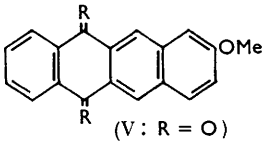
Cyclisation of *o*-(6-methoxy-2-naphthoyl)benzoic acid (I) in a melt of sodium chloride and aluminium chloride yielded after remethylation 8-methoxynaphthacene-5,12-quinone (V), which was reduced by zinc and sodium hydroxide to 6,11-dihydro-2-methoxynaphthacene (VI) and then dehydrogenated by chloranil to 2-methoxynaphthacene.



(I: R = O)
(II: R = H_2)



(III: R = OAc)
(IV: R = H)



(V: R = O)
(VI: R = H_2)

Previously, only benz[*a*]anthracenequinones have been isolated on cyclisation of *o*-(2-naphthoyl)benzoic acids,[2] though in these cases sulphuric acid was the cyclising agent. A different result to be obtained by using a melt of sodium chloride and aluminium chloride was foreshadowed by the direct preparation of naphthacenequinone from *o*-1-naphthoylbenzoic acid by this reagent.[1]

Experimental.—o-(6-*Methoxy*-2-*naphthylmethyl*)*benzoic acid.* *o*-(6-Methoxy-2-naphthoyl)-benzoic acid [1] (1 g.), a solution of sodium hydroxide (10 g.) in water (150 c.c.), zinc dust (30 g.; activated by shaking it with a solution of 1 g. of copper sulphate, then washed), and octanol (to arrest foaming) were refluxed for 48 hr. The mixture was cooled, filtered, washed with ether to remove octanol, then aerated to remove ether, and acidified with hydrochloric acid,

[1] Weizmann, Bergmann, and Bergmann, *J.*, 1935, 1367.
[2] " Elsevier's Encyclopaedia of Organic Chemistry," Vol. 14, Suppl., pp. 73S, 107S, lsevier, Amsterdam, 1951.

which precipitated o-(6-*methoxy*-2-*naphthylmethyl*)*benzoic acid* (0·78 g.), prisms (from ethanol), m. p. 161—164° (Found: C, 78·25; H, 5·75. $C_{19}H_{16}O_3$ requires C, 78·1; H, 5·5%).

12-*Acetoxy*-3-*methoxybenz*[a]*anthracene*. *o*-(6-Methoxy-2-naphthylmethyl)benzoic acid (0·59 g.), glacial acetic acid (10 c.c.), acetic anhydride (4 c.c.), and powdered zinc chloride (30 mg.) were heated under reflux for 1 hr., then poured into cold water and stirred for 5 min. The solid was collected, washed, dried and recrystallised from benzene: 12-*acetoxy*-3-*methoxybenz*[a]-*anthracene*, prisms (0·45 g.), m. p. 166—167° (Found: C, 79·8; H, 5·1. $C_{21}H_{16}O_3$ requires C, 79·73; H, 5·1%), was obtained.

3-*Methoxybenz*[a]*anthracene*. The foregoing acetate (0·36 g.) in pure dioxan (100 c.c.) was run into a suspension of activated zinc dust (80 g.) in 2N-sodium hydroxide (150 c.c.), and refluxed for 18 hr. The product was isolated with benzene, and chromatographed on alumina; light petroleum eluted oil, then benzene eluted 3-*methoxybenz*[a]*anthracene* (0·31 g.), plates (from ethyl acetate–methanol), m. p. 161—162°, principal $\lambda_{max.}$ (in EtOH) 288, 306, 343, 387 mμ (ε 79,800, 20,900, 7100, 1300) (Found: C, 88·65; H, 5·6. $C_{19}H_{14}O$ requires C, 88·3; H, 5·5%).

8-*Methoxynaphthacene*-5,12-*quinone*. *o*-(6-Methoxy-2-naphthoyl)benzoic acid (2·38 g.) was added to a melt of sodium chloride (10 g.) and aluminium chloride (40 g.), stirred and kept at 160—180° for 1 hr., then poured into ice and concentrated hydrochloric acid and warmed to induce solidification of the gum. The black solids were collected, washed, and extracted with cold dilute potassium hydroxide solution; the red extract was filtered and neutralised with carbon dioxide, a yellow solid being precipitated. This was collected, dried, dissolved in chloroform–methanol, freed from insoluble material, and treated with an excess of redistilled ethereal diazomethane. After 1 hr. at room temperature the mixture was evaporated to dryness and the residue was chromatographed in chloroform–benzene on alumina. Ether (2%) in benzene eluted 8-*methoxynaphthacene*-5,12-*quinone* (1·36 g.), recrystallised by dissolution in benzene and dilution with ethyl acetate, as orange-yellow flakes, m. p. 198—203° (Found: C, 78·6; H, 4·2. $C_{19}H_{22}O_3$ requires C, 79·15; H, 4·2%).

6,11-*Dihydro*-2-*methoxynaphthacene*. The methoxynaphthacenequinone (0·84 g.) and activated zinc dust (30 g.) were suspended in a solution of sodium hydroxide (8 g.) and sodium dithionite (2 g.) in water (100 c.c.) and refluxed for 18 hr. The mixture was cooled, and the product isolated with benzene and chromatographed on alumina; light petroleum eluted oil, then benzene eluted 6,11-*dihydro*-2-*methoxynaphthacene* (0·22 g.). Recrystallised twice from ethyl acetate, it had m. p. 205—206°, $\lambda_{max.}$ (in EtOH) 235, 265, 272, 317, 332 mμ (ε 70, 100, 5300, 5100, 1800, 2200) (Found: C, 87·45; H, 5·95. $C_{19}H_{16}O$ requires C, 87·7; H, 6·2%).

2-*Methoxynaphthacene*. 6,11-Dihydro-2-methoxynaphthacene (75 mg.) and chloranil (75 mg.) were refluxed in xylene under nitrogen for 1 hr., then cooled, diluted with benzene, washed twice with alkaline sodium dithionite solution and once with water, dried (Na_2SO_4), and evaporated. Recrystallisation of the residue from chloroform gave 2-*methoxynaphthacene* (45 mg.), orange plates showing green fluorescence in solution, m. p. 324—327°, principal $\lambda_{max.}$ (in $CHCl_3$–EtOH) 276, 280, 330, 349, 366, 386, 409, 434, 461, 532 mμ (ε 175,000, 153,000, 2500, 2000, 2600, 4500, 3600, 5900, 5400, 170) (Found: C, 88·1; H, 5·5. $C_{19}H_{14}O$ requires C, 88·3; H, 5·5%).

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126. 1,1′-*Biphenanthryl and the Structure of the Oxygenated Compound previously so Described.*

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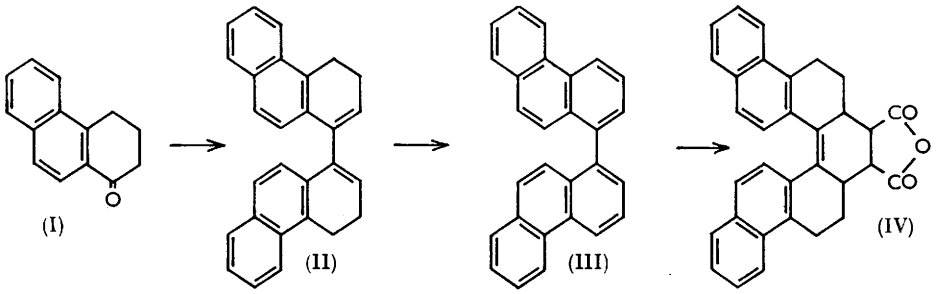
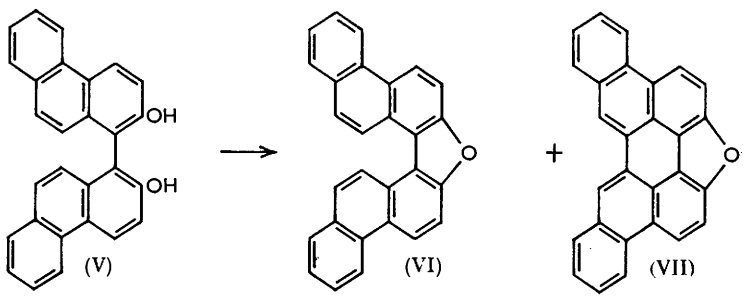
IN an attempt to prepare compounds containing the phenanthreno[2,1-*c*]chrysene system, as in (IV), 1,2,3,4-tetrahydro-1-oxophenanthrene (I) was subjected to pinacol reduction followed by dehydration, which gave 3,3′,4,4′-tetrahydro-1,1′-biphenanthryl (II). This diene on treatment with maleic anhydride did not give the expected adduct (IV), but instead gave a substance of unknown nature containing additional elements of water that could not be converted into the desired compound (IV). The failure of this diene to react normally with maleic anhydride is probably due to steric resistance to coplanarity of the two halves of the molecule.

The diene (II) was, however, readily dehydrogenated to 1,1′-biphenanthryl (III), m. p. 213°, so providing an unambiguous synthesis of the latter. Its structure is supported by the close similarity of its ultraviolet spectrum to that of phenanthrene, when the difference in molecular weight is allowed for (Fig. 1). There is a slight shift to the red and rather less fine structure.



A substance of m. p. 224—226°, claimed as 1,1′-biphenanthryl, was prepared by Yoffe.[1] His method was to distil 2,2′-dihydroxy-1,1′-biphenanthryl (V) with zinc dust, which has been shown in the case of the analogous 2,2′-dihydroxy-1,1′-binaphthyl to give, not 1,1′-binaphthyl, but dinaphtho[2,1 : 1′,2′-*bd*]furan, which has a m. p. only a few degrees higher than that of 1,1′-binaphthyl and has been confused with it.[2] It was therefore reasonable to suppose that Yoffe's compound would also contain oxygen. Its higher m. p. supports this and Yoffe admitted that his analytical results were unsatisfactory. We therefore prepared this compound according to his directions. Elementary analysis indicated that it contained oxygen while a mixed m. p. determination and its absorption of ultraviolet light (Fig. 1) showed that it was different from our 1,1′-biphenanthryl. It is certainly diphenanthro[2,1 : 1′,2′-*bd*]furan (VI).



Yoffe obtained also a by-product of m. p. 315° in the zinc dust distillation, which he claimed to be dibenzo[*b*,*n*]perylene, and pointed out rightly, as is now known,[3, 4, 5] that Clar's 2,3 : 10,11-dibenzoperylene [6] was in reality the 2,3 : 8,9-compound (dibenzo[*fg*,*qr*]-pentacene). Dibenzo[*bn*]perylene has since been prepared and accorded the m. p. 343—345°,[3] 329—332°,[4] 334—336°,[7] and 330—332°.[8] We suspected that Yoffe's by-product was neither of these but an oxygenated compound, 4,5 : 8,9-dibenzoperylo[6,7-*bcd*]furan (VII). Although we obtained only a very small amount of the purified substance, m. p.

[1] Yoffe, *Zhur. obshchei Khim.*, 1933, **3**, 524.
[2] Schoepfle, *J. Amer. Chem. Soc.*, 1923, **45**, 1566.
[3] Zinke and Ziegler, *Ber.*, 1941, **74**, 115.
[4] Schauenstein and Bürgermeister, *Ber.*, 1943, **76**, 205.
[5] Clar, " Aromatische Kohlenwasserstoffe," 2nd edn., Springer, Berlin, 1952, p. 310.
[6] Clar, *Ber.*, 1932, **65**, 846.
[7] Badger, Christie, Pryke, and Sasse, *J.*, 1957, 4417.
[8] Clar and Zander, *J.*, 1958, 1861.

313—315°, its elementary analysis supported this structure. Its ultraviolet absorption spectrum resembles, but is distinct from, that of dibenzo[*bn*]perylene in that the two main peaks around 400 mμ are less intense and those in the 300 mμ region are displaced to the red (Fig. 2). In its infrared absorption spectrum there are strong bands at 1015 and 1240

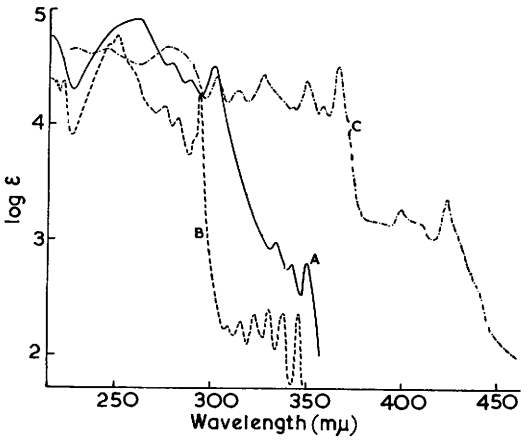


FIG. 1. Ultraviolet spectra of (A) 1,1′-biphenanthryl in hexane, (B) phenanthrene in cyclohexane (curve given by Friedel and Orchin, " Ultraviolet Spectra of Aromatic Compounds," Chapman and Hall, London, 1951), and (C) diphenanthro[2,1 : 1′,2′-*bd*]furan in hexane.

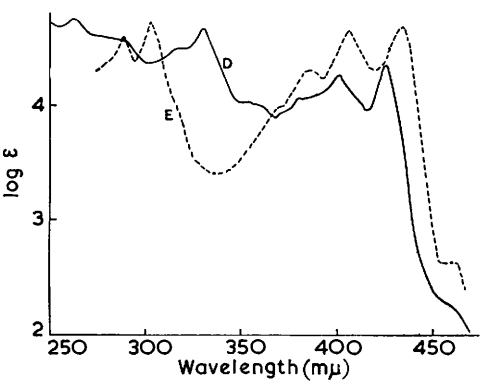


FIG. 2. Ultraviolet spectra of (D) 4,5 : 8,9-dibenzoperylo[6,7-*bcd*]furan in chloroform and (E) dibenzo[*bn*]perylene in benzene (*op. cit.* and refs. 4 and 5).

cm.$^{-1}$ which are also present in the spectrum of the analogous dinaphtho[2,1 : 1′,2′-*bd*]furan but not in that of 1,1′-biphenanthryl. The 1240 cm.$^{-1}$ band is reported to be characteristic of aryl ethers.[9]

Experimental.—*3,3′,4,4′-Tetrahydro-1,1′-biphenanthryl.* 1,2,3,4-Tetrahydro-1-oxophenanthrene (5 g.), prepared by Haworth's method,[10] in dry benzene (20 ml.) and dry ethanol (30 ml.), was treated with aluminium foil (2 g.) and mercuric chloride (0·2 g.) and refluxed for 3 hr. (until solid). Dry ethanol (30 ml.) was added and refluxing continued for another 8 hr. The cooled product was treated with ice and then concentrated hydrochloric acid to dissolve precipitated material, and was extracted with benzene, and the extract was washed with acid and then brine. On removal of the benzene the residue was refluxed with acetic acid (150 ml.) for 3 hr. to dehydrate the pinacol. On cooling, the *diene* (II) (2·3 g.) separated; recrystallised from acetic acid–acetic anhydride and finally from benzene it had m. p. 243—244° (Found: C, 93·9; H, 6·3. $C_{28}H_{22}$ requires C, 93·8; H, 6·2%). On treatment with maleic anhydride this diene gave a pale yellow *product*, m. p. 288—289° (from acetic anhydride) (Found: C, 81·0; H, 5·7. $C_{32}H_{26}O_4$ requires C, 81·0; H, 5·5%).

1,1′-Biphenanthryl. The diene (II) (1 g.) was heated with sulphur (0·3 g.) and palladium–charcoal [11] (0·1 g.) at 300—310° for 7 min. Extraction of the product with chloroform gave *1,1′-biphenanthryl* which after two recrystallisations from benzene had m. p. 213—213·5°, forming colourless needles (0·21 g.) (Found: C, 95·1; H, 5·2. $C_{28}H_{18}$ requires C, 94·9; H, 5·1%).

Diphenanthro[2,1 : 1′,2′-bd]*furan* (cf. Yoffe [1]). 2,2′-Dihydroxy-1,1′-biphenanthryl (1 g.) was heated with zinc dust, not in a retort, but in a flask fitted with a cold-finger condenser. A very small amount of sublimate was obtained. Its benzene solution was extracted with alkali to remove starting material. On concentration and cooling, yellow crystals separated

[9] Bellamy, " The Infra-red Spectra of Complex Molecules," 2nd edn., Methuen, London, 1958, p. 117.
[10] Haworth, *J.*, 1932, 1125.
[11] Blair, Crawford, Spence, and Supanekar, *J.*, 1960, 3313.

(m. p. 270—290°). On further concentration a second crop was obtained (0·22 g.), which after four recrystallisations from light petroleum (b. p. 80—100°) gave *diphenanthro*[2,1 : 1′,2′-bd]-*furan* as yellow needles, m. p. 228—229° (Found: C, 91·6; H, 4·4. $C_{28}H_{16}O$ requires C, 91·3; H, 4·4%. Yoffe [1] obtained colourless needles, m. p. 224—226° (Found: C, 93·91; H, 4·52%).

4,5 : 8,9-*Dibenzoperylo*[6,7-bcd]*furan*. The foregoing first crop was recrystallised from xylene twice, giving the *furan* as dull yellow needles (5 mg.), m. p. 313—315° (Found: C, 90·6; H, 3·85. $C_{28}H_{14}O$ requires C, 91·8; H, 3·85%). Yoffe's product formed yellow needles, m. p. 315° (uncorr.), but he analysed material of m. p. 315—318° (uncorr.), which he obtained in a different way, namely, by treatment of dihydroxybiphenanthryl with aluminium chloride followed by zinc distillation, and which he assumed, without making a mixed m. p. determination, to be the same (Found: C, 95·89; H, 4·14. Calc. for $C_{28}H_{16}$: C, 95·42; H, 4·58%). In spite of this we consider that his preparations of m. p. 315° and 315—318° consisted of dibenzoperylofuran.

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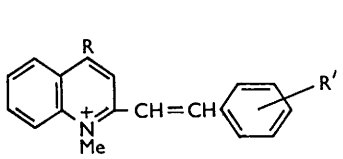
127. *The Search for New Trypanocides. Part VII.*[1] m-*Amidinophenyldiazoaminostyrylquinolinium Salts.*

By S. S. BERG.

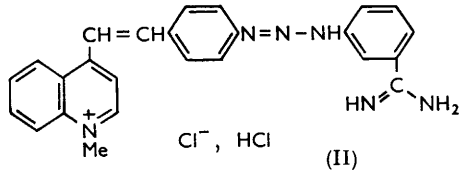
Diazotised 2- and 4-aminostyrylquinolinium salts couple with *m*-aminobenzamidine hydrochloride to give diazoamino-compounds possessing significant babesicidal and trypanocidal activity.

THE trypanocidal activity of a series of 6-substituted 2-styrylquinolinium salts was reported by Browning *et al.*[2] In view of the significant babesicidal and trypanocidal activity of *m*-amidinophenyldiazoamino-quinolinium and -quinazolinium salts,[1] it seemed possible that the introduction of a *m*-amidinophenyldiazoamino-group into similar styrylquinolinium salts might give compounds with interesting biological activity.

The 2- and 4-aminostyrylquinolinium salts were prepared by condensation of the appropriate acetamidobenzaldehyde with the methylquinolinium salt, followed by acid hydrolysis. The products were then diazotised and coupled with *m*-aminobenzamidine hydrochloride, giving the diazoamino-compounds (I) and (II) as water-soluble salts. Their structures were confirmed by evolution of 1 mol. of nitrogen when the compounds were heated with cuprous chloride and 3N-hydrochloric acid.



(I) Cl^-, HCl



Cl^-, HCl (II)

(Ia) R = H, R′ = 3-*m*-amidinophenyldiazoamino. (Ib) R = H or NH_2, R′ = 4-*m*-amidinophenyldiazoamino.

All the products were active against *Trypanosoma rhodesiense*, *T. congolense*, and *Babesia rodhaini* on subcutaneous injection in mice.[3] The most active was 2-4′-*m*-amidinophenyldiazoaminostyryl-1-methylquinolinium chloride hydrochloride (Ia) which had:

[1] Part VI, Berg, *J.*, 1961, 4041.
[2] Browning, Cohen, Ellingworth, and Gullbransen, *Proc. Roy. Soc.*, 1929, *B*, **105**, 99.
[3] Wragg, Washbourn, Brown, and Hill, *Nature*, 1958, **182**, 1005 (method for *T. congolense* and *T. rhodesiense*); Lucas, *Res. Vet. Sci.*, 1960, **1**, 268 (method for *B. rodhaini*).

CD50 0·05 mg./g. (*T. congolense*) and 0·0025 mg./g. (*T. rhodesiense*); ED50 (*B. rodhaini*) 0·019 mg./g.; LD50 1·0 mg./g.

Experimental

Water of crystallisation was determined by the Karl Fischer method.

2-4′-Acetamidostyryl-1-methylquinolinium Methyl Sulphate.—1,2-Dimethylquinolinium methyl sulphate [4] (78 g.), *p*-acetamidobenzaldehyde (49 g.), piperidine (5 ml.), and ethanol (250 ml.) were refluxed together overnight, then cooled in ice. The crystalline salt was collected, washed with ethanol and acetone, and dried at 90°. Recrystallisation from water gave the *salt* (101 g., 83%) as orange needles, m. p. 297—298° (decomp.) (Found: N, 6·75; S, 7·85. $C_{21}H_{22}N_2O_5S$ requires N, 6·75; S, 7·7%). Compounds similarly prepared were: *2-3′-acetamidostyryl-1-methylquinolinium methyl sulphate*, yellow needles (61%) (from water), m. p. 240—242° (Found: N, 6·8; S, 8·05. $C_{21}H_{22}N_2O_5S$ requires N, 6·75; S, 7·7%), and *4-4′-acetamidostyryl-1-methylquinolinium methyl sulphate* (from 1,4-dimethylquinolinium methyl sulphate [5]), golden needles (74%) (from methanol), m. p. 274—275° (decomp.) (Found: N, 6·65; S, 7·6. $C_{21}H_{22}N_2O_5S$ requires N, 6·75; S, 7·7%).

4-Acetamido-1,2-dimethylquinolinium Methyl Sulphate.—4-Acetamidoquinaldine [6] (20 g.) was heated with methyl sulphate (10 ml.) in anhydrous nitrobenzene (200 ml.) for 1 hr. on the steam bath. The *product* separated on cooling and after recrystallisation from ethanol formed colourless prisms (25 g., 76%), m. p. 219—220° (Found: N, 8·6; S, 10·0. $C_{14}H_{18}N_2O_5S$ requires N, 8·6; S, 9·8%).

4-Acetamido-2-4′-acetamidostyryl-1-methylquinolinium Chloride.—4-Acetamido-1,2-dimethylquinolinium methyl sulphate (38 g.), *p*-acetamidobenzaldehyde (20 g.), piperidine (1·6 ml.), and ethanol (100 ml.) were refluxed together for 1 hr. The hot mixture was filtered, and the orange solid was washed with ethanol and dissolved in hot water (1·2 l.) Addition of hot saturated aqueous sodium chloride (600 ml.) then gave the *quinolinium chloride* (27 g., 53%) as orange needles, m. p. 294° (decomp.) (Found: Cl, 8·55; N, 9·9; H_2O, 9·0. $C_{22}H_{22}ClN_3O_2,2{\cdot}25H_2O$ requires Cl, 8·2; N, 9·65; H_2O, 9·3%).

2-4′-Aminostyryl-1-methylquinolinium Chloride Hydrochloride.—2-4′-Acetamidostyryl-1-methylquinolinium methyl sulphate (20 g.) was refluxed with 5N-hydrochloric acid (200 ml.) for 2 hr., then cooled in ice. The solid was filtered off and crystallised from 2N-hydrochloric acid (480 ml.), giving the *chloride hydrochloride* (13·2 g., 78%) as orange needles, m. p. 252° (decomp.) (softens 160°) (Found: Cl, 20·4; N, 8·15; H_2O, 5·1. $C_{18}H_{18}Cl_2N_2,H_2O$ requires Cl, 20·2; N, 8·0; H_2O, 5·15%).

Similar reactions gave *2-3′-aminostyryl-1-methylquinolinium chloride hydrochloride*, brown needles (88%) (from 2N-hydrochloric acid), m. p. 262—264° (decomp.) (Found: Cl, 19·4; N, 8·0; H_2O, 7·25. $C_{18}H_{18}Cl_2N_2,1{\cdot}5H_2O$ requires Cl, 19·6; N, 7·6; H_2O, 7·5%), *4-4′-aminostyryl-1-methylquinolinium chloride hydrochloride*, red prisms (98%) (from ethanol–acetone), m. p. 278° (decomp.) (Found: Cl, 18·6; N, 7·7; H_2O, 11·9. $C_{18}H_{18}Cl_2N_2,2{\cdot}5H_2O$ requires Cl, 18·8; N, 7·45; H_2O, 12·0%), and *4-amino-2-4′-aminostyryl-1-methylquinolinium chloride hydrochloride* (from 4-acetamido-2-4′-acetamidostyryl-1-methylquinolinium chloride) (96%), pale yellow prismatic needles, m. p. 304° (decomp.) (Found: Cl, 19·4; N, 11·4; H_2O, 5·0. $C_{18}H_{19}Cl_2N_3,H_2O$ requires Cl, 19·5; N, 11·6; H_2O, 4·95%).

Coupling Reaction.—The aminostyrylquinolinium salt (0·1 mol.), suspended in N-hydrochloric acid (600 ml.), was diazotised at 5—8° by the addition of sodium nitrite (7·5 g.), and the mixture was stirred at 5—8° for 1 hr. and treated with sulphamic acid to destroy the excess of nitrous acid. A solution of *m*-aminobenzamidine monohydrochloride dihydrate [7] (21 g.) in 2N-hydrochloride acid (40 ml.) and water (60 ml.) was quickly added, followed dropwise by sodium acetate (105 g.) in water (305 ml.). The red solution (or suspension) was stirred at 5—10° for 1 hr., then sodium chloride (51 g.) was added. The red granular solid was filtered off, washed with saturated sodium chloride, and recrystallised. The *products* (pale red or orange) are listed in the Table.

[4] Meisenheimer and Stotz, *Ber.*, 1925, **58**, 2332.
[5] Willems and Nys, *Bull. Soc. chim. belges*, 1957, **66**, 502.
[6] Austin, Potter, and Taylor, *J.*, 1958, 1489.
[7] Easson and Pyman, *J.*, 1931, 2991.

2(or 4)-[3-*m*(or 4-*m*)-Amidinophenyldiazoaminostyryl]-1-methylquinolinium chloride hydrochlorides.

				Yield	Found (%)				Required (%)		
No.	R	Cryst. from	M. p.*	(%)	Cl	N	H_2O	Formula	Cl	N	H_2O
Ib	H	60% w/v Aq.EtOH	229°	70	12·9	16·8	13·25	$C_{25}H_{24}Cl_2N_6,4H_2O$	12·9	15·2	13·1
Ia	H	75% w/v Aq.EtOH	217	37	13·4	15·5	9·7	$C_{25}H_{24}Cl_2N_6,3H_2O$	13·3	15·75	10·1
Ib	NH_2	50% w/v Aq.EtOH	238—240	58	11·6	16·45	16·9	$C_{25}H_{25}Cl_2N_7,5·5H_2O$	11·9	16·5	16·7
II		$MeOH–COMe_2$	238	53	13·95	16·8	3·8	$C_{25}H_{24}Cl_2N_6,H_2O$	14·2	16·85	3·6

* With decomp.

The author thanks Dr. J. N. Ashley, F.R.I.C., for his interest, Mr. S. Bance, B.Sc., F.R.I.C., for the analyses, and Mr. K. N. Brown, B.Sc., Mr. J. Ford-Robertson, B.Sc., and Mr. J. M. S. Lucas, M.R.C.V.S., Dip. Bac., for the biological tests.

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128. *Composition and Solubility of Cerium*(III) *Chloride Alcoholates.*

By F. R. HARTLEY and A. W. WYLIE.

ALTHOUGH the solubility of several anhydrous lanthanon chlorides in alcoholic and other solvents has been measured by Hopkins and Quill [1] and by Matignon,[2] no such data are available for cerium(III) chloride and in few instances have the compositions of the solid phases been established. Earlier knowledge of the lanthanon chloride alcoholates is compared in the first Table with similar data for yttrium and scandium chloride.

The number n of solvate molecules in lanthanon chloride alcoholates, $LnCl_3,n$ROH.

R	La [3,4]	Ce [3]	Nd [2]	Y [2]	Ln [4]	Sc [5]
Me						4 & 3
Et	3 & 2	3	3 & 1	1	3	3 & 2
Pr^n						3 & 2
Bu^n						3 & 2
n-Pentyl						3 & 2
n-Hexyl						3 & 2
Pr^i						1
Bu^t						2

The second Table presents the results of solubility determinations for anhydrous cerium(III) chloride in various aliphatic alcohols and gives the composition of the solid phases where these have been identified. The solubilities of mixed lanthanon chlorides $LnCl_3$, where Ln comprises La 25·6, Ce 45·2, Pr 5·6, Nd 19·9, and Sm 3·75%, are also given.

The solubility of cerium chloride and of the mixed lanthanon chlorides in the normal aliphatic alcohols is seen to decrease from methyl to propyl alcohol, rise at butyl alcohol, and thereafter decrease progressively at least to decyl alcohol. Solubilities are very much smaller in branched-chain than in the corresponding straight-chain alcohols.

The alcoholates are well crystallised compounds, separable from their viscous solutions with some difficulty. Cerium chloride forms trialcoholates with the normal aliphatic alcohols up to pentyl alcohol. With isopropyl alcohol it forms a dialcoholate, but with

[1] Hopkins and Quill, *Proc. Nat. Acad. Sci. U.S.A.*, 1933, **19**, 64.
[2] Matignon, *Ann. Chim. Phys.*, 1906, **8**, 243, 270.
[3] Sheka and Kriss, *Russ. J. Inorg. Chem.*, 1959, **4**, 816.
[4] Meyer and Koss, *Ber.*, 1902, **35**, 2622.
[5] Petrů, Hájek, and Jost, *Croat. Chem. Acta*, 1957, **29**, 457.

Solubility of $CeCl_3$ and of mixed lanthanon chlorides $LnCl_3$ in aliphatic alcohols at 25° ± 0·05°.

	$CeCl_3$ (g./100 g. of soln.)	Solid phase	$LnCl_3$ (g./100 g. of soln.)
Me	39·4 ± 0·2	*	38·4 ± 0·2
Et	27·6 ± 0·2	$CeCl_{3\cdot00}(C_2H_5OH)_{3\cdot11}$	28·8 ± 0·3
Pr^n	25·4 ± 0·3	$CeCl_{2\cdot98}(C_3H_7OH)_{3\cdot10}$	26·7 ± 0·3
Bu^n	34·5 ± 0·2	$CeCl_{3\cdot05}(C_4H_9OH)_{3\cdot07}$	33·0 ± 0·5
n-Pentyl	29·6 ± 0·2	$CeCl_{3\cdot10}(C_5H_{10}OH)_{3\cdot14}$	29·9 ± 0·3
n-Hexyl	26·8 ± 0·4		25·3 ± 0·4
n-Octyl			15·8 ± 0·4
n-Nonyl			8·5 ± 0·2
n-Decyl			5·3 ± 0·1
Pr^t	4·2 ± 0·1	$CeCl_{3\cdot01}(C_3H_7OH)_{2\cdot20}$	
Bu^t	0·5 ± 0·05	$CeCl_3$	

* Compound unstable, but molar ratio $CH_3{\cdot}OH{:}CeCl_3$ probably 4 (see text).

t-butyl alcohol no addition compound is formed. The methyl alcoholates of cerium chloride were investigated by determining the vapour pressure–composition isotherm at 21·3° ± 0·1°. Four equilibrium stages, and a possible fifth, were recognised: at 72·5 mm., corresponding to the saturated solution; at ~71·0 mm., a slight flattening of the curve, which may indicate a labile tetra-alcoholate; at 45·5 mm., corresponding to the tri-alcoholate; at 19·2 mm., corresponding to the dialcoholate; and at ~0·5 mm., corresponding to the monoalcoholate. Thus cerium chloride may combine, according to circumstances, with from one to four molecules of aliphatic alcohol, whereas scandium chloride, according to Petrů *et al.*,[5] forms no monoalcoholate with the normal alcohols.

Experimental.—Cerium chloride was prepared by treating anhydrous cerium benzoate with anhydrous ethyl ether saturated with gaseous hydrogen chloride. Brauman and Takvorian [6] claim that the product of this operation is anhydrous cerium chloride, but a *monoetherate* was isolated at this stage (Found: Ce, 43·4; Cl, 33·4; ether, 22·7. $CeCl_3,C_4H_{10}O$ requires Ce, 43·6; Cl, 33·2; $C_4H_{10}O$, 23·2%). No similar compounds have been reported in the literature. The etherate was converted into anhydrous cerium chloride at 130° in a slow current of nitrogen at 100 mm. The mixed, anhydrous lanthanon chlorides were obtained by chlorination of monazite.[7]

Alcohols were purified before use. Methyl alcohol was treated with sulphanilic acid to remove amines and fractionally distilled over freshly ignited calcium oxide. Ethyl alcohol was dried with aluminium amalgam. Propyl, butyl, pentyl, and hexyl alcohol were distilled from drying agents and fractionated. Benzene was added to t-butyl alcohol to permit separation of water as a ternary azeotrope, b. p. 67·3°; fractional crystallisation finally gave a product of m. p. 25·5°.

Special precautions were taken to exclude moisture during solubility determinations since water notably increased the solubility of lanthanon chlorides in the lower alcohols and decreased the solubility in butyl and pentyl alcohol. Tubes containing the components were sealed with a flame before being shaken in a thermostat bath. Several solubility determinations were carried out with each alcohol and equilibrium was approached from above and below 25° since there was a considerable tendency to supersaturation, especially with the higher alcohols. The saturated solutions were sampled through a preheated filter-tube fitted with a sintered-glass disc. Solids were filtered on sintered glass in a blanket of dry air. At least one sample of each solid was rapidly washed with dry light petroleum to remove adhering mother-liquor. Observations with a microscope and solubility tests established that this procedure did not alter the composition of the solid alcoholate.

Methyl and ethyl alcohol were determined by refluxing the alcoholates with potassium dichromate–sulphuric acid and back-titrating the excess of dichromate. The higher alcohols were determined by difference after gravimetric determination of cerium (or mixed lanthanons) and chloride. Ether in the etherate was determined by keeping the compound *in vacuo* and

[6] Brauman and Takvorian, *Compt. rend.*, 1932, **194**, 1579.
[7] Hartley, *J. Appl. Chem.*, 1952, **2**, 24.

weighing the amount of ether caught in a liquid-air trap. Praseodymium, neodymium, and samarium in the mixed " light " lanthanons were determined spectrophotometrically;[8] cerium was determined volumetrically and lanthanum by difference.

This work was carried out in 1950 when F. R. H. was employed by the Commonwealth Scientific and Industrial Research Organisation.

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[8] Wylie, *J. Soc. Chem. Ind.*, 1950, **69**, 143.

129. *The O-Alkylation of Cyclohexane-1,2-dione.*

By M. S. GIBSON.

THE successful use of 5,5,9-trimethyl-*trans*-decal-1-one (or 6-oxygenated derivatives thereof) for the synthesis of various di- and tri-terpenes depends on the oxygenation of $C_{(2)}$ at some stage.[1] A possible approach involves oxidation by selenium dioxide to the 1,2-dioxodecalin, followed by ethynylation of the dione enol ether to elaborate the side chain at position 1; the 2-ketone group would later be regenerated by treatment with acid. As a model, the alkylation of cyclohexane-1,2-dione was studied.

Direct methylation gave two neutral products: 2-methoxycyclohex-2-enone (11%), which could not be obtained analytically pure; and a crystalline compound, $C_{13}H_{18}O_4$ (6·5%), probably 3-(1-hydroxy-2-oxocyclohexyl)-2-methoxycyclohex-2-enone arising from the dione by aldolisation and methylation. Benzylation gave only one neutral product, 2-benzyloxycyclohex-2-enone, in 35% yield. Sodium acetylide in ammonia converted this into the ethynyl alcohol which was isolated without concomitant dehydration;[2] acid hydrolysis of the latter compound gave only a gum from which no 2-ethynyl-2-hydroxycyclohexanone could be isolated.

Experimental.—Analyses were by Mr. E. Meyer; ultraviolet spectra were measured for ethanol solutions.

Cyclohexane-1,2-dione was freshly prepared[3] and had m. p. 30°, $\lambda_{max.}$ 264 mμ (log ε 3·86); addition of base gave $\lambda_{max.}$ 310 mμ (log ε 3·7).

2-*Methoxycyclohex-2-enone*. Methyl iodide (80 g.) was added to a stirred mixture of cyclohexane-1,2-dione (16 g.), freshly ignited potassium carbonate (80 g.), and " AnalaR " acetone (500 ml.). The stirred mixture was boiled for 4 hr., small amounts of methyl iodide being added from time to time, the ferric chloride test then becoming negative. The cooled mixture was filtered and the solid was washed with acetone. Filtrate and washings were evaporated *in vacuo*, and the residue was extracted with ether. The ether extract was washed with 2N-potassium hydroxide and water, dried, and evaporated. The residue (5·2 g.) was adsorbed on alumina from benzene–pentane; elution gave (i) impure 2-methoxycyclohex-2-enone (2 g.) as an oil; benzene eluted (ii) oil (0·5 g., discarded); and ether eluted a solid fraction (iii) (1·15 g.).

Fraction (i) contained a saturated ketonic impurity, partially removed on further chromatography; the desired *ketone*, which was concentrated into the later fractions, had b. p. (bath) 100—117°/20 mm., n_D^{20} 1·5084 (Found: C, 64·2, 64·0; H, 7·8, 7·9; MeO, 11·0. $C_7H_{10}O_2$ requires C, 66·6; H, 8·0; 1MeO, 11·9%), $\lambda_{max.}$ 259 mμ (log ε 3·79), $\nu_{max.}$ 1630 and 1677 and shoulder (impurity) 1712 cm.$^{-1}$ (in $CHCl_3$). The 2,4-*dinitrophenylhydrazone* separated from ethanol as red needles, m. p. 173—175° (Found: C, 51·1, 51·1; H, 4·4, 4·5; N, 18·6; MeO, 5·1. $C_{13}H_{14}N_4O_5$ requires C, 51·0; H, 4·6; N, 18·3; 1MeO, 4·9%), $\lambda_{max.}$ 375 mμ (log ε 4·51).

Three cystallisations of fraction (iii) from benzene–light petroleum (b. p. 60—80°) gave rhombs, m. p. 127° [Found: C, 65·7, 65·6; H, 7·7, 7·7; MeO, 6·2; active H (toluene; hot),

[1] Danieli, Mazur, and Sondheimer, *Tetrahedron Letters*, 1961, 310.
[2] Ansell and Ducker, *J.*, 1959, 329.
[3] *Org. Synth.*, 1952, **32**, 35.

0·42%; *M* (camphor), 221. $C_{13}H_{18}O_4$ requires C, 65·5; H, 7·6; 1MeO, 6·3; 1 active H, 0·42%; *M*, 238], $\lambda_{max.}$ 249 mμ (log ε 3·93), $\nu_{max.}$ 1630 (C=C), 1680 (conjugated C=O), 1712 (C=O), and 3515 cm.$^{-1}$ (OH) (in $CHCl_3$). This substance, probably 3-(1-*hydroxy*-2-*oxocyclohexyl*)-2-*methoxycyclohex*-2-*enone*, gave no colour with ethanolic ferric chloride and was unaffected by acetic anhydride–pyridine at room temperature; it was rapidly attacked by ethanolic sodium ethoxide with formation of dark acidic products.

In a similar experiment but without methyl iodide, cyclohexane-1,2-dione (1 g.) gave a neutral yellow gum (125 mg.), $\lambda_{max.}$ 286 mμ (log ε 1·24).

2-*Benzyloxycyclohex*-2-*enone*. Freshly distilled benzyl chloride (11 g.) was stirred under reflux with sodium iodide (13·5 g.) in acetone (300 ml.) for 15 min. Potassium carbonate (40 g.) was added to the cooled mixture, followed by cyclohexane-1,2-dione (9·25 g.) in acetone (75 ml.). The mixture was stirred and refluxed for 4 hr., though the ferric chloride test was negative after 1 hr. Isolation of neutral products as above gave a brown lachrymatory oil (19·9 g.). This was adsorbed on alumina, and the excess of benzyl iodide (6·3 g.) was eluted with pentane; benzene–ether (1 : 1) then eluted an oil (8·4 g.) which was further chromatographed on alumina, yielding a series of oily fractions (totalling 3·2 g.) eluted with pentane–benzene and finally benzene, and solid fractions (3·9 g.) eluted with benzene–ether (9 : 1). Further chromatography of the oil gave a further quantity of solid (1 g.). The crude 2-*benzyloxycyclohex*-2-*enone* (4·9 g.) had m. p. 38—42° and gave no colour with ferric chloride. Four crystallisations from light petroleum (b. p. 40—60°) gave needles, m. p. 55—56° (Found: C, 77·4; H, 7·1. $C_{13}H_{14}O_2$ requires C, 77·2; H, 7·0%), $\lambda_{max.}$ 258 mμ (log ε 3·91), $\nu_{max.}$ 1630 and 1678 cm.$^{-1}$ (in $CHCl_3$). The ether eluates from the chromatograms afforded only gums.

2-*Benzyloxy*-1-*ethynylcyclohex*-2-*ene*-1-*ol*. 2-Benzyloxycyclohex-2-enone (2 g.) in dry ether (30 ml.) was added to a stirred solution of sodium acetylide (from 2 g. of sodium) in liquid ammonia (150 ml.) cooled to −35° to −40°. After 4½ hr. at this temperature, ammonium chloride (10 g.) was added. The ammonia was allowed to evaporate, and ether and water were added. The ether extract was washed with 5% hydrochloric acid, sodium hydrogen carbonate solution, and water, dried, and evaporated, leaving a brown oil (2 g.). This was chromatographed on alumina in pentane, giving recovered starting material (260 mg.), eluted with benzene–ether (9 : 1), and thick oily fractions (totalling 1·33 g.), eluted with benzene–ether (1 : 1) and finally with ether, which gave on distillation 2-*benzyloxy*-1-*ethynylcyclohex*-2-*enol*, b. p. (bath) 120°/0·1 mm. (Found: C, 79·3; H, 7·2; acetylenic H, 0·42. $C_{15}H_{16}O_2$ requires C, 78·9; H, 7·1; 1 acetylenic H, 0·44%), $\nu_{max.}$ 1662, 3320, and 3622 cm.$^{-1}$ (in $CHCl_3$).

2-Benzyloxycyclohex-2-enone was recovered unchanged after attempted reaction with sodium acetylide in liquid ammonia at −50°.

Attempted preparation of 2-*ethynyl*-2-*hydroxycyclohexanone*. The acetylenic alcohol (202 mg.) was left for 20 hr. in dioxan (2·2 ml.) and 2N-sulphuric acid (0·8 ml.) at room temperature. Ether and water were added, and the ether solution was washed with sodium hydrogen carbonate solution and water, dried, and evaporated, giving a yellowish oil (200 mg.), $\nu_{max.}$ 1675, 1730, 3335, and 3535 cm.$^{-1}$ (in $CHCl_3$). Attempts to separate the desired product through Girard T reagent or through the silver derivative were unsuccessful.

The author thanks Professor F. Sondheimer for interesting discussions relating to this work, which was carried out during tenure of a Weizmann Memorial Fellowship.

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130. *The Synthesis of Disulphides by Displacement Reactions.*

By Brian Milligan and J. M. Swan.

The well-known reaction of thiols with sodium tetrathionate in aqueous solution to give disulphides [1] involves two successive nucleophilic displacements:

$$RS^- + {}^-O_3S{\cdot}S{\cdot}S{\cdot}SO_3^- \longrightarrow RS{\cdot}S{\cdot}SO_3^- + {}^-S{\cdot}SO_3^-$$

$$RS^- + RS{\cdot}S{\cdot}SO_3^- \longrightarrow RS{\cdot}SR + {}^-S{\cdot}SO_3^-$$

Difficulties are encountered with sparingly soluble thiols. In such cases we have found that the reaction can be carried out more conveniently in *NN*-dimethylformamide with pyridine or cyclohexylamine as the base. Alternatively, disulphides can be prepared in high yield by heating thiols with anilinium tetrathionate and a base in ethanol.

Thiouronium salts, which give rise to thiols in alkaline solution, also react with tetrathionate to give the corresponding disulphides. *S*-Benzylthiouronium chloride and aqueous sodium tetrathionate gave the sparingly soluble *S*-benzylthiouronium tetrathionate which at pH 10 was rapidly converted into dibenzyl disulphide, though in other cases pH 12 was necessary for rapid formation of disulphides. In this way diethyl, diallyl, dibenzyl, and di-4-nitrobenzyl disulphide were prepared in overall yields of 42—95% from the corresponding alkyl halides, isolation of the intermediate thiouronium salts being unnecessary.

Pirie [2] and Toennies [3] prepared cystine by reaction of cysteine with 1,1′-dithiodiformamidine dihydrochloride in aqueous solution. This reaction also proceeds by two successive nucleophilic displacements: [3]

$$RS^- + {}^+NH_2{:}(NH_2)C{\cdot}S{\cdot}S{\cdot}C(NH_2){:}NH_2^+ \longrightarrow RS{\cdot}S{\cdot}C(NH_2){:}NH_2^+ + CS(NH_2)_2$$

$$RS^- + RS{\cdot}S{\cdot}C(NH_2){:}NH_2^+ \longrightarrow RS{\cdot}SR + CS(NH_2)_2$$

Using the same reagent Preisler and Bateman [4] converted dithiobiuret into 2,5-di-imino-1,2,4-dithiazolidine.

We have converted water-insoluble thiols into their disulphides by reaction with 1,1′-dithiodiformamidine dihydrochloride in 80% pyridine. The reaction is complete in 5 min. at 50°, yields being generally 90—100%. The reaction can be carried out equally well in boiling aqueous ethanol, or less satisfactorily in glacial acetic acid.

In an attempt to extend this reaction to the synthesis of trisulphides, we have treated thiols with 1,1′-trithiodiformamidine dihydrochloride under the same conditions. However, the crude products contained mainly disulphides; only from the reaction with toluene-*p*-thiol was a small amount of the corresponding trisulphide isolated.

Experimental.—Reaction of thiols with sodium tetrathionate. The thiol (20 mmoles) was added to a solution of sodium tetrathionate dihydrate (11 mmoles) in *NN*-dimethylformamide (10 ml.) containing pyridine or cyclohexylamine (50 mmoles). After 15 min. water (100 ml.) was added and the product was filtered off, washed with water, and dried. Yields of the corresponding disulphides are shown in the annexed Table.

Thiol	Yield (%) of disulphide in pyridine	Yield (%) of disulphide in cyclohexylamine
Benzenethiol	46	75
p-Bromobenzenethiol	85	—
Toluene-ω-thiol	80	90
L-Cysteine hydrochloride	54	—
Naphthalene-2-thiol	98	100

[1] Foss, *Acta Chem. Scand.*, 1947, **1**, 307; Chinard and Hellerman, "Methods of Biochemical Analysis," ed. Glick, Interscience Publ., Inc., New York, Vol. I, 1.
[2] Pirie, *Biochem. J.*, 1933, **27**, 1181.
[3] Toennies, *J. Biol. Chem.*, 1937, **120**, 297.
[4] Preisler and Bateman, *J. Amer. Chem. Soc.*, 1947, **69**, 2632.

Anilinium tetrathionate. Concentrated aqueous solutions of aniline hydrochloride (17·3 g.) and sodium tetrathionate dihydrate (20·4 g.) were mixed, and the resulting precipitate (29 g.) was filtered off and crystallized from ethanol. *Anilinium tetrathionate* (21·5 g., 78%) was obtained as needles, m. p. 220° (decomp.) (Found: C, 35·4; H, 4·1; S, 31·2. $C_{12}H_{16}N_2O_6S_4$ requires C, 34·9; H, 3·9; S, 31·1%).

Oxidation of thiols with anilinium tetrathionate. A solution of anilinium tetrathionate (5 mmoles) in hot 90% ethanol (25 ml.) was added slowly to the thiol (10 mmoles) and cyclohexylamine (1·0 ml.) in ethanol (15 ml.). The mixture was heated to boiling and then set aside for 1 hr. The product was isolated by either (1) filtering off the precipitate and washing it free from thiosulphate with water, or (2) evaporating the mixture to dryness and extracting the product with ethyl acetate. In this way toluene-ω-thiol gave dibenzyl disulphide in 56% yield after purification by chromatography on alumina. Benzenethiol, *p*-bromobenzenethiol, and naphthalene-2-thiol were also converted into the corresponding disulphides, in yields of 74, 90, and 91%, respectively. When cyclohexylamine was replaced by pyridine or aniline, the yields of disulphide derived from naphthalene-2-thiol were 77 and 81%, respectively.

S-*Benzylthiouronium tetrathionate.* This *salt* separated on mixing aqueous solutions of potassium tetrathionate and *S*-benzylthiouronium chloride. It crystallized from ethanol as prisms, m. p. 170° (Found: C, 34·7; H, 4·0; O, 17·4. $C_{16}H_{22}N_4O_6S_6$ requires C, 34·4; H, 4·0; O, 17·2%). Crystallization from water gave plates, m. p. 175—177° (Found: C, 34·3; H, 4·1%). From a solution of this salt at pH 10, a quantitative yield of dibenzyl disulphide was precipitated.

Conversion of alkyl halides into dialkyl disulphides. A solution of the alkyl halide (0·1 mole) and thiourea (0·1 mole) in ethanol (100 ml.) was heated under reflux for 1 hr., the solvent evaporated *in vacuo*, and the residue dissolved or suspended in water (250 ml.). After addition of sodium tetrathionate dihydrate (0·05 mole) the pH of the mixture was adjusted to 12 and maintained thereat for ½ hr. by addition of 4N-sodium hydroxide, and the resulting product was isolated by filtration or by extraction with ether. In this way ethyl bromide gave diethyl disulphide (42%), b. p. 154—156°, allyl chloride gave diallyl disulphide (60%), b. p. 78—83°/13 mm., benzyl chloride gave dibenzyl disulphide (95%), m. p. 69—70°, and 4-nitrobenzyl bromide gave di-4-nitrobenzyl disulphide (71%), m. p. 123°. Dimethyl disulphide, b. p. 108—111°, was obtained in 55% yield from *S*-methylthiouronium sulphate.

Reaction of thiols with 1,1′*-dithiodiformamidine dihydrochloride.* (i) 1,1′-Dithiodiformamidine dihydrochloride,[5] m. p. 174—175° (decomp.) (5 mmoles), was added to a boiling solution or suspension of the thiol (10 mmoles) in 66% v/v ethanol (25 ml.), and the mixture was heated under reflux for 10—30 min. The resulting disulphide was filtered off after evaporation of most of the ethanol. (ii) 1,1′-Dithiodiformamidine dihydrochloride (5 mmoles) was added to a solution of the thiol (10 mmoles) in 80% pyridine (20 ml.) at 50°. After 5 min. the mixture was cooled, acidified with N-hydrochloric acid, and the product filtered off. Yields and melting points of the derived disulphides are shown in the annexed Table.

	Method (i)		Method (ii)	
Thiol	Yield	M. p.	Yield	M. p.
Toluene-ω-thiol	85	69°	93	68° *
Benzenethiol	97	59—60	94	59 *
Naphthalene-2-thiol	86	138—140	94	138—140
L-Cysteine	—	—	99 †	—

* After one crystallization. † The nitroprusside test for thiol was negative.

Dibenzyl disulphide (0·95 g., 77%) was also prepared by heating a solution of toluene-ω-thiol (1·24 g.) and 1,1′-dithiodiformamidine dihydrochloride (1·12 g.) in acetic acid (20 ml.) on a steam-bath for 15 min.

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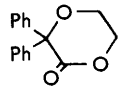
[5] Preisler and Berger, *J. Amer. Chem. Soc.*, 1947, **69**, 322.

131. *Reactions of 2-Bromoethyl Benzilate and 2-Bromoethyl Mandelate with Secondary Amines.*

By G. P. Ellis, J. King, and T. B. Lee.

The established methods of preparing basic esters of benzilic acid require either the basic alkyl halide or the basic alcohol.[1] An attempt to vary this procedure by condensing various secondary amines with 2-bromoethyl benzilate (I) failed, giving a halogen-free, non-basic, saturated compound, shown to be 2,2-diphenyl-3-oxo-1,4-dioxan (II). Cyclization of 2-bromoethyl benzilate to this compound, reported [2] to be formed by reaction of 2-dimethylaminoethyl chlorodiphenylacetate with ethylene glycol, was found to be

$Ph_2C(OH)\cdot CO\cdot O\cdot CH_2\cdot CH_2Br$ (I)



(II)

independent of the nature of the secondary amine used. The oxodioxan (II) did not depress the melting point of a sample prepared from ethylene glycol, and on hydrolysis with ethanolic sodium hydroxide it gave (2-hydroxyethoxy)diphenylacetic acid (cf. ref. 2).

In view of the above unexpected cyclisation, the analogous reaction of 2-bromoethyl mandelate with secondary amines has been investigated. Condensation proceeded normally, and the expected substituted aminoethyl mandelates were obtained. 2-Bromoethyl mandelate with piperidine gave 2-piperidinoethyl mandelate.[3] 2-Morpholinoethyl mandelate has also been prepared from 2-bromoethyl mandelate.

Experimental.—*2-Bromoethyl benzilate* (I). Benzilic acid (22·8 g., 0·1 mole) and 2-bromoethanol (12·5 g., 0·1 mole) were added to carbon tetrachloride (200 ml.) containing concentrated sulphuric acid (5 drops) and heated under reflux in a flask attached to a water entrainment apparatus. The benzilic acid dissolved, and after 4—5 hr. water (1·8 ml., 0·1 mole) had collected and the mixture was set aside overnight. The crystals (29·5 g.), m. p. 97—103° (decomp.), were filtered off, washed with a little carbon tetrachloride, and dried. The crude product was dissolved in hot benzene, the solution filtered, and light petroleum (b. p. 40—60°) was added to the filtrate. The ester (18·8 g., 56%), m. p. 148—149°, crystallised (Found: C, 57·4; H, 4·6; Br, 23·3. Calc. for $C_{16}H_{15}BrO_3$: C, 57·3; H, 4·5; Br, 23·8%). It was previously [4] described as an oil.

2,2-Diphenyl-3-oxo-1,4-dioxan (II). 2-Bromoethyl benzilate (6·7 g., 0·02 mole) was heated under reflux with piperidine (3·40 g., 0·04 mole) in benzene (60 ml.) overnight. After cooling, ether was added and piperidine hydrobromide (3·10 g.), m. p. 240—242°, was filtered off and washed with ether. The filtrate was treated with an excess of ethereal hydrogen chloride, and the solid obtained (2·65 g.), on crystallisation from ethanol–ether, was shown to be piperidine hydrochloride (1·70 g.; m. p. 244—246°). The ether–benzene filtrate was washed with water and dried (Na_2SO_4); filtration and removal of the solvent gave the oxodioxan which crystallised from light petroleum (b. p. 60—80°) in rosettes (3·40 g., 67%), m. p. 100—101° (Found: C, 75·5; H, 5·3. Calc. for $C_{16}H_{14}O_3$: C, 75·6; H, 5·6%). A chloroform solution did not decolorise bromine and the halogen test was negative.

When the piperidine was replaced by morpholine or diethylamine, the oxodioxan, m. p. 99—100°, was obtained in 64—68% yield.

2-Bromoethyl mandelate. Mandelic acid (15·2 g., 0·1 mole), 2-bromoethanol (12·5 g., 0·1 mole), benzene (150 ml.), and sulphuric acid (4 ml.; 20% v/v) were heated under reflux in a Dean and Stark apparatus. When no more water distilled, the cooled solution was washed with water, dilute sodium carbonate solution, and water, dried (Na_2SO_4), filtered, and evaporated. Distillation gave the *ester* (16·7 g., 64%), b. p. 142—144°/0·5 mm., m. p. 50—52° (Found: C, 45·8; H, 4·5; Br, 30·4. $C_{10}H_{11}BrO_3$ requires C, 46·3; H, 4·3; Br, 30·8%).

[1] Horenstein and Pählicke, *Ber.*, 1938, **71**, 1645; Ford-Moore and Ing., *J.*, 1947, 55; King and Holmes, *J.*, 1947, 64; Blicke and Biel, *J. Amer. Chem. Soc.*, 1954, **76**, 3163; Klosa, *Arch. Pharm.*, 1955, **288**, 75.

[2] Chubb, Frangatos, and Nissenbaum, *Canad. J. Chem.*, 1960, **38**, 1231.

[3] Blicke and Maxwell, *J. Amer. Chem. Soc.*, 1942, **64**, 428; Blicke and Kaplan, *ibid.*, 1943, **65**, 1967.

2-Piperidinoethyl mandelate. 2-Bromoethyl mandelate (2·50 g., 0·01 mole), piperidine (1·70 g., 0·02 mole), and benzene (30 ml.) were heated under reflux for 15 hr. After cooling and addition of ether, the piperidine hydrobromide (1·56 g.) was filtered off. The filtrate was washed with water and dried (Na_2SO_4). After filtration and addition of ethereal hydrogen chloride to the concentrated filtrate, the precipitated ester hydrochloride (2·20 g.) was filtered off and crystallised from ethanol–ether as a colourless solid (1·55 g., 52%), m. p. 156—157° (Blicke and Maxwell [4] give m. p. 159—160°) (Found: C, 59·6; H, 7·6; Cl, 11·7. Calc. for $C_{15}H_{21}NO_3$,HCl: C, 60·1; H, 7·4; Cl, 11·8%).

2-Morpholinoethyl mandelate. The preparation was carried out as in the last paragraph but with morpholine (1·74 g., 0·02 mole). *2-Morpholinoethyl mandelate* (0·9 g., 30%), crystallised from ethanol–ether, had m. p. 152—156° (Found: C, 56·0; H, 6·8; Cl, 12·0. $C_{14}H_{19}NO_4$,HCl requires C, 55·7; H, 6·7; Cl, 11·8%).

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[4] Yoshida and Iwashige, *Pharm. Bull.* (*Japan*), 1955, **3**, 417.

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132. *Reaction of Diazonium Tetrafluoroborates with Nickel Carbonyl.*

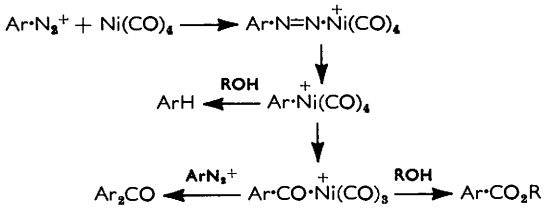
By J. C. CLARK and R. C. COOKSON.

As a possible route to aryl carboxylic acids and their derivatives we have examined the reaction of diazonium tetrafluoroborates with transition-metal carbonyls.

The diazonium salts did not react with nickel carbonyl. Addition of ether, dioxan, or water to a suspension of the salt in the carbonyl also produced no reaction, but ethanol, acetone, t-butyl alcohol, or acetic acid induced vigorous effervescence of nitrogen and carbon monoxide. The yields of pure products separated by chromatography on silica gel are given in the Table. Gradual addition (A) of nickel carbonyl to a suspension of the salt in the solvent favoured reduction against carboxylation, in contrast with addition (B) of the solvent to the salt in the carbonyl, which preserves a higher concentration of carbonyl and carbon monoxide (compare 1 and 7 with 2 and 8). Dimethylformamide (17 and 20), in which the diazonium salts are soluble, seemed to offer no advantage over the other liquids in which they are almost insoluble.

The reaction of diazonium tetrafluoroborates with acetic acid and nickel carbonyl, which forms the aromatic acid in 20—75% yields (except 1-naphthyl, which gave much tar), may sometimes provide a useful, single-step alternative to the Sandmeyer reaction,[1] especially where the nitriles from the latter contain other groups susceptible to hydrolysis. In some cases (*e.g.*, 13) the diaryl ketones were formed from reaction of an intermediate with another molecule of diazonium salt.

Although it is not certain whether the reaction goes mainly through radicals or ions, intermediates such as the following may be involved (the probable reaction of the nickel atom with the hydroxylic solvent is omitted for simplicity):



[1] Saunders, "The Aromatic Diazo Compounds," Arnold, London, 1948, p. 348; Cowdrey and Davies, *Quart. Rev.*, 1952, **6**, 358.

Evidently the acylnickel carbonyl is not a strong enough acylating agent to attack t-butyl alcohol to give the t-butyl ester (Nos. 6 and 11). The failure of the *p*-carboxy- or *p*-ethoxycarbonyl-salts to yield any diaryl ketone (compare Nos. 2 and 8 with 13, 15, and 18) may be partly caused by withdrawal of electrons by the *para*-substituent, which would speed up reaction of the acyl–nickel complex with solvent and slow down its reaction with diazonium ion: against that, however, is the lower yield of ketone from the *p*-tolyl (No. 13) than from the *p*-methoxyphenyl salt (No. 18).

Addition of acetic acid to a suspension of 4-carboxybenzenediazonium tetrafluoroborate in iron pentacarbonyl caused effervescence. From the red, viscous product terephthalic acid was isolated in 14% yield. The diazonium salts did not react appreciably with molybdenum hexacarbonyl during the time taken for completion with nickel carbonyl; longer periods led to dark tars.

After we had finished our experiments Schrauzer [2] reported that aqueous diazonium chlorides reacted with iron pentacarbonyl in acetone or methanol to give the carboxylic acids (0—40%), accompanied by the diaryl ketones and aryl chlorides.

Experimental.—*p*-Ethoxycarbonylbenzenediazonium tetrafluoroborate was made by Schiemann and Winkelmüller's method; [3] preparation of the other diazonium fluoroborates followed Starkey's directions.[4] Typical examples of procedures A and B are described:

Procedure A. A mixture (made with care) of nickel carbonyl (40 ml.) and ethanol (60 ml.) was added dropwise to a suspension of *p*-ethoxycarbonylbenzenediazonium tetrafluoroborate (14 g.) in ethanol (50 ml.) cooled in ice. The addition was made at a rate sufficient to maintain a steady effervescence (if it is made too fast the mixture becomes warm and the diazonium salt decomposes). After about 18 ml. of the carbonyl solution had been added (*ca.* 1 mol.) effervescence had almost ceased, and rapid addition of the rest of the carbonyl caused the evolution of only a little gas. Ether (150 ml.) was added to the mixture, which was then warmed (with care) on a water-bath to co-distil nickel carbonyl and ether. After removal of

No.	Diazonium salt $RN_2^+BF_4^-$	Solvent and procedure	Products (molar % yield) $R{\cdot}CO_2H$	$R{\cdot}CO_2Et$	R_2CO	RH
1	*p*-Ethoxycarbonylphenyl-	EtOH (A)	—	37	—	54
2	,, ,, ,,	EtOH (B)	—	53	—	16
3	,, ,, ,,	EtOH–H_2O (1 : 5) (B)	41	—	—	21
4	,, ,, ,,	AcOH (B)	52	—	—	—
5	,, ,, ,,	Me_2CO–H_2O (1 : 1) (A)	38	—	—	—
6	,, ,, ,,	Me_2CO or $Me_3C{\cdot}OH$	47	—	—	—
7	*p*-Carboxyphenyl-	EtOH (A)	—	1·2	—	85 *
8	,, ,,	EtOH (B)	46	39	—	3 *
9	,, ,,	AcOH (A)	23	—	—	—
10	,, ,,	AcOH (B)	76·5	—	—	—
11	,, ,,	$Me_3C{\cdot}OH$–dioxan (1 : 1) (A)	18	—	—	—
12	,, ,,	$Me_3C{\cdot}OH$–dioxan (1 : 1) (B)	68	—	—	—
13	*p*-Tolyl-	EtOH (B)	5	16	33	—
14	,,	AcOH (B)	19	—	—	—
15	*p*-Chlorophenyl-	EtOH (B)	4	20	12	—
16	,, ,,	AcOH (B)	39	—	—	—
17	,, ,,	$Me_2N{\cdot}CHO$ (A)	20	—	—	—
18	*p*-Methoxyphenyl-	EtOH (B)	4	20	4	—
19	,,	AcOH (B)	74	—	—	—
20	,, ,,	$Me_2N{\cdot}CHO$ (A)	31	—	—	—
21	1-Naphthyl-	EtOH (B)	2	—	—	—
22	,,	AcOH (B)	4	—	—	—

* As ethyl benzoate.

ethanol under reduced pressure the resulting viscous mass was shaken with water (200 ml.) and ether (100 ml.). The green aqueous layer was extracted three times more with ether. The viscous orange oil remaining from evaporation of the combined ether extracts was chromatographed on silica gel (150 g.). Light petroleum containing 25% of benzene eluted ethyl

[2] Schrauzer, *Chem. Ber.*, 1961, **94**, 1891.
[3] Schiemann and Winkelmüller, *Org. Synth.*, 1933, **13**, 52.
[4] Starkey, *Org. Synth.*, 1939, **19**, 40.

benzoate (4·23 g., 54%), identified by its infrared spectrum. Benzene eluted a solid, m. p. 43—45° after recrystallisation (4·32 g., 54%), unchanged when mixed with diethyl terephthalate: the infrared spectra of the two samples were identical. Further elution with more polar solvents yielded amorphous products with strong bands at 1730, 1715, 1695, 1290, and 1115 cm.$^{-1}$.

Procedure B. *p*-Ethoxycarbonylbenzenediazonium tetrafluoroborate (4·0 g.) in nickel carbonyl (20 ml.) did not react. When ethanol (15 ml.) was slowly dropped into the cooled mixture vigorous effervescence occurred. The product was worked up as before, to give ethyl benzoate (0·364 g., 16%) and diethyl terephthalate (1·78 g., 53%).

The yields given in the Table refer to purified compounds, which were identified with authentic samples by mixed m. p. (if crystalline) and by infrared spectra. Monoethyl terephthalate (Nos. 3—8) had m. p. 169—171°; *p*-toluic acid, m. p. 180—181°; 4,4′-dimethylbenzophenone, m. p. 94—95°; *p*-chlorobenzoic acid, m. p. 244·5—245°; 4,4′-dichlorobenzophenone, m. p. 147—149°; *p*-anisic acid, m. p. 183—184°; 4,4′-dimethoxybenzophenone, m. p. 142—143°; 1-naphthoic acid, m. p. 160—161°.

Our attention was concentrated on the products of carbonylation, so that small quantities of toluene, chlorobenzene, and anisole resulting from reduction may have been overlooked.

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