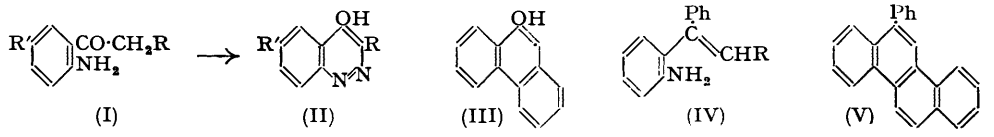
NOTES.

745. *Cinnolines. Part XXXIII.* Some 3-Aryl-4-hydroxycinnolines.*

By D. W. Ockenden and K. Schofield.

The synthesis of 4-hydroxycinnolines (II) from 2-aminoaryl ketones (I) (cf. Schofield and Simpson, *J.*, 1945, 520) is widely applicable, and proceeds efficiently with the amines (I; R = H, halogen, or alkyl) (Schofield and Simpson, *loc. cit.*; *J.*, 1948, 1170; Keneford and Simpson, *J.*, 1948, 354). Hitherto, diazotisation of (I; R = aryl) has not been described; such reactions would be interesting because formally they present the possibility of competition between cinnoline formation and the Pschorr types of cyclisation (Pschorr, *Ber.*, 1896, **29**, 496). Thus, *o*-aminophenyl benzyl ketone (I; R = Ph, R′ = H) might



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

provide either 4-hydroxy-3-phenylcinnoline (II; R = Ph, R′ = H) or 9-phenanthrol (III). The latter possibility was first suggested by Lothrop and Goodwin (*J. Amer. Chem. Soc.*, 1943, **65**, 363). We have recently synthesised some amines of the type (I; R = aryl) (Ockenden and Schofield, to be published) and now describe their behaviour on diazotisation.

Diazotisation of *o*-aminophenyl benzyl ketone in concentrated hydrochloric acid, and cyclisation of the diazonium compound, rapidly gave 4-hydroxy-3-phenylcinnoline in high yield. Under a variety of conditions appropriate to the Pschorr reaction (see Experimental) the cinnoline was the only product isolable. Similarly, the appropriate amines provided 4-hydroxy-6-methyl- (II; R = Ph, R′ = Me) and 4-hydroxy-6-nitro-3-phenyl-cinnoline (II; R = Ph, R′ = NO_2).

The behaviour of *o*-aminophenyl benzyl ketone in the present type of cinnoline synthesis recalls that of 1-*o*-aminophenyl-1 : 2-diphenylethylene (IV; R = Ph) which, upon diazotisation and cyclisation of the diazonium compound, gave only 3 : 4-diphenylcinnoline (Simpson,

* Part XXXII, *J.*, 1953, 3700.

J., **1943**, 447). In contrast Simpson (*loc. cit.*) showed that diazotisation of 1-*o*-aminophenyl-2-α-naphthyl-1-phenylethylene (IV; R = 1-$C_{10}H_7$) gave either 3-α-naphthyl-4-phenylcinnoline or 2-phenylchrysene (V), depending on the conditions. For this reason we examined *o*-aminophenyl α-naphthylmethyl ketone (I; R = 1-$C_{10}H_7$, R′ = H). By diazotisation in concentrated hydrochloric acid and cyclisation of the diazonium compound this gave 4-hydroxy-3-α-naphthylcinnoline. Neither under any of the conditions mentioned for the phenyl analogue, nor by decompositions of the diazonium borofluoride (Heacock and Hey, *J.*, 1952, 1508) was 2-chrysenol produced.

Clearly, in amines of the type (I; R = aryl), the methylene group is highly activated, presumably so much so that cinnoline formation is rapid enough to exclude Pschorr cyclisation.

Experimental.—*3-Aryl-4-hydroxycinnolines.* The appropriate amine was diazotised at 0° with aqueous sodium nitrite, and the diazonium solution was then heated at 60° for 3 hr. The cinnoline quickly separated (Yield " A "). Alternatively the diazonium solution was kept at room temperature for 4 days (Yield " B ") (cf. Leonard and Boyd, *J. Org. Chem.*, 1946, **11**, 419).

Treatment of the diazonium chloride solution from *o*-aminophenyl benzyl ketone or *o*-aminophenyl α-naphthylmethyl ketone with copper powder (Pschorr, *loc. cit.*), or with sodium hypophosphite (Ruggli and Staub, *Helv. Chim. Acta*, 1937, **20**, 37), or diazotisation in alcoholic sulphuric acid with amyl nitrite and addition of copper powder (*idem*, *ibid.*) gave diminished yields of impure cinnolines.

No.	Cinnoline	Amine, g.	Conc. HCl, c.c.	$NaNO_2$, g.[a]	" A," %	" B," %
1	4-Hydroxy-3-phenyl-	0·2	5	0·07	64	90
2	4-Hydroxy-6-methyl-3-phenyl-	0·1	,,	0·04	67	86
3	4-Hydroxy-6-nitro-3-phenyl-...	0·25	10[b]	0·08	50	61
4	4-Hydroxy-3-α-naphthyl-	0·1	5	0·03	77	87

[a] In 1 c.c. of water, except in the third example (0·5 c.c.). [b] Acetic acid (6 c.c.) was also added. 1. White leaflets (Found: C, 76·7; N, 4·8; N, 12·1. Calc. for $C_{14}H_{10}ON_2$: C, 76·7; H, 4·5; N, 12·6%), m. p. 265—267° alone and mixed with a specimen prepared according to Schofield and Swain (*J.*, 1949, 2393). 2. Cream-coloured plates (Found: C, 77·7; H, 5·2. $C_{15}H_{12}ON_2$ requires C, 76·2; H, 5·1%), m. p. 310—312°. 3. The *compound* formed small yellow needles (Found: C, 64·1; H, 3·6. $C_{11}H_8O_3N_3$ requires C, 63·3; H, 3·4%), m. p. 347—348°. (4) The *compound* was obtained as small plates (Found: C, 78·2; H, 4·6. $C_{18}H_{12}ON_2$ requires C, 79·4; H, 4·4%), m. p. 285—286°.

We are indebted to the Council of University College, Exeter, and to Imperial Chemical Industries Limited for financial support, and to D.S.I.R. for a maintenance grant to one of us (D. W. O.).

WASHINGTON SINGER LABORATORIES,
PRINCE OF WALES RD., EXETER.

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746. *A New Synthesis of Arsonic Acids. Part IV.* Stilbene-3-arsonic Acid.*

By WALTER FREUND and ALFRED KOMZAK.

A SOLUTION of *m*-arsanilic acid (8·6 g.) in aqueous sodium hydrogen carbonate (60 c.c. containing 3·5 g.) was added to one of sodium nitrite (2·85 g.) in water (10 c.c.), and then diazotised with 25% hydrochloric acid (32·33 c.c.) in the usual manner. The filtered solution was added to cinnamic acid (5·9 g.) in acetone (120 c.c.), in which sodium acetate (approx. 32 g.) was suspended, the mixture was well shaken or stirred until the pH became approx. 6, and aqueous cupric chloride (8 g. in 18 c.c.) then added dropwise at room temperature. After 50 min. the precipitate was separated and purified by conventional methods. *Stilbene-3-arsonic acid* separated from acetic acid as pale yellow plates, which did not melt below 300° (Found: C, 55·55; H, 4·7, 4·7; As, 24·4, 24·3. $C_{14}H_{13}O_3As$ requires C, 55·3; H, 4·3; As, 24·6%).

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* Part III, *J.*, 1952, 3073.

747. *Studies with Phenylbutadiene. Part I. A New Synthesis of Naphthalene.*

By S. A. Faseeh.

A suspension of 4-phenylbutadiene-1-carboxylic acid (Doebner, *Ber.*, 1902, **35**, 2129) in carbon tetrachloride absorbs chlorine in sunlight (but not unless so irradiated), to yield successively 2 : 3-dichloro-5-phenylpent-4-enoic and 2 : 3 : 4 : 5-tetrachloro-5-phenylpentanoic acid (for a similar stepwise addition to 1-phenylbutadiene see Strauss, *Ber.*, 1909, **42**, 2866, and Muscat and Huggins, *J. Amer. Chem. Soc.*, 1929, **51**, 2496). Heating the former product with sodium carbonate solution yields 1-chloro-4-phenylbutadiene which affords naphthalene in 82% yield when heated with vacuum-dried stannous chloride.

This simple synthesis of naphthalene parallels that of phenanthrene from 2-formyldiphenyl (*Pakistan J. Sci. Res.*, 1951, **3**, 37; *J. Indian Chem. Soc.*, 1945, **22**, 181).

Experimental.—2 : 3-*Dichloro-5-phenylpent-4-enoic acid.* Chlorine was passed into 4-phenylbutadiene-1-carboxylic acid (43·5 g., 0·25 mole) in carbon tetrachloride (435 g.) in sunlight (37°). Absorption of 0·25 mole of chlorine required 1 hr., the suspension clearing and the temperature reaching 57°. A further 0·125 mole of chlorine was introduced during a further hour, and the solution was left for a third hour in sunlight. The yellow colour was lost and a small quantity of colourless crystals was deposited. The solution was filtered and evaporated in air to a viscous paste which was stirred with light petroleum–xylene. The resulting colourless precipitate, crystallised from the same mixture, yielded the *dichloro-acid* (57·7 g., 80%), m. p. 126—127° (Found: C, 53·5; H, 4·2; Cl, 29·3. $C_{11}H_{10}O_2Cl_2$ requires C, 53·9; H, 4·1; Cl, 29·0%).

2 : 3 : 4 : 5-*Tetrachloro-1-phenylpentanoic acid.* The foregoing conditions, modified by a final exposure to sunlight for 5 hr., gave the *tetrachloro-acid* (38·0 g., 95%), m. p. 180° (Found: C, 41·9; H, 3·3; Cl, 44·6. $C_{11}H_{10}O_2Cl_4$ requires C, 41·8; H, 3·2; Cl, 44·9%).

1-*Chloro-4-phenylbutadiene.* The dichloro-acid was heated in 5% sodium carbonate solution (225 c.c.) on the water-bath for 2 hr. An oil separated which was extracted with ether and on distillation yielded 1-chloro-4-phenylbutadiene (15·1 g., 92%), b. p. 113°/2—3 mm. (Found: C, 72·55; H, 5·1; Cl, 21·8. Calc. for $C_{10}H_9Cl$: C, 73·0; H, 5·5; Cl, 21·6%).

Naphthalene. 1-Chloro-4-phenylbutadiene (20·6 g.) and stannous chloride (2·35 g.; vacuum-dried) were gradually heated in an oil-bath. At 95° the mixture suddenly became brown and copious evolution of acid vapours took place. The temperature was kept at 95° for 2 hr., at the end of which evolution of acid vapours slackened. The temperature was then raised to *ca.* 220° and kept thereat for 0·5 hr. during which the evolution of gas came to an end. The product was heated with water and extracted with ether. The ethereal extract on distillation yielded naphthalene (13·1 g., 82%), m. p. and mixed m. p. 79° (from alcohol) [picrate, m. p. and mixed m. p. 149° (Found: C, 54·0; H, 3·2; N, 11·4. Calc. for $C_{16}H_{11}O_7N_3$: C, 53·8; H, 3·1; N, 11·8%)].

The author is indebted to Dr. Bashir Ahmad, Director of this Institute, for encouragement and facilities and to Mr. M. S. F. A. Abidi for assistance with the experiments.

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University of the Panjab, Lahore, Pakistan. [*Received, May 18th*, 1953.]

748. *Attempted Preparation of Cyanogen Fluoride.*

By H. J. Callomon, H. W. Thompson, F. Allan Andersen, and Börge Bak.

The study of the infra-red and microwave spectra of cyanogen fluoride is of considerable interest, and attempts have been made to prepare it for this purpose in both Oxford and Copenhagen. Since the method described by Cosslett (*Z. anorg. Chem.*, 1931, **201**, 75) has been proved not to lead to this product, and other possible methods of preparation have also been unfruitful, a brief report seems desirable.

Cosslett's procedure, using the reaction $AgF + ICN = AgI + FCN$, was closely followed. Great care was taken to use only highly purified silver fluoride (Andersen, Bak, and Hillebert, *Acta Chem. Scand.*, 1953, **7**, 236) and cyanogen iodide (Bak and Hillebert, *Org. Synth.*, 1952, **32**, 29). The apparatus was so designed that volatile products were immediately trapped and not allowed to recycle over the silver fluoride with unchanged cyanogen iodide. This minimizes the chance of polymerization of any cyanogen fluoride formed. The products thus obtained were examined at Oxford in a Perkin-Elmer 12C infra-red spectrometer. Bands of carbon dioxide, nitrous oxide, silicon tetrafluoride, and carbonyl fluoride were identified in the complex spectrum. Essentially similar results were found at Copenhagen where a Beckman I.R.2 spectrometer was used, and where the gaseous products were also examined with a microwave spectroscope covering the range 18,000—26,000 Mc. Cyanogen fluoride should show the transition $J = 0 \longrightarrow J = 1$ at about 20,550 Mc if bond lengths r_{CF} and r_{CN} are 1·30 Å and 1·16 Å. No such absorption line could be found, although tests of the sensitivity with nitrous oxide proved quite satisfactory. The walls of the glass furnace were subsequently found to have been corroded in the vicinity of the silver fluoride. This could only have occurred after the introduction of cyanogen iodide gas into the furnace, for a preliminary baking out of the furnace with the silver fluoride *in situ* in high vacuum yielded only minute traces of gas.

At Oxford the experiments were then repeated, closely fitting liners of quartz and Monel-metal stainless steel tube being used, with the silver fluoride suspended on platinum gauze. The products were examined in a mass spectrometer. Those obtained from the experiment in quartz were identical with those obtained originally. Those obtained from the experiment in metal showed a decrease in the proportion of carbon dioxide, nitrous oxide, and silicon fluoride, but contained an appreciable proportion of carbon–fluorine and nitrogen–fluorine fragments. About 3% of a component with molecular weight 45 was found. Since no other combination of the possible atoms would correspond to this mass, after allowance for the ^{13}C and ^{15}N isotopes in carbon dioxide and nitrous oxide, the presence of a little cyanogen fluoride is indicated. A peak corresponding to the trimer $(FCN)_3$ was also obtained. Finally, the experiment was repeated with use of a liner of copper and mercuric fluoride, prepared from mercuric chloride and fluorine by Henne's method (*J. Amer. Chem. Soc.*, 1936, **58**, 884). The reaction proceeded at 100—150° and, in addition to products similar to those found previously, the mass-spectrum indicated the presence of components which appeared to arise from fluorination of the silicone tap-grease used on cone and socket joints on the external (cold) parts of the apparatus. A little cyanogen fluoride was again detected. A small amount of a blue gas, condensed by liquid air but not by solid carbon dioxide, was also formed which may have been CF_3NO (see Ruff, *loc. cit.*).

At Copenhagen a number of experiments were carried out in brass containers. Since preliminary experiments had shown that on use of such metal tubes the formation of $(FCN)_3$ was evident, implying a polymerization of the cyanogen fluoride first formed, attempts were made to freeze out the latter as quickly as possible. Silver fluoride and cyanogen iodide were mixed intimately and placed in the brass container which was immediately evacuated. The container was then placed in an oil-bath at 240° and the gases formed were withdrawn continuously through freezing traps. The product gave no indication of cyanogen fluoride in either the infra-red or the microwave spectrum.

During the attempts to mix silver fluoride and cyanogen iodide, it was noticed that they

form a complex compound very easily if mixed together in aqueous or anhydrous methanol. Yellow precipitates are formed, the composition corresponding to the formula $ICN,(AgF)_n$ where $1{\cdot}2 < n < 2{\cdot}8$, but no well-defined compound was ever obtained. These mixtures all exploded when heated to 220°, giving off mainly nitrogen, but no sign of cyanogen fluoride.

It would appear, therefore, that cyanogen fluoride cannot be prepared, except in very small yield, by direct fluorination of cyanides with strong fluorinating agents of the type here described. The point of attack appears to be the triple bond of the cyanide, for in the largest proportion of the products the carbon and nitrogen are separated. It appears unlikely that the active intermediate which attacks glass and quartz is cyanogen fluoride itself, for the presence of the latter was measured after some days of storage in a glass bulb. It would also be difficult to account for the formation of 10% of nitrous oxide with two nitrogen atoms adjacent, and very little nitrogen. Such cyanogen fluoride as is formed appears to polymerise very readily at higher temperatures to a stable trimer.

It is noteworthy that Ruff and Giese (*Ber.*, 1936, **69**, 598, 604, 684), by passing fluorine over silver or mercurous cyanides, obtained a mixture of carbon–nitrogen–fluorine compounds very similar to those reported here. Hückel (*Nachr. Akad. Wiss. Göttingen*, 1946, 36) attempted to fluorinate cyanogen iodide with mercuric fluoride under pressure in a steel bomb, and obtained the trimer $(FCN)_3$ in good yield. Attempts to prepare cyanogen fluoride by a reaction analogous to the Hofmann reaction starting with trifluoroacetyl chloride $CF_3{\cdot}COCl$, *viz.*, $CF_3{\cdot}COCl \longrightarrow CF_3{\cdot}CO{\cdot}NH_2 \longrightarrow CF_3{\cdot}N{:}CO \longrightarrow CF_3{\cdot}NH_2 \longrightarrow FCN$, stopped at $CF_3{\cdot}N{:}CO$, which is surprisingly stable.

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THE CHEMICAL LABORATORY, UNIVERSITY OF COPENHAGEN. [*Received, May 20th*, 1953.]

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749. *The Synthesis of Monofluorocitric Acid.*

By D. E. A. RIVETT.

THE interest in monofluorocitric acid, suspected of being the metabolite responsible for the toxicity of fluoroacetate (for a recent review see Peters, *Proc. Roy. Soc.*, 1952, *B*, **139**, 143), has prompted its synthesis. Of the various methods used for the synthesis of citric acid that of Lawrence (*J.*, 1897, **71**, 457) appeared to be best suited for the preparation of a substituted citric acid even though a poor yield was to be expected. Thus, a Reformatsky reaction between ethyl ethoxalylfluoroacetate ($EtO{\cdot}CO{\cdot}CO{\cdot}CHF{\cdot}CO_2Et$) and ethyl bromoacetate produced ethyl monofluorocitrate, converted by acid hydrolysis into the extremely hygroscopic acid. Although the yield of ester is only about 12%, the starting materials are easily prepared.

Experimental.—Ethyl ethoxalylfluoroacetate. Ethyl fluoroacetate (122 g.) was added dropwise with stirring at room temperature during 1½ hr. to a mixture of ethyl oxalate (174 g.) and ether (400 ml.) containing alcohol-free sodium ethoxide (from 23 g. of sodium). 2 Days later 5N-hydrochloric acid (240 ml.), cooled to −20°, was rapidly added (slow addition results in greatly reduced yield of ester), the ether layer separated, and the residue twice extracted with ether. The combined ether extracts were washed with saturated sodium hydrogen carbonate solution, dried (Na_2SO_4), and evaporated. Distillation of the residue gave *ethyl ethoxalylfluoroacetate* as a pale yellow liquid (130 g., 55%), b. p. 99°/3 mm., n_D^{25} 1·4203 (Found: C, 47·2; H, 5·45. $C_8H_{11}O_5F$ requires C, 46·6; H, 5·4%). It gave a reddish-brown solution with ferric chloride, failed to form a copper derivative when shaken in chloroform solution with aqueous copper acetate, and, when kept with a buffered aqueous alcoholic solution of semicarbazide, gave a violet-coloured solution but no solid. The 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol in yellow needles, m. p. 145° (Found: C, 43·6; H, 4·0; N, 14·7. $C_{14}H_{15}O_8N_4F$ requires C, 43·5; H, 3·9; N, 14·5%).

Ethyl monofluorocitrate. A mixture of ethyl ethoxalylfluoroacetate (36·0 g.), ethyl bromo-

acetate (27·3 g.), and benzene (50 ml.) was added to activated zinc (13·6 g.) at such a rate as to maintain gentle reflux. After boiling under reflux for 1 hr. the solution was cooled and 3N-sulphuric acid (100 ml.) added, and the benzene layer was washed with aqueous sodium carbonate, dried, and evaporated. Distillation of the residue at 120°/10^{-1} mm. and redistillation *in vacuo* gave pure *ester* (6·0 g., 12%), n_D^{25} 1·4392 (Found: C, 49·4; H, 6·6. $C_{12}H_{19}O_7F$ requires C, 49·0; H, 6·5%), which crystallised after several weeks at 0°, forming needles, m. p. 41°. The yield of ester was not improved by increasing the proportion of zinc and of ethyl bromoacetate.

The ester (0·5 g.) was boiled under reflux with 3N-hydrochloric acid (15 ml.) for 6 hr. The acid was isolated by continuous extraction with ether and dried *in vacuo* for several days over phosphoric oxide. It forms very hygroscopic needles and because of difficulty in handling was converted into the barium salt. The acid was neutralised with 0·5N-sodium hydroxide, and hot aqueous barium chloride (0·8 g.; 5 ml.) was then added. The cooled solution was filtered and the residue washed with cold water till free from chloride ions, and the *barium fluorocitrate* (0·65 g.) dried at 110°/10 mm. [Found: Ba, 49·3. $(C_6H_4O_7F)_2Ba_3$ requires Ba, 49·9. $(C_6H_4O_7F)_2Ba_3,\frac{1}{2}H_2O$ requires Ba, 49·3%). For comparison barium citrate, prepared in the same way, was also analysed (Found: Ba, 51·5. Calc. for $(C_6H_5O_7)_2Ba_3$: Ba, 52·1. Calc. for $(C_6H_5O_7)_2Ba_3,\frac{1}{2}H_2O$: Ba, 51·6%).

The analyses were by Mr. F. E. Charlton. This paper is published by permission of the Chief Scientist, Ministry of Supply.

CHEMICAL DEFENCE EXPERIMENTAL ESTABLISHMENT,
PORTON, NR. SALISBURY.

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750. *A Method of Iodination.*

By K. T. POTTS.

IT has been customary in most types of iodination to employ in the reaction a third substance capable of acting as an hydrogen iodide acceptor. Ammonia has been used with success mainly by Datta and Prosad (*J. Amer. Chem. Soc.*, 1917, **39**, 441) and Bordeianu (*Ann. Sci. Univ. Jassy*, 1935, **20**, 131; *Chem. Abs.*, 1936, **30**, 1760) who found that phenol could be iodinated in the presence of ammonia, methylamine, or tetramethylammonium hydroxide. Clayton, Hems, and Borroughs (*J.*, 1949, 3424; 1950, 840) have substituted a primary amine for ammonia and have successfully developed a method of using iodine–potassium iodide solution in the presence of ethylamine; they found that the primary amine was more suitable than the corresponding secondary and tertiary amines.

Reactant	Product *	Yield, %	M. p.
Aniline	*p*-Iodoaniline	76	61—62°
p-Toluidine	3-Iodo-*p*-toluidine	35	40
Dimethylaniline	*p*-Iododimethylaniline	86	78—79
Phenol	2 : 4 : 6-Tri-iodophenol	72	155—156
o-Cresol	4 : 6-Di-iodo-*o*-cresol	quant.	67
m-Cresol	2 : 4 : 6-Tri-iodo-*m*-cresol	73	121
p-Cresol	2 : 6-Di-iodo-*p*-cresol	quant.	60
β-Naphthol	1-Iodo-2-naphthol	96	92
o-Nitrophenol	2 : 4-Di-iodo-6-nitrophenol	66	96
p-Nitrophenol	2 : 6-Di-iodo-4-nitrophenol	34	153—155
p-Hydroxybenzoic acid	3 : 5-Di-iodo-4-hydroxybenzoic acid	53	264—265 †
Salicylic acid	3 : 5-Di-iodosalicylic acid	—	decomp. 220—240
Anthranilic acid	2-Amino-5-iodobenzoic acid	76	212
Pyrrole	Tetraiodopyrrole	41	decomp. 150—160

Products had m.p.s agreeing with the literature values, except for that from salicylic acid [lit.: values range from 212° (decomp.) to 235—236°] and from pyrrole (lit.: 145°).
* Cresols are numbered OH = 1. † Loses iodine above 200°.

In an investigation of the iodination of a derivative of tyrosine, use was made of iodine–potassium iodide solution in the presence of ethylenediamine. This reagent was found to

be very satisfactory for the iodination of phenols, amines, and hydroxybenzoic and other acids. The scope of the method is largely limited by the ease with which the compounds to be iodinated undergo substitution which depends on the presence of electron-repelling groups in the nucleus. Highly reactive compounds, such as phenol, always gave the tri-substituted compound even when one equivalent of the reagent was used. Ethers, such as anisole and methyl β-naphthyl ether, failed to react (cf. Jones and Richardson, *J.*, 1953, 713); acetanilide, *p*-nitroaniline, and thiophen did not react appreciably. The method is of particular value for preparing *p*-iodoaniline. The table summarizes the main results obtained.

Experimental.—It was found convenient to use a stock 4N-solution of iodine in potassium iodide and a 60% aqueous solution of ethylenediamine. In most experiments a solution of iodine in potassium iodide (0·1 mole) was added, with constant shaking, to a solution of the aromatic compound (0·1 mole) in ethylenediamine solution (0·05 mole). Alcohol (*ca.* 10 ml.) was added if necessary to form a homogeneous phase. The solution was allowed to decolorize before the next addition of iodine was made. After 2 hr. at room temperature the mixture was poured into water containing sodium thiosulphate. If a crystalline product separated, it was filtered off and recrystallized from a suitable solvent, usually alcohol or acetic acid. If the product separated as an oil, a slight excess of alkali was added, and the product steam-distilled.

THE UNIVERSITY OF SYDNEY, SYDNEY, AUSTRALIA. [*Received, June 16th,* 1953.]

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751. *Infra-red Absorptions of the* iso*Cyanate Group.*

By W. H. T. DAVISON.

THE infra-red absorptions of the *iso*cyanate group have not been previously characterised, apart from a general (and erroneous) assignment of the region 2050—2200 cm.$^{-1}$ to "*iso*-cyanates, 1 : 2-dienoid, etc." (Colthup, *J. Opt. Soc. Amer.*, 1950, **40**, 397), and assignments for cyanic acid (Herzberg and Reid, *Discuss. Faraday Soc.*, 1950, **9**, 92) and methyl *iso*cyanate (Eyster and Gillette, *J. Chem. Phys.*, 1940, **8**, 369). The last two papers discuss in some detail the interaction of the pseudo-symmetrical vibrations $\nu_{C=O}$ and $\nu_{C=N}$ to give one very strong anti-symmetrical absorption $\nu_{a(NCO)}$ at about 2250 cm.$^{-1}$ and a weaker symmetrical absorption $\nu_{s(NCO)}$ at about 1350 cm.$^{-1}$ (the convenient notation is that of Thomas, *Chem. and Ind.*, 1953, 567). The spectra of eight *iso*cyanates have been

	cm.$^{-1}$	prism	ε *
1. Cyanic acid [a]	2289, 2260	LiF	(vs)
2. Methyl *iso*cyanate [b]	2230 [c]	KBr	(s)
3. Phenyl *iso*cyanate	2274, 2263	LiF	(vs)
	2270	NaCl	(vs)
4. 1-Naphthyl *iso*cyanate ...	2275	LiF	2000
	2270	NaCl	1200
5. 2-Naphthyl *iso*cyanate	2267	LiF	(vs)
6. Octadecyl *iso*cyanate	2270	NaCl	(vs)
7. Naphthalene 1 : 5-di*iso*-cyanate	2265	LiF	1900
	2270	NaCl	1400
8. Toluene di*iso*cyanate	2265	LiF	(vs)
9. Methylenebis-(*p*-phenyl *iso*cyanate)	2272	LiF	(vs)
10. Hexamethylene di*iso*-cyanate	2270	LiF	(vs)

[a] Herzberg and Reid, *loc. cit.*; measured as a gas. [b] Eyster and Gillette, *loc. cit.*; measured as a gas. [c] Of doubtful accuracy since the prism has poor dispersion in this region.

* $\varepsilon = \log_{10}(I_0/I)/nbc$ where n is the number of NCO groups per molecule, b is the path length in cm., and c is the concentration in moles/l. Where not measured quantitatively, (vs) denotes very strong and (s) strong absorption.

examined for these stretching vibrations; the absorptions associated with the bending modes, which would probably be in the potassium bromide region, were not investigated.

Spectra of solutions in carbon tetrachloride were measured with a double-beam Grubb-

Parsons spectrometer, sodium chloride and lithium fluoride prisms being used; the results for $\nu_{a(NCO)}$ are given in the Table, together with those for cyanic acid and methyl *iso*cyanate, from the literature. Frequency calibration was based upon the rotational fine structure of carbon monoxide and carbon dioxide.

The results show that $\nu_{a(NCO)}$ gives an extremely intense characteristic absorption at 2269 ± 6 cm.$^{-1}$. In all cases, the frequency was re-measured with a capillary thickness of the undiluted liquid, or a paraffin mull of the solid *iso*cyanate; although it was difficult to obtain samples thin enough for accurate measurements, the frequencies were the same as those of the carbon tetrachloride solutions. Values of the group molar absorptivity (ε) were about 1300 with the normal slits required for sodium chloride working and about 2000 for lithium fluoride working. While it might have been expected that ε would be of the order of twice that for a typical $\nu_{C=O}$, or $\nu_{C=N}$, the measured values are much stronger, and so permit extremely sensitive analyses (the more so as the 2270-cm.$^{-1}$ region is spectrally transparent for most compounds). Nitriles absorb in the same region (Kitson and Griffith, *Analyt. Chem.*, 1952, **24**, 334), but they have in general lower frequencies (2250 ± 10 cm.$^{-1}$ for unconjugated nitriles) and very much weaker absorptions ($\varepsilon \sim 13$). Unlike $\nu_{C\equiv N}$, $\nu_{a(NCO)}$ is apparently unaffected by adjacent unsaturation.

It would obviously be of value to be able to distinguish *iso*cyanates from nitriles by means of other characteristic bands of the former, and so the 1300—1400 cm.$^{-1}$ region was examined for $\nu_{s(NCO)}$. Tentative assignments of weak absorptions occurring at 1380—1395 (in compounds 3—5 and 7) were made, but the bands were too weak to be of general diagnostic value, especially as they were liable to be hidden by the 1375-cm.$^{-1}$ bands associated with methyl and methylene deformations. This assignment corresponds to that of $\nu_{s(NCO)}$ at 1377 cm.$^{-1}$ in methyl *iso*cyanate (Eyster and Gillette, *loc. cit.*).

The author thanks Mr. G. R. Bates for experimental assistance, and the Dunlop Rubber Co. Ltd. for permission to publish this note.

CHEMICAL RESEARCH DIVISION, DUNLOP RESEARCH CENTRE,
BIRMINGHAM, 24. [*Received, June 19th*, 1953.]

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752. *The Interaction of Iodine Bromide and Phenol or Aniline.*

By A. G. SHARPE.

IODINE BROMIDE and phenol react in carbon tetrachloride according to equation (1) (Militzer, *J. Amer. Chem. Soc.*, 1938, **60**, 256):

$$C_6H_5{\cdot}OH + 2IBr \longrightarrow p\text{-}C_6H_4Br{\cdot}OH + HBr + I_2 \quad . \; . \; (1)$$

The formulation of the overall reaction as the sum of (2) and (3) appeared to be supported by the formation (in unspecified yield) of *p*-bromoaniline hydriodide in the interaction of

$$C_6H_5{\cdot}OH + Br \longrightarrow p\text{-}C_6H_4Br{\cdot}OH + HI \quad . \; . \; . \; (2)$$
$$HI + IBr \longrightarrow HBr + I_2 \quad . \; . \; . \; . \; . \; . \; . \; (3)$$

iodine bromide and aniline. Reaction (2), however, would imply polarization of the iodine–bromine bond in the unlikely direction I^-Br^+; and it has been suggested [Lambourne and Robertson, *J.*, 1947, 1167; Bennett and Sharpe, *J.*, 1950, 1383 (where physicochemical data are given)] that reaction (1) is one of bromination by the bromine formed in the thermal dissociation of iodine bromide, which takes place to the extent of 9·5% in carbon tetrachloride at 25°. A third suggestion, that the mechanism of (1) is represented by (4) and (5), has recently been made by Pearson and Ross (*J. Amer. Chem. Soc.*, 1952, **74**, 2933).

$$C_6H_5{\cdot}OH + IBr \longrightarrow p\text{-}C_6H_4I{\cdot}OH + HBr \quad . \; . \; . \; . \; (4)$$
$$2p\text{-}C_6H_4I{\cdot}OH + HBr \longrightarrow p\text{-}C_6H_4Br{\cdot}OH + C_6H_5{\cdot}OH + I_2 \quad . \; (5)$$

These authors have shown that, in carbon tetrachloride, reaction (5) is complete after 85 min. at 45° or 8—10 hr. at room temperature—conditions similar to those described by Militzer for the bromination of α-naphthol with iodine bromide in carbon tetrachloride.

It is now shown by quantitative analysis that phenol and iodine bromide in carbon tetrachloride react rapidly at room temperature. There is immediate evolution of hydrogen bromide, and the colour of iodine at once appears in the solution; after 10 min., half of the oxidising power of the iodine bromide has disappeared, and half of the bromine (but no iodine) has entered the aromatic nucleus. No further change occurs during 24 hr. Even after 30 sec., the reaction is about 80% complete. These periods are so much shorter than that required for (5) that Pearson and Ross's mechanism appears untenable.

After iodine bromide and excess of aniline have been allowed to react during 2 min. at room temperature, the solution possesses no oxidising properties, and a mole of iodine bromide yields 0·5 g.-ion each of Br^- and I^-. Aniline forms a complex with iodine in carbon tetrachloride solution, and then reacts with it even at room temperature (Hofmann, *Annalen*, 1848, **67**, 61; Hodgson and Marsden, *J.*, 1937, 1365); when solutions of aniline (0·02 mol.) and iodine bromide (0·04 mol.) are mixed, however, a strong but transient iodine colour appears. It seems possible, therefore, that thermal dissociation of the iodine bromide is followed by a very fast reaction between bromine and aniline and a somewhat slower reaction between iodine and aniline. The overall change is expressed by the equation,

$$2C_6H_5{\cdot}NH_2 + 2IBr \longrightarrow C_6H_4Br{\cdot}NH_2 + C_6H_4I{\cdot}NH_2 + HBr + HI \quad . \quad (6)$$

The stoicheiometry of (6) is therefore fundamentally different from that of (1); and Militzer's isolation of *p*-bromoaniline hydriodide may thus be explained without postulating that the iodine bromide reacts as I^-Br^+. Although the experiments described here do not eliminate the possibility of iodine bromide reacting as I^-Br^+, they do appear to show that the established thermal dissociation of iodine bromide affords a satisfactory alternative explanation for the course of its reactions with aromatic compounds.

Experimental Methods.—A solution of iodine bromide in carbon tetrachloride was standardised by shaking it with aqueous potassium iodide and titrating the liberated iodine with 0·2N-thiosulphate. Aliquot portions were allowed to react with phenol or aniline in carbon tetrachloride, and residual oxidising power was determined as before. Control experiments showed that when the iodine bromide solution was shaken with an aqueous solution containing both phenol and potassium iodide, iodine liberation was 95% of the theoretical; the possibility that any significant part of the reaction with phenol took place after addition of the potassium iodide solution was thereby eliminated.

For the determination of halides after reactions, the carbon tetrachloride solution was shaken with sulphurous acid. Total halide in the aqueous extract was determined by Volhard's method, and iodine by selective oxidation with excess of hydrogen peroxide and acetic acid (Mitchell, " Sutton's Volumetric Analysis," J. and A. Churchill, London, 1935, p. 256). In a typical experiment with phenol, in which solutions of 5 g. (excess) of phenol and 0·0240 mole of iodine bromide in 100 ml. carbon tetrachloride at 20° were allowed to react during 10 min., the products (*a*) liberated 0·0122 mole of iodine from potassium iodide and (*b*) after reduction with sulphurous acid contained 0·0355 g.-ion of total halide, of which 0·0230 g.-ion were iodide. With a reaction period of 30 sec., the products liberated 0·0146 mole of iodine. Other results are presented in outline above.

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753. *Bond Type in Trisacetylacetonecobalt*(III).

By Richard O. Whipple, Robert West, and Kenneth Emerson.

B. West (*J.*, 1952, 3122) has recently indicated the need for a redetermination of the magnetic susceptibility of trisacetylacetonecobalt(III) in order to make clear the nature of the bonding in this compound. The only previously reported measurement, by Ishiwara (*Rep. Tohoku Univ.*, 1914, **3**, 309), indicates paramagnetism amounting to 0·93 Bohr magneton. This is not consistent with either d^2sp^3 hybrid bonds (which should lead to diamagnetism) or with the "ionic" structure (which should have four unpaired electrons).*

The present authors have determined the magnetic susceptibility of trisacetylacetonecobalt(III) and find it to be diamagnetic. Therefore, the compound is very probably an octahedral penetration complex of the usual type with d^2sp^3 hybrid covalent bonding. The slow cobalt exchange noted by West (*loc. cit.*) for this compound is not surprising in view of the large electronegativity difference between cobalt and oxygen, and the resulting ionic character of the Co–O bonds.

An interesting parallel to this case of conflicting magnetic data is afforded by the related compound, tripotassium cobalt(III) oxalate. The original report of diamagnetism for this compound (Wiedemann, *Ann. Physik*, 1887, **32**, 459) was first contradicted (Berkman and Socher, *Z. phys. Chem.*, 1926, **124**, 324) and later confirmed (Johnson, *Trans. Faraday Soc.*, 1932, **28**, 848). The results of Berkman and Socher and those of Ishiwara (*locc. cit.*) can probably be ascribed to paramagnetic or ferromagnetic impurities, which are often persistent contaminants in compounds of the transition metals.

Experimental.—Trisacetylacetonecobalt(III). Chloropentamminocobalt(III) dichloride (10 g.) was dissolved in hot water (400 ml.), and the pH adjusted to approx. 8 by addition of 2N-sodium hydroxide. Acetylacetone (50 g.) was added, and the solution was heated on the steam-bath until long, green needles of product appeared (about 30 min.). The mixture was then cooled and extracted several times with benzene. The combined extracts were dried and evaporated to give black crystals. The product (from several similar preparations) was recrystallized three times from absolute ethanol and twice from benzene; the final recrystallization was carried out shortly before the magnetic measurements were made. The compound melted at 198·5° (corr.) (Found: Co, 16·3; C, 50·7; H, 6·1. Calc. for $C_{15}H_{21}O_6Co$: Co, 16·5; C, 50·6; H, 5·9%). West (*loc. cit.*) found m. p. 196° (uncorr.) and Urbain and Debierne (*Compt. rend.*, 1899, **129**, 302) give 240°.

Magnetic measurements. These were made by the Gouy split-tube method, water and air being used as standards. Three packings of the tube were made, and measurements were carried out at six field strengths between 7000 and 12,000 gauss. The susceptibilities obtained were independent of field strength. The volume susceptibility at 27·4° was $-0{\cdot}159 \times 10^{-6}$ c.g.s. unit, corrected for air in the sample. This corresponds to a gram-susceptibility of $-0{\cdot}167 \times 10^{-6}$ and a molar susceptibility of $-59{\cdot}4 \times 10^{-6}$ c.g.s. unit.

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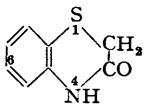
* West suggests a third possible structure involving d^3 hybrid bonds. Such a structure would, however, be diamagnetic, and not paramagnetic as he suggests.

754. *Preparation of 2 : 3-Dihydro-3-oxobenzo-1 : 4-thiazine Derivatives as Possible Anthelmintics. Part II.**

By ALEXANDER MACKIE and A. ANTHONY CUTLER.

SINCE many derivatives of 2 : 3-dihydro-3-oxobenzo-1 : 4-thiazine (I) show distinct anthelmintic effects when tested *in vitro* against liver fluke (*Fasciola hepatica*) (Mackie and Raeburn, *Brit. J. Pharmacol.*, 1952, **7**, 219), the earlier work in this series (*idem*, *J.*, 1952, 787; Mackie and Cutler, *Rec. Trav. chim.*, 1952, **71**, 1198) has been extended, particularly to 6-substituted compounds.

The 6-bromo-, 6-methyl, and 6-*tert.*-butyl derivatives were obtained by reduction of the corresponding *para*-substituted (*o*-nitrophenylthio)acetic acids. These acids were prepared by treating the appropriate diazotised *o*-nitro-amine with mercaptoacetic acid in presence of aqueous sodium acetate and decomposing the (phenyldiazothio)acetic acids thus obtained by hot aqueous sodium carbonate (cf. Friedlaender and Chwala, *Monatsh.*, 1907, **28**, 279). Previous attempts to prepare the 6-bromo-compound either by Sandmeyer reaction or by decomposition of the diazonium perbromide resulted only in highly impure material.


(I)

6-Toluene-*p*-sulphonamido-, 6-acetamidobenzenesulphonamido-, and 6 : 7-diethoxy-derivatives of (I) were also prepared.

Analogy with known anthelmintics led to unsuccessful attempts to condense the 6-chloro-derivative of (I) with 2-diethylaminoethylamine, and the 6-amino-derivative with 10-chloroacetylphenothiazine, and to prepare the 6 : 7-dichloro-derivative of (I) from the 6 : 7-dihydroxy-compound.

The derivatives prepared showed only depressant or no effect when tested against anterior preparations of the roundworm *Ascaris lumbricoides*, but some had a paralysant effect on liver fluke (*Fasciola hepatica*) *in vitro*, the 6-bromo-derivative being very effective (1 : 20,000). Details of these tests will be published elsewhere.

Experimental.—6-*Chloroacetoamido*-2 : 3-*dihydro*-3-*oxobenzo*-1 : 4-*thiazine*. Chloroacetyl chloride (6 g.) was slowly added to a boiling glacial acetic acid solution (150 c.c.) of 6-amino-2 : 3-dihydro-3-ketobenzo-1 : 4-thiazine (7 g.), and the mixture refluxed for 30 min. Pouring the cooled product into cold water gave the pale brown *chloroacetoamido*-derivative, which crystallised from aqueous ethanol as colourless needles (4 g.), m. p. 240—241° (decomp.) (Found : N, 11·1. $C_{10}H_9O_2N_2ClS$ requires N, 10·9%).

6-*Benzamido*-2 : 3-*dihydro*-3-*oxobenzo*-1 : 4-*thiazine*. Benzoyl chloride (15 c.c.) was added portionwise to vigorously agitated 6-amino-2 : 3-dihydro-3-oxobenzo-1 : 4-thiazine (5 g.) suspended in aqueous sodium hydroxide (175 c.c.). The precipitated *benzamido*-derivative crystallised from acetic acid in colourless needles (3 g.), m. p. 269—270° (decomp.) (Found : N, 9·6. $C_{15}H_{12}O_2N_2S$ requires N, 9·9%).

2 : 3-*Dihydro*-3-*oxo*-6-*toluene*-p-*sulphonamidobenzo*-1 : 4-*thiazine*. A pyridine solution (30 c.c.) of the 6-amino-compound (4·5 g.) was refluxed with toluene-*p*-sulphonyl chloride (7 g.) for 2 hr. The dark brown precipitate was dissolved in 0·1N-sodium hydroxide (200 c.c.), diluted to 600 c.c., refluxed with charcoal, and filtered. The filtrate was added slowly to excess of dilute sulphuric acid and recrystallization of the resulting precipitate from aqueous ethanol gave colourless needles (3 g.) of the pure *toluenesulphonamido-thiazine*, m. p. 235—236° (decomp.) (Found : N, 8·3. $C_{15}H_{14}O_3N_2S_2$ requires N, 8·4%).

6-p-*Acetamidobenzenesulphonamido*-2 : 3-*dihydro*-3-*oxobenzo*-1 : 4-*thiazine*. *p*-Acetamidobenzenesulphonyl chloride (6 g.) was refluxed for 1 hr. with a pyridine solution (15 c.c.) of the 6-amino-derivative (4·5 g.). The product was refluxed with acetone (200—250 c.c.), then filtered hot, and, on addition of water, the required *compound* was precipitated. It formed pale yellow feathery needles (5 g.), m. p. 305° (decomp.), from nitrobenzene (Found : N, 10·9. $C_{16}H_{15}O_4N_3S_2$ requires N, 11·1%).

6 : 7-*Diethoxy*-2 : 3-*dihydro*-3-*oxobenzo*-1 : 4-*thiazine*. A solution of 2 : 3-dihydro-6 : 7-di-

* *J.*, 1952, 787, is considered to be Part I of this series.

hydroxy-3-oxobenzo-1 : 4-thiazine (5 g.) (Mackie and Raeburn, *J.*, 1952, 787) in ethanolic sodium ethoxide (50 c.c.) was refluxed (2—3½ hr.) with ethyl sulphate (12 g.) in an inert atmosphere. After cooling and dilution with water, the product was filtered off, dissolved in hot benzene (charcoal), and filtered. Light petroleum (b. p. 60—80°) precipitated the 6 : 7-*diethoxythiazine* which formed pale yellow rectangular prisms (0·3 g.), m. p. 136—137°, from aqueous ethanol (Found : C, 56·4; H, 6·1. $C_{12}H_{15}O_3NS$ requires C, 56·2; H, 6·3%).

6-*Bromo*-2 : 3-*dihydro*-3-*oxobenzo*-1 : 4-*thiazine*. 4-Bromo-2-nitroaniline (40 g.) was diazotised and the solution added to a well-cooled mixture of mercaptoacetic acid (25 g.) and aqueous sodium acetate (containing 60 g.). A solution in aqueous sodium carbonate of the thick red oil obtained was decomposed on warming, and acidification of the aqueous solution of the product afforded a bright yellow precipitate of the crude (4-*bromo*-2-*nitrophenylthio*)*acetic acid* (19 g.), which was sufficiently pure for the reduction. It crystallised from aqueous ethanol as yellow needles, m. p. 216—217° (Found : C, 33·3; H, 2·0; N, 4·9. $C_8H_6O_4NBrS$ requires C, 32·9; H, 2·1; N, 4·8%).

Reduction of this acid gave the 6-bromo-thiazine, colourless needles (8 g.), m. p. 204—205° (from aqueous ethanol) (Found: C, 39·3; H, 2·5; N, 5·5. Calc. for C_8H_6ONBrS: C, 39·3; H, 2·5; N, 5·7%). Mackie and Raeburn (*loc. cit.*) gave the m. p. of the supposedly impure bromo-compound as 220°, with a nitrogen content of 5·0%, but there appears to be no doubt that the compound obtained by the above method is pure bromo-derivative.

(4-*Methyl*-2-*nitrophenylthio*)*acetic acid*, similarly prepared from 3-nitro-4-aminotoluene (20 g.), crystallised from aqueous ethanol as yellow needles (6 g.), m. p. 182—183° (Found : C, 47·7; H, 4·0; N, 6·2. $C_9H_9O_4NS$ requires C, 47·6; H, 4·0; N, 6·2%), and on reduction afforded the 6-*methyl-thiazine*, pale cream-coloured needles (4 g.) (from aqueous acetic acid), m. p. 178—179° (partial decomp.) (Found : C, 60·6; H, 5·1; N, 8·0. C_9H_9ONS requires C, 60·3; H, 5·0; N, 7·8%).

6-tert.-*Butyl*-2 : 3-*dihydro*-3-*oxobenzo*-1 : 4-*thiazine*.—4-*tert.*-Butyl-2-nitroaniline (10 g.) (Shoesmith and Mackie, *J.*, 1928, 2336) gave (4-tert.-*butyl*-2-*nitrophenylthio*)*acetic acid*, yellow needles (1 g.), m. p. 162—163° (from aqueous ethanol) (Found : C, 53·4; H, 5·6. $C_{12}H_{15}O_4NS$ requires C, 53·5; H, 5·6%), and thence the 6-tert.-*butyl-thiazine*, colourless plates (0·2 g.), m. p. 170—171° (from aqueous ethanol) (Found : C, 63·7; H, 6·8; N, 6·0. $C_{12}H_{15}ONS$ requires C, 65·2; H, 6·8; N, 6·3%).

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755. *Phenylthiohydantoins from Serine and Threonine.*

By V. M. INGRAM.

DURING the stepwise degradation of peptides by Edman's method (*Acta Chem. Scand.*, 1950, **4**, 283) the amino-acids appear as the corresponding substituted 3-phenyl-2-thiohydantoins. Authentic samples of most of these derivatives are readily prepared (*idem, ibid.*, p. 277), but threonine has so far only yielded the dehydrated analogue, 5-ethylidene-3-phenyl-2-thiohydantoin, and attempts to isolate the serine derivative were unsuccessful (*idem, locc. cit.*; Swan, *Australian J. Sci. Res., A*, 1952, **5**, 719). By using milder conditions the pure phenylthiohydantoins from these two amino-acids have now been isolated, and the products of hydrolysis have been briefly examined.

Experimental.—From serine. DL-Serine (1·0 g.) was treated with phenyl *iso*thiocyanate, Edman's method (*ibid.*, p. 277) being used at room temperature. Excess of reagent was removed by several extractions with benzene, and acid was added until the pH was 1; some pink oil separated and was discarded. 5-*Hydroxymethyl*-3-*phenyl*-2-*thiohydantoin* was deposited during 2 days at room temperature and was recrystallised from ethanol; the derivative

(0·9 g.) then had m. p. 176—178° (Found: C, 53·9; H, 4·5; N, 12·5. $C_{10}H_{10}O_2N_2S$ requires C, 54·1; H, 4·5; N, 12·6).

From threonine. By the same procedure DL-threonine (0·5 g.) was converted into 5-1′-*hydroxyethyl*-3-*phenyl*-2-*thiohydantoin*, which formed felted needles (0·55 g.) (from ethanol), m. p. 194° (decomp.; after charring at 150°) (Found: C, 55·5; H, 4·9; N, 11·8. $C_{11}H_{12}O_2N_2S$ requires C, 55·9; H, 5·1; N, 11·9).

Both phenylthiohydantoins were examined by paper chromatography in two of the solvent systems recommended by Sjöquist (*Acta Chem. Scand.*, 1953, **7**, 447). The following relative R_F values (3-phenyl-2-thiohydantoin, $R_F = 1·00$) were found for the serine and the threonine derivatives: in heptane–pyridine, 0·77 and 1·00, respectively; in heptane–*n*-butanol–formic acid (2 : 2 : 1), 0·82 and 0·97, respectively.

Hydrolysis. Hydrolysis at 150° of the phenylthiohydantoin (10 micromoles) from serine in hydrobromic acid (47%; 1 c.c.; 24 hr.) or aqueous barium hydroxide (0·25 N; 2 c.c.; 48 hr.) yielded a mixture of alanine and serine in variable proportions. Under similar conditions the threonine compound formed mainly α-aminobutyric acid and some glycine in hydrobromic acid; when heated with aqueous barium hydroxide, threonine appeared together with smaller quantities of glycine and α-aminobutyric acid. The amino-acids were identified by paper chromatography, *n*-butanol–acetic acid–water (3 : 1 : 1) and Hausmann's *sec*-butanol–ammonia and *sec*.-butanol–formic acid (*J. Amer. Chem. Soc.*, 1952, **74**, 3181) being used.

MEDICAL RESEARCH COUNCIL UNIT FOR THE STUDY OF THE MOLECULAR STRUCTURE OF BIOLOGICAL SYSTEMS, CAVENDISH LABORATORY, CAMBRIDGE.

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756. *Azulenes. Part I. A Synthesis of Azulene.*

By DOUGLAS LLOYD and FREDERICK ROWE.

bicyclo[5 : 3 : 0]DEC-7-EN-9-ONE, prepared by the method described by Islam and Raphael (*J.*, 1952, 4086) for *bicyclo*[4 : 3 : 0]non-6-en-8-one, has been converted into the corresponding *bicyclo*[5 : 3 : 0]decenol and *bicyclo*[5 : 3 : 0]decadiene. The latter, when dehydrogenated over palladium–charcoal in a vacuum (see Gordon, *Chem. Reviews*, 1952, **50**, 168), yielded a main product which was identified as azulene by means of its ultraviolet spectrum.

Experimental.—Ethyl 1-*acetonyl*-2-*oxo*cyclo*heptane*-1-*carboxylate.* This was prepared essentially by Islam and Raphael's method (*loc. cit.*). Propargyl bromide was condensed with the sodium derivative of ethyl 2-oxo*cyclo*heptane-1-carboxylate to give ethyl 2-oxo-1-propargyl-*cyclo*heptane-1-carboxylate, which was then converted into ethyl 1-acetonyl-2-oxo*cyclo*heptane-1-carboxylate, b. p. 134°/2 mm. The *bis*-2 : 4-*dinitrophenylhydrazone* formed yellow prisms, m. p. 175°, from methanol–ethyl acetate (Found: C, 50·1; H, 4·9; N, 18·7. $C_{25}H_{28}O_{10}N_8$ requires C, 50·0; H, 4·7; N, 18·7%). The *disemicarbazone* could not be satisfactorily recrystallised, but a dust-free sample, purified by washing it, had m. p. 223° (decomp.) (Found: C, 51·3; H, 7·7; N, 23·2. $C_{15}H_{26}O_4N_6$ requires C, 50·8; H, 7·35; N, 23·7%).

bicyclo[5 : 3 : 0]*Dec*-7-*en*-9-*one.* Ethyl 1-Acetonyl-2-oxo*cyclo*heptane-1-carboxylate (4·2 g.) was heated under reflux with aqueous potassium hydroxide solution for 6 hr. in nitrogen (cf. Islam and Raphael, *loc. cit.*). The product (2·0 g., 76%), b. p. 94°/2 mm., formed a *dinitrophenylhydrazone* as red needles [from light petroleum (b. p. 80—100°)], m. p. 185° (Found: C, 58·6; H, 5·5; N, 16·8. $C_{16}H_{18}O_4N_4$ requires C, 58·2; H, 5·45; N, 17·0%).

bicyclo[5 : 3 : 0]*Dec*-7-*en*-9-*ol.* The *bicyclo*[5 : 3 : 0]decenone (2·0 g.) was reduced with lithium aluminium hydride, giving a faintly yellow oil, b. p. 88—92°/2 mm. (1·55 g., 76·5%). Various attempts to dehydrogenate this oil, by using sulphur, selenium, chloranil, and palladium–charcoal, were ineffective; heating of a sample under reflux with nitrobenzene and iodine (cf. Treibs, *Annalen*, 1952, **576**, 110) produced an intense green material, which was soluble in phosphoric acid, and could be separated readily by paper chromatography, but faded rapidly in air.

bicyclo[5 : 3 : 0]*Deca*-7 : 9-*diene*. *bicyclo*Decanol (1·2 g.) was heated with freshly fused, powdered potassium hydrogen sulphate (1 g.). Much charring occurred but a brown oil (0·3 g.), b. p. 80—90°/2 mm., was obtained as distillate.

Present work				P. and H. (*loc. cit.*)			
$\lambda_{max.}$	log ε	$\lambda_{max.}$	log ε	$\lambda_{max.}$	log ε	$\lambda_{max.}$	log ε
2380	4·29	3260	3·58	2380	4·22	3260	3·48
2620	4·60	3380	3·70	2730	4·74	3360	3·58
2730	4·83	3510	2·96	2790	4·69	3410	3·64
2790	4·79	3610	2·16	2950	3·58	3510	3·18
2950	3·59					3610	2·34

Azulene. This brown oil was distilled, at 1 mm. pressure in an atmosphere of nitrogen, over palladium–charcoal (20%) heated to 350°. Deep blue needles of azulene formed in the receiver. The product was purified by fractionation on alumina, and its ultra-violet spectrum recorded. This coincided with that previously recorded by Plattner and Heilbronner (*Helv. Chim. Acta*, 1948, **31**, 804) (see the Table).

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757. *Constituents of the Higher Fungi. Part III.* Agrocybin.*

By E. R. H. JONES and J. D. BU'LOCK.

SINCE the characterisation of " Lachnophyllum ester " as methyl dec-2-en-4 : 6-diynoate (Wiljams, Smirnov, and Goljmov, *J. Gen. Chem. Russia*, 1935, **5**, 1195), the conjugated polyacetylenes have been shown to constitute a considerable group of natural products with a surprisingly wide distribution. Of outstanding importance has been the work of Sörensen and his collaborators on the isolation of a series of polyacetylenic compounds from plants of the Compositae family, where they are of widespread occurrence (cf. Sörensen, *Chem. and Ind.*, 1953, 240). Polyacetylene structures have also been established for the plant poisons, oenanthotoxin and cicutoxin (from Umbelliferae) (Anet, Lythgoe, Silk, and Trippett, *J.*, 1953, 309), and the component acids of certain seed oils (cf. Black and Weedon, *J.*, 1953, 1785). The occurrence of such compounds is not, however, confined to the higher plants, as polyacetylene compounds are also produced by certain fungi. A number of antibiotics isolated from various Basidiomycetes exhibit the characteristic ultra-violet absorption of poly-ynes; to those described by Anchell (*J. Amer. Chem. Soc.*, 1952, **74**, 1588) may be added two compounds from *Coprinus quadrifidus* (Doery, Gardner, Burton, and Abraham, *Antibiotics and Chemotherapy*, 1951, **1**, 409). Mycomycin, from the soil actinomycete *Nocardia acidophilus* and having the structure trideca-3 : 5 : 7 : 8-tetraen-10 : 12-diynoic acid (Celmer and Solomons, *J. Amer. Chem. Soc.*, 1952, **74**, 1860, 3838; 1953, **75**, 1372), has hitherto been the only polyacetylene antibiotic of known structure. In this paper we describe the characterisation of a second antibiotic, agrocybin, as octa-2 : 4 : 6-triynamide.

Through the courtesy of Dr. W. J. Robbins, Director of the New York Botanical Gardens, and Dr. M. Anchell, we were supplied with cultures of several fungi, on the metabolic products of which preliminary work had been done. From one of these, *Agrocybe dura*, Kavanagh, Hervey, and Robbins (*Proc. Nat. Acad. Sci.*, 1950, **36**, 102) had isolated an antibiotic, agrocybin, for which they reported details of biological activity and some physical properties, including the ultra-violet absorption spectrum. Using a process similar to theirs, we were able to isolate agrocybin from culture liquids in yields of *ca.* 30 mg./l., although not reproducibly.

Agrocybin formed crystals which decomposed explosively at 130—140° without

* Part II, *J.*, 1940, 1491.

melting, and blackened in a few hours when exposed to light. The ultra-violet absorption spectrum (see table) is characteristic of the chromophore ·[C:C]$_3$·R', where R' is a carboxyl

Agrocybin in ethanol [1]	$\lambda_{max.}$, Å	2150	2240	2690	2860	3040	3250
	10^{-3} ε	68·0	86·5	1·75	2·40	3·05	1·95
Octa-2 : 4 : 6-triynoic acid in ethanol [2] ...	$\lambda_{max.}$, Å	—	2200	2700	2860	3050	3260
	10^{-3} ε	—	62·0	2·4	2·8	2·5	2·1

[1] Positions of maxima agree with those previously reported by Kavanagh *et al.* (*loc. cit.*). [2] From Jones, Whiting, Armitage, Cook, and Entwistle, *Nature*, 1951, **168**, 900.

group or its spectroscopic equivalent. Comparison of the observed absorption intensities with the molecular-extinction coefficients for octa-2 : 4 : 6-triynoic acid indicated a molecular weight of *ca.* 150, assuming that agrocybin contains only one chromophore; on the same assumption, the hydrogenation equivalent gave a more accurate value of 135 ± 5. Analytical data (see Experimental) indicated the presence of one atom of nitrogen in a molecule of this size; this, coupled with the observation that agrocybin is a neutral compound, suggested that the chromophore might be ·[C:C]$_3$·CO·NH$_2$. (Other work in these laboratories, as yet unpublished, has shown that the absorption spectrum of hepta-2 : 4-diynoic acid closely resembles that of its amide.) This was confirmed by the infra-red absorption spectrum of the compound, measured in Nujol suspension, which shows bands at 2125 and 2210 cm.$^{-1}$, characteristic of a conjugated poly-yne, and at 1420, 1620, and 1680 cm.$^{-1}$, characteristic of a conjugated primary amide. The spectrum also showed that ethynyl groups were absent, so that a structure of the type R·[C:C]$_3$·CO·NH$_2$ was indicated. The nature of the non-chromophoric group R was established by the hydrogenation of agrocybin, which was rapid and quantitative, to give a compound identified by m. p., mixed m. p., and infra-red spectrum as octanamide. Thus agrocybin is octa-2 : 4 : 6-triynamide.

Agrocybin was not affected by contact with dilute aqueous alkali at 25°, but during 30 minutes of treatment with 1% potassium hydroxide in ethanol the optical density around 3000 Å increased about tenfold, the resulting solution having absorption maxima at 2850 (infl.), 2970, 3120, and 3270 Å (infl.) (relative intensities 0·8, 1·0, 1·0, 0·75). Changes of this type, which have been observed with other, similar, poly-ynes, are probably to be ascribed to a base-catalysed addition of ethanol to the conjugated poly-yne system, and are to be distinguished from the ready isomerisation, in aqueous alkali, of polyacetylenes containing an allene group (cf. Celmer and Solomons, *loc. cit.*). Studies of both types of reaction are in progress in these laboratories and will be reported in due course.

Experimental.—Isolation. Cultures of *A. dura* were grown on a corn-steep medium as described by Kavanagh *et al.* (*loc. cit.*). The culture liquid was extracted twice with 1/10 volume of ethyl acetate, the combined extracts evaporated to a small volume, the concentrate washed with 2% aqueous sodium hydrogen carbonate, and the ethyl acetate finally removed by evaporation over a small volume of water, all evaporations being carried out under reduced pressure. This procedure gave substantially pure agrocybin (yield, *ca.* 30 mg./l. of culture liquid). The product, recrystallised (to constant extinction coefficient) from aqueous ethanol, decomposed explosively at 130—140° [Found: C, 66·1; H, 3·9; N, 10·7; OMe, absent. C_8H_5ON requires C, 73·3; H, 3·8; N, 10·7%. Kavanagh *et al.* (*loc. cit.*) found C, 65·6; H, 4·3%; accurate analyses are frequently difficult to obtain with compounds of this type, particularly when, as in this case, only a limited amount of material is available].

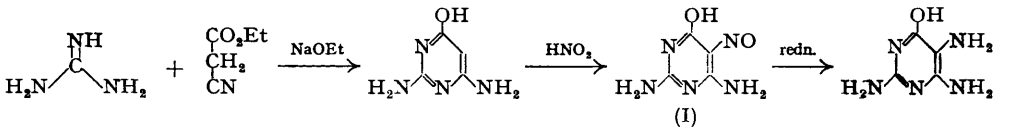
Hydrogenation. Agrocybin (10·0 mg.), hydrogenated over Adams's platinum catalyst in ethanol, rapidly took up the calculated volume of hydrogen (Found: 11·2 c.c. at 22°/757 mm. C_8H_5ON, three triple bonds, requires 11·2 c.c.). The filtered solution was evaporated and the solid residue recrystallised from light petroleum to give octanamide, m. p. 103—105°, not depressed by admixture with authentic material, m. p. 105—106°, and depressed to 92—98° by admixture with nonanamide, m. p. 99°.

THE UNIVERSITY, MANCHESTER, 13. [*Received, July 18th*, 1953.]

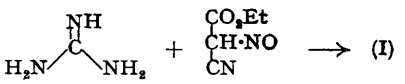
758. *A Convenient Synthesis of Some 4-Substituted 5-Aminopyrimidines.*

By PHYLLIS D. LANDAUER and H. N. RYDON.

5-AMINOPYRIMIDINES containing hydroxyl or amino-groups in the 4- or 6-positions have usually been prepared (cf. Lythgoe, *Quart. Reviews*, 1949, **3**, 181) by a three-stage process involving condensation of an active methylene compound with urea or a derivative, followed by nitrosation (or coupling with a diazonium salt) and reduction, *e.g.*, 2 : 4 : 5-triamino-6-hydroxypyrimidine was prepared as follows (Traube, *Ber.*, 1900, **33**, 1371) :



We now report work on a shorter route in which the intermediate nitroso-compound is prepared by direct condensation of the urea derivative with the readily available ethyl hydroxyiminocyanoacetate (Conrad and Schulze, *Ber.*, 1909, **42**, 735) or ethyl hydroxyiminomalonate (*iso*nitrosomalonate) (Cerchez, *Bull. Soc. chim.*, 1930, **47**, 1279), *e.g.* :



The condensation of ethyl hydroxyiminocyanoacetate with, *inter al.*, urea and guanidine is described in a German patent (D.R.P. 206453; "Friedländer," **9**, 1005) and that of ethyl hydroxyiminomalonate with thiourea by Johnson and Nicolet (*J. Amer. Chem. Soc.*, 1914, **36**, 354), but the possibilities of this method appear to have been overlooked by most workers in the pyrimidine field.

The method is very simple and convenient, and gives overall yields which are often superior to those obtained by using the more usual procedure; the method is especially valuable for the preparation of 2 : 4 : 5-triamino-6-hydroxypyrimidine, a key intermediate in the preparation of pteroic and folic acids. In the initial condensation with the hydroxyimino-compound either one or two equivalents of sodium ethoxide are used, the choice depending on the relative solubilities of the resulting 5-nitrosopyrimidine and its sodium salts; in certain cases we have found efficient stirring to be essential. The reduction of the 5-nitrosopyrimidine to the amino-compound can be conveniently effected by using either sodium hydrosulphite (dithionite) or Raney nickel; the former is convenient in cases when the 5-aminopyrimidine can be isolated as an insoluble sulphate but the latter is preferable in cases where the sulphate of the product is freely soluble in water or where it is desired to eliminate a thiol group simultaneously with the reduction. We outline below satisfactory procedures for the preparation of 2 : 4 : 5-triamino-6-hydroxy-, 4 : 5-diamino-6-hydroxy-2-methyl-, 4 : 5-diamino-6-hydroxy-, 4 : 5-diamino-2 : 6-dihydroxy-, and 2 : 5-diamino-4 : 6-dihydroxy-pyrimidine (divicine).

Experimental.—2 : 4 : 5-*Triamino-6-hydroxypyrimidine.* Finely powdered guanidine hydrochloride (19·1 g., 0·2 mole) was added to ethanolic sodium ethoxide, prepared from sodium (9·1 g., 0·4 mole) and ethanol (125 ml.). After 30 min. at room temperature with occasional shaking, sodium chloride was filtered off and ethyl hydroxyiminocyanoacetate (28·4 g., 0·2 mole) added to the filtrate; the mixture was shaken vigorously and then kept at room temperature overnight. The precipitated 2 : 4-diamino-6-hydroxy-5-nitrosopyrimidine (I) was filtered off, washed with water, and suspended in hot water (750 ml.); sodium dithionite (40 g.) was added and the mixture boiled for 5 min., the red colour of the nitroso-compound being discharged. Slow addition of concentrated sulphuric acid (180 ml.) precipitated 2 : 4 : 5-triamino-6-hydroxypyrimidine sulphate, which was filtered off after cooling (29·0 g.;

59%); it crystallised from 2N-sulphuric acid in needles (Found: N, 28·1, 28·2. Calc. for $C_4H_7ON_5,H_2SO_4,\frac{1}{2}H_2O$: N, 28·2%).

4 : 5-*Diamino*-6-*hydroxy*-2-*methylpyrimidine*.—Acetamidine hydrochloride (9·45 g., 0·1 mole) was condensed as usual with ethyl hydroxyiminocyanoacetate (14·2 g., 0·2 mole) by using sodium ethoxide from sodium (4·6 g., 0·2 mole) and ethanol (100 ml.). The pale violet sodium salt of 4-amino-6-hydroxy-2-methyl-5-nitrosopyrimidine (14 g., 79%) was filtered off, washed with a little ethanol, and dried at 100°. On a larger scale it was essential to add the hydroxyimino-ester with efficient mechanical stirring. This salt (4·4 g.) was dissolved in water (100 ml.), and the solution warmed to 70°; wet Raney nickel catalyst was added in portions until no further colour change occurred. The mixture was then heated on the steam-bath for an hour, and the nickel filtered off and washed thoroughly with hot water. The filtrate and washings were acidified with sulphuric acid and concentrated under reduced pressure to 50 ml. Basification with ammonia solution precipitated 4 : 5-diamino-6-hydroxy-2-methylpyrimidine in sparkling platelets (2·5 g., 72%); recrystallisation from 2N-sulphuric acid gave the sulphate in needles, m. p. 265° (Found: N, 23·6. Calc. for $C_5H_8ON_4,H_2SO_4$: N, 23·5%).

4 : 5-*Diamino*-6-*hydroxypyrimidine*. Thiourea (38 g., 0·5 mole) was condensed with ethyl hydroxyiminocyanoacetate (71 g., 0·5 mole), by using sodium ethoxide, from sodium (23 g., 1 mole) and ethanol (1 l.). The brown-red sodium salt of 4-amino-6-hydroxy-2-mercapto-5-nitrosopyrimidine (75 g., 77%) was filtered off, washed with a little ethanol, and dried at 100°. This salt (4·9 g.) was reduced with Raney nickel as described for the 2-methyl compound; the concentrate, after being kept at 0° overnight, deposited 4 : 5-diamino-6-hydroxypyrimidine (2·0 g., 63%) which yielded the hemisulphate as needles, m. p. 268°, on crystallisation from 2N-sulphuric acid (Found: N, 31·6; S, 9·0. Calc. for $C_4H_6ON_4,\frac{1}{2}H_2SO_4$: N, 32·0; S, 9·2%).

4 : 5-*Diamino*-2 : 6-*dihydroxypyrimidine*. Urea (6·0 g., 0·1 mole) was condensed with ethyl hydroxyiminocyanoacetate (14·2 g., 0·1 mole) and sodium ethoxide, from sodium (4·6 g., 0·2 mole) and ethanol (150 ml.). The precipitated nitroso-compound was filtered off and suspended in 4% sodium hydroxide solution (400 ml.) at 60°; sodium dithionite was added in small portions until the solution was clear and no further colour change occurred. The solution was boiled with charcoal, filtered, cooled to room temperature, and treated with concentrated sulphuric acid (25 ml.); the precipitated 4 : 5-diamino-2 : 6-dihydroxypyrimidine sulphate was filtered off and recrystallised from 2N-sulphuric acid; the yield was 11 g. (46%).

2 : 5-*Diamino*-4 : 6-*dihydroxypyrimidine* (*divicine*). Guanidine hydrochloride (9·55 g., 0·1 mole) was added to sodium ethoxide, from sodium (6·9 g., 0·3 mole) and ethanol (150 ml.). After 30 min. at room temperature, the mixture was refluxed while ethyl hydroxyiminomalonate was added during 10 min. with rapid mechanical stirring; refluxing and stirring were continued for a further hour. The precipitated nitroso-compound was filtered off, suspended in water (400 ml.) at 60°, and reduced, as described above, with sodium dithionite. Concentrated sulphuric acid (25 ml.) was added to the cooled solution, and the precipitated divicine hemisulphate was filtered off, washed, and dried (8·6 g., 45%).

The sulphate (1·45 g.) was triturated with water (10 ml.), and 2N-sodium hydroxide (4 ml.) added dropwise to bring the pH to 8. The base was filtered off and at once warmed with N-hydrochloric acid (30 ml.); after the solution had been filtered, while hot, from a little sulphate, ethanol (30 ml.) was added, followed by sufficient water (10 ml.) to re-dissolve the precipitated hydrochloride. The solution was boiled with charcoal, filtered, and more ethanol (40 ml.) added to the hot filtrate. Divicine hydrochloride (1·03 g., 69%) crystallised in beautiful flattened needles. Recrystallisation from 2N-hydrochloric acid (25 ml.) and ethanol (25 ml.) gave analytically pure material (0·73 g.) (Found: N, 28·5; Cl, 18·1. Calc. for $C_4H_6O_2N_4,HCl,H_2O$: N, 28·5; Cl, 18·1%).

We are grateful to Messrs. H. G. Baxter and R. H. Doust for experimental assistance and to the Department of Scientific and Industrial Research for a Maintenance Allowance (to P. D. L.). Analyses were carried out in the microanalytical laboratory (Mr. F. H. Oliver) of this Department.

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759. *Methanesulphonic Anhydride.*

By L. N. Owen and S. P. Whitelaw.

For the synthesis of certain types of methanesulphonates the use of methanesulphonic anhydride, rather than the chloride, may be advantageous (compare Linstead, Owen, and Webb, *J.*, 1953, 1225). The only method so far described for the preparation of the anhydride involves the interaction of silver methanesulphonate with methanesulphonyl chloride (Billeter, *Ber.*, 1905, **38**, 2018). Aromatic sulphonic anhydrides have been obtained by reaction of a sulphonic acid, or its sodium salt, with thionyl chloride (Meyer and Schlegl, *Monatsh.*, 1913, **34**, 561; Meyer, *Annalen*, 1923, **433**, 335; Fichter and Stocker, *Helv. Chim. Acta*, 1924, **7**, 1072), but such methods have not been applied to aliphatic sulphonic acids. We have now found that methanesulphonic anhydride can be simply prepared in over 80% yield by treatment of methanesulphonic acid with boiling thionyl chloride.

Experimental.—Methanesulphonic acid (35 g.), b. p. 140°/2 mm., and thionyl chloride (100 c.c.) were boiled under reflux for 3 hr., and then evaporated to a dark solid residue which was extracted with boiling dry ether. Evaporation of the extracts gave the crude anhydride, which after recrystallisation from dry ether formed prisms (26 g., 82%), m. p. 70—71° (Billeter, *loc. cit.*, gives m. p. 71°).

Poor yields of anhydride (<20%) were obtained by reaction of (i) sodium methanesulphonate with boiling thionyl chloride, (ii) methanesulphonic acid or its sodium salt with methanesulphonyl chloride at 160°, (iii) methanesulphonyl chloride (2 mol.) and water (1 mol.) at 160°.

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760. *The Condensation of Glyoxal and* iso*Nicotinoylhydrazine (Isoniazid).*

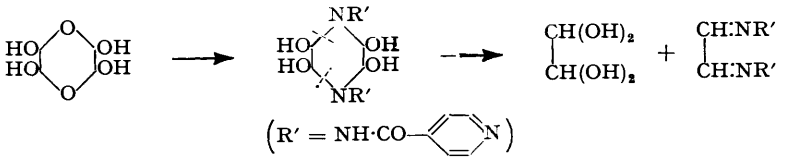
By Vincent C. Barry and P. W. D. Mitchell.

Isoniazid condenses with a variety of aldehydes and ketones to give crystalline hydrazones, many of which have been prepared for evaluation of their activity against *Mycobacterium tuberculosis* (Offe, Siefken, and Domagk, *Z. Naturforsch.*, 1952, **76**, 462; Yale, Losee, Martins, Holsing, Perry, and Bernstein, *J. Amer. Chem. Soc.*, 1953, **75**, 1933). With glyoxal the nature of its condensation product has been found to depend on the concentration of the solutions (Table 2). Thus when glyoxal (0·0086 mole) and isoniazid (0·022 mole) were condensed in 25 c.c. of water, the product was the monohydrazone (I), while the same quantities of reactants in 400 c.c. of water gave the bis-

(I) R·CO·NH·N:CH·CHO $\left(R = \text{}\right)$ $(R\cdot CO\cdot NH\cdot N{:}CH\cdot)_2$ (II)

hydrazone (II). Both compounds were obtained as crystalline solids melting above 360°. The bishydrazone is insoluble in water and organic solvents but may be recrystallised from 50% aqueous acetic acid. Attempts at recrystallising the monohydrazone, which is slightly soluble in water and ethanol always yielded the bis-compound. The conversion of (I) into (II) can also be readily effected by 5 min.' boiling in 50% acetic acid or by dissolution at room temperature in dilute aqueous sodium hydroxide or in dilute mineral acids. Formation of the bishydrazone, in this way, was found to be accompanied by the liberation of glyoxal. In order to explain this reaction, it is suggested that the mono-

hydrazone arises from condensation of isoniazid with the dimeric form of glyoxal to give a dimeric monohydrazone which could then undergo cleavage, as shown, with the formation of the bishydrazone and glyoxal.



The *p*-nitrophenylhydrazone from 1-hydroxydioxan has been shown by Summerbell and Rochen (*J. Amer. Chem. Soc.*, 1941, **63**, 3241), to give glyoxal bis-*p*-nitrophenylhydrazone when refluxed with 25% aqueous acetic acid for 4 hr. In this case the authors suggested that the reaction proceeded by an autoxidation process.

The products obtained from glyoxal and isoniazid were identified by means of ultra-violet light-absorption measurements. In 0·1N-hydrochloric acid, the bishydrazone has a maximum at 267 mμ which moves to a higher wave-length in alkali. Thus in 0·1N-sodium hydroxide the yellow solution has a maximum at 366 mμ. These two maxima are probably those of the tautomeric forms of the bishydrazone, $(\cdot CH{:}N\cdot NH\cdot COR)_2 \rightleftharpoons (\cdot CH{:}N\cdot N{:}CR\cdot OH)_2$ (R as above). The monohydrazone in 0·1N-sodium hydroxide gives a yellow solution, having an absorption maximum at 366 mμ. The value of $E^{1\%}_{1\,cm.}$ corresponded well with that expected from a solution in which two molecules of the monohydrazone had given one of the bishydrazone. Measurements were also made on the hydrochloride and sulphate of (II) which are obtained when the monohydrazone is crystallised from dilute hydrochloric and sulphuric acid respectively. The molecular weights of these salts were confirmed by titration with alkali.

*Experimental.—Glyoxal mono*iso*nicotinoylhydrazone* (I). An excess of 50% aqueous syrupy glyoxal was added to a concentrated aqueous solution of isoniazid. The solution immediately became yellow and after a few minutes a yellow precipitate was formed. This was washed with water, ethanol, and ether and dried in the vacuum-oven at 100° (P_2O_5). The cream-yellow *hydrazone* had m. p. >360° (Found: C, 54·2; H, 4·4; N, 23·2. $C_8H_7O_2N_3$ requires C, 54·2; H, 4·0; N, 23·8%).

*Glyoxal bis*iso*nicotinoylhydrazone* (II). Dilute aqueous solutions (less than 1%) of glyoxal and isoniazid were mixed and kept overnight; the solution yielded well-defined colourless crystals of the hydrazone, m. p. >360° (Found: C, 56·3; H, 4·3; N, 27·9. Calc. for $C_{14}H_{12}O_2N_6$: C, 56·7; H, 4·1; N, 28·4%).

Conversion of (I) *into* (II). (*a*) The monohydrazone was boiled for 5 min. with 50% acetic acid. The pale yellow solution, on cooling, gave colourless rectangular plates, m. p. >360° (Found: C, 56·3; H, 4·4; N, 27·6%).

(*b*) A saturated solution of (I) in hot 0·1N-sodium hydroxide, on cooling, gave deep yellow crystals [presumably the *lactim* form of (II)], m. p. 329—331° (Found: C, 56·3; H, 4·2; N, 27·4%).

(*c*) A solution of (I) in hot dilute hydrochloric acid gave on cooling deep yellow crystals of the *hydrochloride*, m. p. >360° (Found: equiv., 188·7. $C_{14}H_{12}O_2N_6,2HCl$ requires equiv., 184·5). The *sulphate* (Found: equiv., 122·5. $C_{14}H_{12}O_2N_6,2H_2SO_4$ requires equiv., 123) was prepared in a similar way from dilute sulphuric acid and had m. p. 323° (decomp.). Both the hydrochloride and the sulphate were washed with ethanol and ether only, since they dissociate readily in water.

The salts (50 mg.), suspended in water (20 c.c.), were titrated with N/30-sodium hydroxide to chlorophenol-red.

Ultra-violet light absorption. The compounds described above (30 mg.) were dissolved in 0·1N-sodium hydroxide (10 c.c.) and diluted to 250 c.c. with water, and 10 c.c. of this solution diluted to 250 c.c. with 0·1N-sodium hydroxide. Extinctions were measured in 1·0-cm. cells with a Beckman photo-electric spectrophotometer (Model DU). The highest value of $E^{1\%}_{1\,cm.}$ obtained (1128) was, as expected, that of the bishydrazone (II). This value was used in calculations of the molecular weights of the other compounds (Table 1).

The values of $E^{1\%}_{1\,cm.}$ at 366 mμ given for the mono- and the bis-hydrazone in 0·1N-sodium hydroxide were used to disclose the nature of the products obtained when glyoxal and isoniazid were allowed to react at ordinary temperatures (see Table 2).

TABLE 1.

Substance	$E^{1\%}_{1\,cm.}$ at 366 mμ	Molecular weight: Required	Molecular weight: Calc. from u.-v. data
(II), m. p. >360°	1128	296	—
(II), m. p. 329°	1120	296	300
(II), hydrochloride	906	369	368
(II) sulphate	693	496	482
(I)	929	354	359

TABLE 2.

Glyoxal (g.) [c]	Isoniazid (g.)	H_2O (c.c.)	Yield (g.) after (*t*) hr.	$E^{1\%}_{1\,cm.}$	Comment
1	3	25	2·38 [a] (¼)	892	Mono-
1	3	400	2·69 (2½)	1074	Mainly bis-
			0·91 [b] (18)	860	Mono-
0·5	3	25	1·93 (48)	968	Mainly mono-
0·5	3	400	1·53 (24)	1060	Mainly bis-
0·5	0·5	400	0·31 (24)	1035	Mixture

[a] 1 g., boiled with 50% acetic acid (40 c.c.) for 5 min., gave the bishydrazone (0·82 g.; $E^{1\%}_{1\,cm.}$ at 366 mμ = 1069; calcd. yield, 0·84 g.). The filtrate from this experiment contained glyoxal since the bishydrazone (0·25 g.; $E^{1\%}_{1\,cm.}$ at 366 mμ = 1110) was obtained on addition of isoniazid (1 g.). [b] This was a second crop of crystals separating from the filtrate after 18 hr. 300 mg., when boiled with ethanol (300 c.c.), gave the bishydrazone (160 mg.; $E^{1\%}_{1\,cm.}$ at 366 mμ = 1153). The filtrate, on evaporation to dryness, gave a yellow residue (137 mg.), readily soluble in water. The solution (25 c.c.), on addition of isoniazid (0·7 g.), yielded the bishydrazone of glyoxal (72 mg.; $E^{1\%}_{1\,cm.}$ at 366 mμ = 1126). [c] Solid polymer separating from 50% aqueous solution.

One of us (P. W. D. M.) is indebted to University College, Dublin, for a Lasdon Foundation Research Fellowship.

LABORATORIES OF THE MEDICAL RESEARCH COUNCIL OF IRELAND,
TRINITY COLLEGE, DUBLIN.

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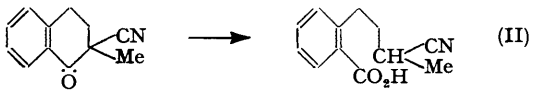
761. *Ring Fission of 2-Cyano-1 : 2 : 3 : 4-tetrahydro-2-methyl-1-oxonaphthalene.*

By D. B. COWELL, W. H. LINNELL, and D. W. MATHIESON.

DURING attempts to condense 2-cyano-1 : 2 : 3 : 4-tetrahydro-2-methyl-1-oxonaphthalene (I) with diethyl or dimethyl succinate in presence of potassium *tert.*-butoxide, the only product isolated under a large variety of conditions was diethyl or dimethyl 2 : 5-dioxo-*cyclo*hexane-1 : 4-dicarboxylate. None of the expected tricyclic ketones was formed and no starting material was recoverable. Under the conditions normally used for such



condensations the main reaction in this case appears to be ring fission (cf. Johnson, Petersen, and Gutsche, *J. Amer. Chem. Soc.*, **1947**, **69**, 2942). Thus it has been found that when the cyano-ketone (I) is treated with potassium *tert.*-butoxide alone, even under relatively mild conditions (55°; 5 hr.), cleavage of the alicyclic ring takes place with formation of

the cyano-acid (II). The structure of (II) was confirmed by hydrolysis to the dicarboxylic acid, followed by ring closure to 1 : 2 : 3 : 4-tetrahydro-2-methyl-1-oxonaphthalene.

Experimental.—*2-Cyano-1 : 2 : 3 : 4-tetrahydro-2-methyl-1-oxonaphthalene.* This *ketone* was obtained (85% yield) from 2-cyano-1 : 2 : 3 : 4-tetrahydro-1-oxonaphthalene by a route similar to that described by Johnson, Petersen, and Gutsche (*J. Amer. Chem. Soc.*, 1947, **69**, 2942) for the corresponding tetrahydro-oxophenanthrene, and had b. p. 128°/1 mm., m. p. 28° (Found : C, 77·6; H, 5·6; N, 7·6. $C_{12}H_{11}ON$ requires C, 77·8; H, 5·9; N, 7·6%).

γ-o-Carboxyphenyl-α-methylbutyronitrile (II). The above cyano-ketone (1·87 g.) was heated for 5 hr. at 55° with potassium (2 g.) in *tert.*-butyl alcohol (50 ml.). After addition of water and removal of solvent the residue was extracted with sodium carbonate. The *acid* fraction (1·48 g.) had b. p. 144—146°/0·06 mm., m. p. 42—45° (Found : C, 71·0; H, 6·5; N, 6·6. $C_{12}H_{13}O_2N$ requires C, 70·9; H, 6·5; N, 6·9%).

Hydrolysis of the cyano-acid with 30% sulphuric acid for 10 hr. gave *γ-o-carboxyphenyl-α-methylbutyric acid*, crystallising from aqueous acetic acid in needles, m. p. 133—134° (Found : C, 65·6; H, 6·1. $C_{12}H_{14}O_4$ requires C, 64·9; H, 6·4%).

1 : 2 : 3 : 4-*Tetrahydro-2-methyl-1-oxonaphthalene.* The dicarboxylic acid (0·25 g.) was refluxed for 8 hr. with acetic anhydride, and the residue obtained after removal of the reagent was heated at 250°/4 mm. until no further carbon dioxide was evolved. On addition of Brady's reagent to the residue the 2 : 4-*dinitrophenylhydrazone* of the ketone was obtained, crystallising from dioxan–alcohol in prisms, m. p. 235—236° (Found : C, 59·9; H, 4·8; N, 16·6. $C_{17}H_{16}O_4N_4$ requires C, 60·0; H, 4·7; N, 16·5%). This gave no m. p. depression on admixture with a sample prepared from an authentic specimen of 1 : 2 : 3 : 4-tetrahydro-2-methyl-1-oxonaphthalene (Sah and Brüll, *Ber.*, 1940, **73**, 1430). The ultra-violet absorption characteristics of both samples were identical, *viz.*, $\lambda_{max.}$ 390 mμ (ε 29,000) (main band only, in $CHCl_3$).

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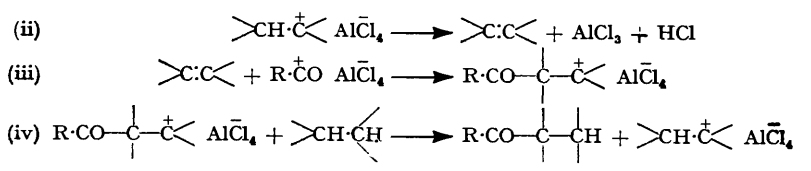
762. *Transfer of Hydride Ion.*

By G. BADDELEY and W. PICKLES.

*iso*PROPYL BROMIDE, *iso*propyl alcohol, and di*iso*propyl ether are decomposed by aluminium chloride at room temperature and evolve propane; decomposition of diethyl ether with evolution of ethane requires higher temperatures. These reactions are related on the one hand to the alkylation and acylation of aliphatic hydrocarbons and on the other to the acid-catalysed conversion of alcohols and ethers into hydrocarbon and carbonyl compound. It is suggested that *all* these reactions are effected by transfer of hydride ion.

Transfer of hydride ion is fundamental in the alkylation and acylation of aliphatic and alicyclic hydrocarbons by the Friedel–Crafts method (Schmerling, " Catalytic Re-



actions of Hydrocarbons—Ionic Mechanism," Symposium No. 24, Sept., 1952, New Jersey; Bartlett, Condon, and Schneider, *J. Amer. Chem. Soc.*, 1944, **66**, 1531; Baddeley, Wrench, and Williamson, *J.*, 1953, 2110); for example, acylation, the simpler process, involves at least a chain-initiating reaction (i) and a chain reaction (ii)—(iii)—(iv), of which (i) and (iv) are effected by transfer of hydride ion. A similar scheme with acyl replaced by alkyl cation represents some of the reactions occurring in the alkylation process.

Mixtures of aluminium chloride and alkyl halide, alcohol, ether, or olefin, and hydrogen halide are frequently used for the nuclear alkylation of aromatic compounds, but when these are not readily alkylated, *e.g.*, aryl ketones (*J.*, 1949, S229), or when they are absent the alkylating agent extracts hydride ion from an aliphatic side-chain (unpublished observation) or from the compound providing the alkylating agent. The latter reaction was first reported by Friedel and Crafts (*Ann. Chim.*, 1884, **1**, 451) : they obtained hydrogen chloride and a mixture of *saturated* hydrocarbons from *iso*amyl and aluminium chlorides. We find that *iso*propyl bromide, with catalytic amounts of reagent, evolves propane (0·5 mol.) and hydrogen halide (cf., Meyer, *Ber.*, 1894, **27**, 2766); the reaction is given the following tentative inperpretation :

$$Me_2CHX + AlX_3 \longrightarrow Me_2\overset{+}{C}H\ Al\overset{-}{X}_4$$

$$Me_2C(X)\text{–}H \rightarrow \overset{+}{C}HMe_2\ Al\overset{-}{X}_4 \longrightarrow Me_2\overset{+}{C}X\ Al\overset{-}{X}_4 + Me_2CH_2$$

$$Me_2\overset{+}{C}X\ Al\overset{-}{X}_4 \longrightarrow HX + AlX_3 + CH_2{:}CMeX \longrightarrow \text{Polymer}$$

This type of reaction occurs less readily with ethyl bromide since this, probably, loses hydride ion less readily than does *iso*propyl bromide; this view is supported by the fact that, in the presence of aluminium chloride, nitrobenzene is reduced by *iso*propyl but not by ethyl bromide (Gilman, Burtner, Calloway, and Turck, *J. Amer. Chem. Soc.*, 1935, **57**, 907).

Whereas *iso*propyl alcohol affords the chloride on addition of a molecular proportion of reagent (formulated as $AlCl_3$), reaction (v) (Norris and Sturgis, *ibid.*, 1939, **61**, 1413), we find that, even at room temperature, excess of reagent provides propane. Since ketones are also formed, the reaction is formulated as in (vi) and (vii). Di*iso*propyl ether also reacts at room temperature with evolution of propane; the reaction is suitably represented by (viii) followed by (vi) and (vii). Similarly, diethyl ether evolves ethane but reaction occurs only on warming (90—100°).

(v) $Me_2CH{\cdot}OH + AlCl_3 \longrightarrow Me_2CH{\cdot}OH,AlCl_3 \longrightarrow HCl + Me_2CH{\cdot}O{\cdot}AlCl_2 \longrightarrow Me_2CHCl + AlOCl$

(vi) $Me_2C(OAlCl_2)\text{–}H \rightarrow \overset{+}{C}HMe_2\ Al\overset{-}{Cl}_4 \longrightarrow Me_2\overset{+}{C}OAlCl_2\ Al\overset{-}{Cl}_4 + Me_2CH_2$

(vii) $Me_2\overset{+}{C}{\cdot}O{\cdot}AlCl_2\ Al\overset{-}{Cl}_4 \longrightarrow Me_2C{:}O,AlCl_3 + AlCl_3$ ↓ Condensation products

(viii) $(Me_2CH)_2O,AlCl_3 \longrightarrow Me_2CH{\cdot}O{\cdot}AlCl_2 + Me_2CHCl$

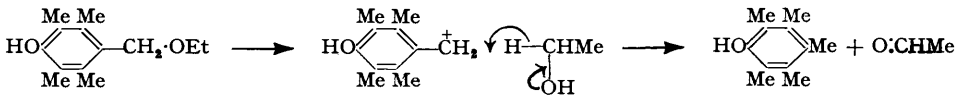
Decomposition of ethers and alcohols into hydrocarbon and carbonyl compound has often been described and, when catalysed by acid, is, in our opinion, closely related to the above observations and best represented by the general expression :

$$R'R''CH{\cdot}OR \underset{H^+}{\rightleftharpoons} R'R''C(OH)\text{–}H \rightarrow \overset{+}{R} \xrightarrow{-H^+} R'R''C{:}O + RH$$

$$R'R''CH{\cdot}OH + ROH \xrightarrow[-H_2O]{H^+} R'R''C(OH)\text{–}H \rightarrow \overset{+}{R}$$

It relates the reaction to the Cannizzaro reaction, incorporates the fact that alkylating agent is formed (for numerous illustrations see Price " The Alkylation of Aromatic Compounds by the Friedel–Crafts Method," Organic Reactions, Vol. III), and implies that rate of reaction is directly related to the ease with which hydride ion is released by the alcohol R'R''CH·OH. This implication is readily substantiated; for example, since ethyl alcohol is a more powerful reducing agent than methyl alcohol, alkyl and aralkyl cations should be more readily reduced to hydrocarbon in the former alcohol. This is the case; 4-ethoxy-

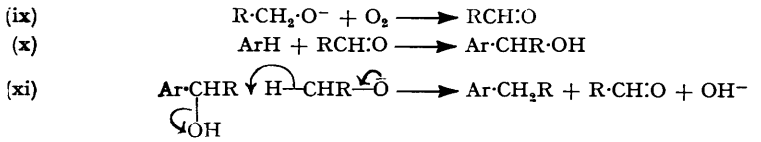
methyltetramethylphenol (I) provides pentamethylphenol and acetaldehyde in ethanolic hydrogen chloride but is not reduced when methanol is used (Burawoy and Chamberlain, *J.*, 1949, 626):



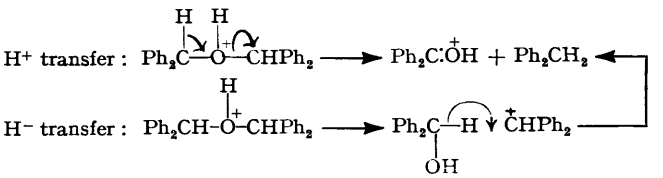
(I)

Similarly, tri- and di-phenylmethanol are reduced to the corresponding methane derivatives by mineral acid and ethyl alcohol, and triphenylmethyl chloride, in diethyl ether, is reduced in the presence of zinc chloride or aluminium chloride (Norris and Young, *J. Amer. Chem. Soc.*, 1924, **46**, 2580).

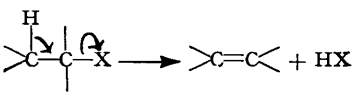
Transfer of hydride ion is a recognised feature of termination of chain-reaction in acid-catalysed polymerisation of olefins, of many oxidation reduction processes, *e.g.*, reduction of ketones with aluminium alkoxide, and of alkylation with alkoxide ion (Cornforth, Cornforth, and Robinson, *J.*, 1942, 682). In the last instance, the mechanism of reaction provided by the authors can be represented by (ix)—(x)—(xi); (ix) initiates the chain reaction (x)—(xi).



Some of the above oxidation–reduction processes can be formulated as though hydrogen is transferred as proton instead of as hydride ion; this is illustrated by the *acid*-catalysed conversion of bisdiphenylmethyl ether into benzophenone and diphenylmethane:

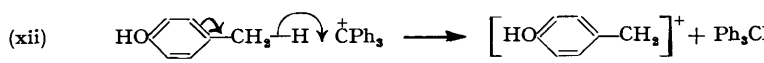


These formulations may represent alternative mechanisms and we plan to provide data which will distinguish between them; *e.g.*, the latter requires that this reaction, like the Cannizzaro reaction (Fredenhagen and Bonhoeffer, *Z. physikal. Chem.*, 1938, *A*, **181**, 379), should occur without exchange of hydrogen between organic reactant and hydroxylic solvent. Burton and Cheeseman (*J.*, 1953, 986) prefer the former since it resembles the well-known elimination reactions:



Transfer of hydride ion sometimes obstructs or competes with aromatic substitution. We conclude with a few examples.

(*a*) Whereas *o*-cresol is alkylated by triphenylmethanol in acetic–sulphuric acid, *p*-cresol reduces the alcohol to the corresponding methane and is oxidised to " polymerised



quinomethane " (Boyd and Hardy, *J.*, 1928, 630; Schorigin, *Ber.*, 1927, **60**, 2373). The reaction is now represented by (xii); the 4-hydroxybenzyl cation combines with phenolic material, as in the preparation of phenol–formaldehyde resins.

(*b*) Benzoyl cation oxidises 9 : 10-dihydroanthracene to anthracene; this gives the 9-benzoyl derivative which is reduced by dihydroanthracene to the final product, 9-benzoyl-9 : 10-dihydroanthracene (Nenitzescu, Gavăt, and Cocora, *Ber.*, 1939, **72**, 819; Baddeley, Wrench, and Williamson, *loc. cit.*).

(*c*) Acetyl cation oxidises 5-acetylindane and 6-acetyltetralin to the corresponding indene and 1 : 2-dihydronaphthalene derivatives, and these are acetylated (Baddeley, Wrench, and Williamson, *loc. cit.*).

(*d*) Alkylation of benzene by diphenylmethyl chloride and aluminium chloride provides mainly diphenylmethane and triphenylmethyl chloride (Boesekin, *Rec. Trav. chim.*, 1903, **22**, 311). Triphenylmethane is formed but, by losing hydride ion to the diphenylmethyl cation, forms the more stable triphenylmethyl cation which does not readily attack benzene.

$$PhH + Ph_2\overset{+}{C}H\ \overline{AlCl_4} \longrightarrow Ph_2CH + HCl + AlCl_3$$

$$Ph_2CH + Ph_2\overset{+}{C}H\ \overline{AlCl_4} \longrightarrow Ph_3\overset{+}{C}\ \overline{AlCl_4} + Ph_2CH_2$$

A full account of the reactions which are reported for the first time in this paper will form part of a later communication.

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