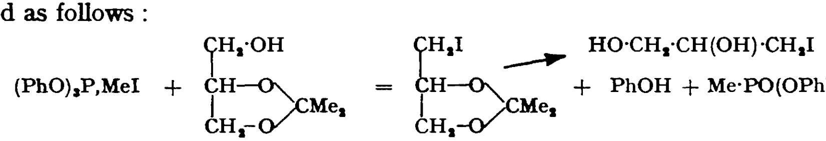
The Preparation of Glycerol Iodides.

By T. H. Bevan, T. Malkin, and D. B. Smith.

[Reprint Order No. 5866.]

Glycerol α-iodide [glycerol α-iodohydrin], a starting material for the preparation of diglycerides (Fischer, *Ber.*, 1920, **53**, 1621) and phosphatidic acids (Hessel, Morton, Todd, and Verkade, *Rec. Trav. chim.*, 1954, **73**, 150), is prepared by replacement of chlorine in 2 : 3-*iso*propylidenedioxypropyl chloride (Fischer and Pfähler, *Ber.*, 1920, **53**, 1606), or of the toluene-*p*-sulphonyl group in 2 : 3-*iso*propylidenedioxypropyl toluene-*p*-sulphonate (Fischer and Baer, *J. Amer. Chem. Soc.*, 1948, **70**, 609) by heating in a sealed tube with sodium iodide in acetone, followed by hydrolysis of the resulting *iso*propylidene iodide. In order to avoid the use of sealed tubes, we used the new method for preparing iodides described by Landauer and Rydon (*J.*, 1953, 2224), and we find that yields of 75% are readily obtained as follows:



The iodide, which is soluble in water, is readily separated from the insoluble diphenyl methylphosphonate.

Similarly, 1 : 3-benzylideneglycerol gives glycerol β-iodide in 56% yield. Glattfield and Klaas (*J. Amer. Chem. Soc.*, 1933, **55**, 1114) obtained an 18% yield by heating glycerol β-chloride with sodium iodide in acetone under pressure.

Experimental.—*Glycerol α-iodide.* Under anhydrous conditions, 1 : 2-*O*-*iso*propylideneglycerol (35 g., 0·26 mole) (Malkin and Shurbagy, *J.*, **1936**, 1634) was added to triphenyl phosphite methiodide (90 g., 0·22 mole), and the temperature was kept below 50°. After 6 hr., the brown viscous oil was freed from phenol and iodine, by vigorous shaking with 5% sodium hydrate solution, followed by washing with water. 5N-Sulphuric acid (5 ml.) in 86% ethanol (125 ml.) was added to the well-drained oil, and after 20 hr. hydrolysis was completed by 5 minutes' refluxing. The cold solution was neutralised with barium carbonate, filtered, and evaporated on the water-bath under reduced pressure to an oil, from which the iodohydrin was extracted by several washings with water. After the addition of common salt to the combined washings, the iodide was extracted with ether, the ether solution was dried (Na_2SO_4), and the ether was distilled off. The residual oil, crystallised from chloroform and then from chloroform–light petroleum (b. p. 40—60°), yielded colourless platelets (29·2 g.), m. p. 48·5—49·5°.

If the intermediate *iso*propylidene iodide is required the initial reaction product is taken up in ether, freed from phenol and iodine, and dried. After removal of ether, the product is distilled. 2 : 3-*iso*Propylidenedioxypropyl iodide boils at 70—72°/2 mm. The by-product, diphenyl methylphosphonate, boils 85—90° higher.

Glycerol β-iodide. Triphenyl phosphite (24·3 g., 0·079 mole) and methyl iodide (15 g., 0·12 mole) were refluxed under anhydrous conditions for 36 hr. After cooling, the still warm liquid was washed several times with anhydrous ether, which was decanted and, whilst the phosphite methiodide was still liquid 1 : 3-*O*-benzylideneglycerol (12 g., 0·067 mole) (Verkade and van Roon, *Rec. Trav. chim.*, 1942, **61**, 831) was added, the temperature being kept below 50°. After 8 hr. the dark brown liquid was washed several times with sodium hydroxide solution and taken up in ether for further washing with alkali and water. The ether was removed, and the residual oil was hydrolysed by 5N-sulphuric acid (3 ml.) in 85% ethanol (75 ml.) at 40° for 30 hr. The procedure from this point is as described for the α-iodide, yielding white platelets (7 g.) m. p. 53° (Glattfield and Klaas, *loc. cit.*, found m. p. 53°) (Found : I, 63·3. Calc. for $C_3H_7O_2I$: I, 62·9%). The slight difference in technique from the previous preparation is due to the fact that 1 : 3-*O*-benzylideneglycerol is a solid, whereas 1 : 2-*O*-*iso*propylideneglycerol is a liquid.

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The Preparation of the Mononitrocinnamaldehydes.

By W. DAVEY and J. R. GWILT.

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MONONITROCINNAMALDEHYDES have been prepared by alkali-catalysed condensation of acetaldehyde with the appropriate nitrobenzaldehyde in aqueous-alcohol (Kinkelin, *Ber.*, 1885, **18**, 483) or in solution in the acetaldehyde itself (Baeyer and Drewsen, *Ber.*, 1883, **16**, 2205; Kinkelin, *loc. cit.*; Göhring, *Ber.*, 1885, **18**, 371, 719). Nitration of cinnamaldehyde in sulphuric acid with potassium nitrate (Diehl and Einhorn, *ibid.*, p. 2335; Mohlau and Adam, *Z. Farbst. Industr.*, 1906, **5**, 402) gave *o*- and *p*-nitrocinnamaldehydes whilst nitration in acetic anhydride (Mills and Evans, *J.*, 1920, **117**, 1037) gave *o*-nitrocinnamaldehyde in 36% yield. The results of condensation and nitration are discussed below under the individual aldehydes.

By a method substantially that of Baeyer and Drewsen (*loc. cit.*) a 61% yield of *o*-nitrocinnamaldehyde was obtained, in agreement with the findings (70% yield) of Diehl and Einhorn (*loc. cit.*). Kinkelin's method (*loc. cit.*) gave no more than 26% though Diehl and Einhorn (*loc. cit.*) reported 40%. In both condensations a gum proved difficult to remove from the product. Previous work by the present authors (*J.*, 1950, 204, 3348) had shown the value of diacetate formation for the protection of the aldehyde group and nitration of cinnamylidene diacetate by modifications of the method of Mills and Evans (*loc. cit.*) gave an 85% yield of *o*-nitrocinnamaldehyde. Diacetate formation has usually been achieved by use of sulphuric acid as catalyst but not more than 50% of cinnamylidene diacetate was thus obtained; the diacetate was however obtained in 95% yield by the use of orthophosphoric acid and could be used ***in situ*** for nitration. The dilute hydrochloric acid added to the final reaction mixture in the method of Mills and Evans (*loc. cit.*)

hydrolysed the *o*-nitrocinnamylidene diacetate; the observed rise in temperature is not due solely to the reaction between acetic anhydride and water under these conditions.

Kinkelin (*loc. cit.*) reported that Baeyer and Drewsen's method (*loc. cit.*) gave poor yields of *m*-nitrocinnamaldehyde whilst Göhring (*loc. cit.*) claimed almost quantitative yields. In the present work yields of only 32% were obtained by Baeyer and Drewsen's method, but the alternative method developed by Kinkelin and claimed by him to give a 50% yield was found to give a 61% yield and the product was readily purified, though some evidence of further condensation was obtained. Variations in the method, or use of alternative methods, in general gave lower yields.

p-Nitrocinnamaldehyde proved the most difficult isomer to obtain pure. Yields of 38% and 48% were obtained by the methods of Göhring (*loc. cit.*) and of Kinkelin (*loc. cit.*) respectively. Waley (*J.*, 1948, 2010) has reported yields of 72% by a modification of Göhring's method and his method appears to be the most satisfactory though the experimental conditions are apparently somewhat critical. Attempts to prepare the aldehyde by direct nitration did not lead to a practicable method and increasing severity in nitration conditions gave oxidation to *p*-nitrobenzaldehyde and then to *p*-nitrobenzoic acid. Dilution of the reagents before reaction, *e.g.*, with acetic acid, prevented nitration, unchanged cinnamaldehyde being recovered.

o-Nitrocinnamaldehyde has been readily converted by reduction into quinoline in 82% yield and this represents a convenient preparative method.

EXPERIMENTAL

Preparation of Diacetates.—Acetic anhydride (500 ml.) and orthophosphoric acid (5 ml.; *d* 1·75) were mixed at 20° and the aldehyde (1 mole) added during 5—10 min. with stirring. After a further 30 minutes' stirring, during which the temperature rose only to *ca.* 30°, the mixture was poured into a large excess of water, and the product isolated and purified. By this method cinnamylidene and *o*-, *m*-, and *p*-nitrobenzylidene diacetate were obtained in 95—97% yield and ethylidene diacetate in 90% yield.

Nitration of Cinnamylidene Diacetate.—Cinnamaldehyde (105 g.) was dissolved in acetic anhydride (500 ml.), and phosphoric acid (5 ml.; *d* 1·75) was added with cooling and stirring. After 1 hr., the solution was held at $-5°$ to 0° by the addition of solid carbon dioxide whilst nitric acid (35 ml.; *d* 1·52) was added during 30 min. The solution was then allowed to reach room temperature during 2 hr. with stirring and poured into ice-water (4 l.). Hydrochloric acid (250 ml.; *d* 1·16) was added during 15 min. and the mixture left overnight. The product consisted of a mixture of *o*-nitrocinnamaldehyde and *o*-nitrocinnamylidene diacetate. It was dissolved in ethanol (600 ml.), sulphuric acid [40 ml. (*d* 1·84) +400 ml. of water] was added, and the whole refluxed for 2 hr. On cooling, *o*-nitrocinnamaldehyde separated as sandy needles and dilution with water gave a further crop. The total yield was recrystallised twice from ethanol (charcoal), to give pale yellow needles of *o*-nitrocinnamaldehyde (103 g., 84%), m. p. and mixed m. p. 128°. Alternatively the mixture of aldehyde and diacetate was hydrolysed by 2 hours' refluxing with 5N-hydrochloric acid (500 ml.) or 1·5 hours' with magnesium hydroxide suspension (40 g. in 500 ml. of water).

Reduction of o-*Nitrocinnamaldehyde.*—*o*-Nitrocinnamaldehyde (10 g.), water (250 ml.), ferrous sulphate heptahydrate (150 g.), and hydrochloric acid (1 ml.; *d* 1·18) were together heated to 90° under reflux. Ammonia solution (*d* 0·88) was added through the condenser at two-minute intervals in portions of 25, 10, 10, and 10 ml., with vigorous shaking after each addition. The mixture was held at 90° for 1 hr. and then steam-distilled. The distillate was extracted with ether, the extract washed with a little water, and dried (Na_2SO_4) and the ether was removed. The residual liquid was distilled, to yield quinoline (6·0 g., 82%), b. p. 123—128°/18 mm. (tartrate, m. p. 126°; picrate, m. p. 203°).

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The Preparation of 1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-*Octahydrodibenzothiophen.*

By W. COOPER.

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1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-OCTAHYDRODIBENZOTHIOPHEN has been synthesised by Cagniant and Cagniant (*Bull. Soc. chim., France*, 1952, 326) from 1 : 2 : 3 : 4-tetrahydrothionaphthen. The intermediates in this synthesis are not readily available, but it has now been found that this octahydro-compound can be prepared conveniently by direct reaction of sulphur with *cyclo*hexanone or 2-*cyclo*hex-1′-enyl*cyclo*hexanone. The latter is probably an intermediate in the formation of the dibenzothiophen from *cyclo*hexanone.

Experimental.—1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-*Octahydrodibenzothiophen.* (*a*) From *cyclo*hexanone. Sulphur (32 g.) and *cyclo*hexanone (200 g.) were heated under reflux (nitrogen atmosphere; in air some oxidation occurred to give adipic acid) for 20 hr.; hydrogen sulphide was steadily evolved. After cooling, unchanged sulphur (16 g.) was removed, and dissolved sulphur, polysulphides, and thiols were extracted with aqueous sodium hydroxide. Fractionation of the neutral layer gave: (i) *cyclo*hexanone (110 g.); (ii) 2-*cyclo*hex-1′-enyl*cyclo*hexanone (9 g.), b. p. 152—154°/18 mm., n_D^{20} 1·5117, d_{20}^{20} 1·026 (oxime, m. p. 148°) [Found: O in CO (by reaction with hydroxylamine hydrochloride and titration of the acid liberated), 8·8. Calc. for $C_{12}H_{18}O$: O in CO, 9·0%] (infra-red spectrum identical with that of a sample prepared by Rapson's method, *J.*, 1941, 15); (iii) 1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-octahydrodibenzothiophen (20 g.), m. p. 32° after recrystallisation from alcohol (Cagniant and Cagniant, *loc. cit.*, report m. p. 31°), b. p. 120°/1 mm., n_D^{20} 1·5702 {Found: C, 74·4; H, 8·2; S, 17·0%; *M* (ebullioscopic in benzene), 195; $[R]_D$, 59·0. Calc. for $C_{12}H_{16}S$: 3, 74·9; H, 8·4; S, 16·7%; *M*, 192·2; $[R]_D$, 58·8}, light absorption (by Mr. C. E. KENDALL), max. at 2400 Å (ε 7560); and (iv) a high-boiling viscous residue (12 g.) containing much combined sulphur and not examined in detail.

The infra-red spectrum of the octahydrodibenzothiophen has been deposited with the Society (C.S. No. 175) * by Mr. W. H. T. DAVISON.

Heating the octahydrodibenzothiophen (1 g.) with selenium (3 g.) at 360° for 4 hr. gave a crystalline sublimate (0·6 g.) of dibenzothiophen, m. p. 97° (picrate, m. p. 123°), the ultra-violet spectrum of which was identical with that given by Sawicki and Ray (*J. Amer. Chem. Soc.*, 1952, **74**, 4120).

(*b*) From 2-*cyclo*hex-1′-enyl*cyclo*hexanone. Sulphur (8 g.) and this ketone (30 g.) were heated for 10 hr. at 170°. Water and hydrogen sulphide were formed. The red-brown product, when washed with alkali and fractionated, gave unchanged ketone (5 g.), the octahydrodibenzothiophen (16 g., 45%), and a high-boiling residue.

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Thermodynamic Indicator Constants of Dinitrophenols in Dioxan–Water Mixtures.

By S. KERTES.

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FOR the measurements and calculation of the thermodynamic indicator constants Kolthoff and Guss's method (*J. Amer. Chem. Soc.*, 1938, **60**, 2516) was used. Judson and Kilpatrick (*ibid.*, 1949, **71**, 3110) used a similar method for determination of ionization constants for 2 : 5-dinitrophenol in aqueous solution. Although there is an extensive literature on nitrophenols in aqueous solution, there is little on the behaviour of those indicator acids in non-aqueous media (Eisenbrand and Halban, *Z. phys. Chem.*, 1930, **146**, *A*, 30; Halban and Kortüm, *ibid.*, 1934, **170**, *A*, 351; Kortüm, *ibid.*, 1937, **38**, *B*, 1; 1939, **42**, *B*, 39; *Ber.*, 1941, **74**, *B*, 409; Halban and Szigeti, *Helv. Chim. Acta*, 1937, **20**, 746). These authors,

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* Photocopies, price 3*s*. each, may be obtained from the General Secretary, The Chemical Society, Burlington House, Piccadilly, London, W.1, on application quoting the C.S. no.

whose approach is the closest to that used in this Note, and others, did not measure the ionization constants by the method and under the conditions now described.

In a buffered system containing a small amount of acid–base indicator the thermodynamic equilibrium constant K' is given by the equation

$$K' = a_{\mathrm{I},b}a_{\mathrm{A}}/a_{\mathrm{I},a}a_{\mathrm{B}} = Kf_{\mathrm{I},b}f_{\mathrm{A}}/f_{\mathrm{I},a}f_{\mathrm{B}}$$

where the subscripts A, B, and I*a*, I*b* refer to the acid or basic form of the buffer and indicator respectively. On introduction of the Debye–Hückel equation for sufficiently dilute solution, *viz.*, $-\log f_{\mathrm{ion}} = \alpha Z^2\sqrt{\mu}$, it follows that

$$\mathrm{p}K' = \mathrm{p}K - \log f_{\mathrm{I},b}f_{\mathrm{A}}/f_{\mathrm{I},a}f_{\mathrm{B}} = \mathrm{p}K - 2\alpha(Z_{\mathrm{I},a} - Z_{\mathrm{A}})\sqrt{\mu}$$

where $Z_{\mathrm{I},a}$ and Z_{A} are the charges of the indicator acid and the buffer acid respectively. The value of α is given by $\alpha = 1{\cdot}826 \times 10^6/(DT)^{3/2}$, where D is the dielectric constant of the medium.

By plotting the experimental values of pK against the square root of ionic strengths and by calculating the limiting slope by use of $2\alpha(Z_{\mathrm{I},a} - Z_{\mathrm{A}})$ the pK' values are found. Since the indicator acid in the case of nitrophenols is uncharged, the value of $Z_{\mathrm{I},a}$ is equal to zero. Therefore, the values of the expression $2\alpha(Z_{\mathrm{I},a} - Z_{\mathrm{A}})$ depend on the term Z_{A} only, which can be -1, 0, or 1 depending upon whether the buffer acid is of cation, uncharged, or anion type, respectively.

Table 1 shows the calculated values of the slope $2\alpha(Z_{\mathrm{I},a} - Z_{\mathrm{A}})$ as a function of medium and the type of the buffer acid.

TABLE 1. *Calculated values of the slope* $2\alpha(Z_{\mathrm{I},a} - Z_{\mathrm{A}})$.

Solvent		Type of the buffer acid : *		Solvent		Type of the buffer acid : *	
Dioxan, wt. %	*D*	cation	anion	Dioxan, wt. %	*D*	cation	anion
0	81·07	−1·020	1·020	70	18·20	− 9·368	9·368
20	62·38	−1·472	1·472	82	9·77	−23·822	23·822
45	39·57	−2·922	2·922				

* Value for uncharged species = zero.

Experimental.—If the dissociation constant of the buffer acid K_{A} is known in the chosen medium, the thermodynamic ionization constant of the dinitrophenol indicators K_{I} can be calculated from the equation pK_{I} = pK' + pK_{A}. The buffer system acetic acid–sodium acetate (Harned and Owen, "The Physical Chemistry of Electrolytic Solutions," Reinhold Publ. Corp., New York, 1950, p. 581) was used for 2 : 5-dinitrophenol, and formic acid–sodium formate (*idem, ibid.*) for 2 : 4- and 2 : 6-dinitrophenol.

For the indicators, the ratios between acid and base forms were determined spectrophotometrically at 20°, a Beckman DU Spectrophotometer with water circulation being used. In order to determine the most convenient wave-length for the measurements, full absorption spectra (220—500 mμ) of the sodium dinitrophenoxides were obtained in all the dioxan–water mixtures used. The measurements were made at five different wave-lengths close to the maximum absorption (420—480 mμ) and the ratios found were averaged. The maximum error at a mean pK value was 0·2%. The buffer solutions and 2 ml. of the indicator, all in aqueous solution, were added to the desired amounts of dioxan in a 50-ml. volumetric flask, and the mixtures made up to the mark with water. The solution was then kept in a thermostat at 20° for at least 2 hr. The fraction of indicator in alkaline form was determined by comparing each solution with a corresponding solution of identical ionic strength in which the buffer was replaced by sodium hydroxide.

The values of pK for every system were determined over an ionic strength from about 1×10^{-1} to 5×10^{-4}. Greater ionic strengths than 1×10^{-2} were obtained by addition of lithium chloride or sodium nitrate. In solutions of high dioxan content (70% and 82%) and below an ionic strength of 5×10^{-3} the intermediate yellow colour of the indicator does not appear, and therefore no measurements could be made.

The dinitrophenols were B.D.H. indicator solutions with a concentration of 0·05% for 2 : 4- and 2 : 5-dinitrophenol and of 0·02% for 2 : 6-dinitrophenol. The dioxan was a chemically pure reagent (May and Baker). All other reagents were "Baker's Analyzed c.p.".

Table 2 shows the values of the thermodynamic indicator constants obtained at 20° in different dioxan–water mixtures. The pK values plotted against the mole-fraction of dioxan

TABLE 2. *Thermodynamic indicator constants* (log p$K_{\text{therm.}}$) *at* 20°.

	Dinitrophenol				Dinitrophenol		
Dioxan, wt. %	2 : 4-	2 : 5-	2 : 6-	Dioxan, wt. %	2 : 4-	2 : 5-	2 : 6-
0	4·13	3·75	5·23	70	7·75	7·05	9·45
20	4·75	4·20	5·90	82	9·50	8·80	11·40
45	5·80	5·10	7·15				

give a linear function for 2 : 5- and 2 : 4-dinitrophenol and a very nearly linear function for 2 : 6-dinitrophenol.

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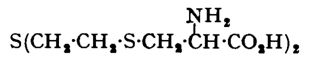
Sulphonium Compounds related to Aryldi-2-halogenoalkylamines.

By J. J. ROBERTS and W. C. J. ROSS.

[Reprint Order No. 5935.]

THE sulphonium dichloride (I) prepared from di-2-chloroethyl sulphide (" mustard gas ") and thiodiglycol $S(CH_2{\cdot}CH_2{\cdot}OH)_2$ possesses a necrotising action approximately one-tenth that of " mustard gas " (Stein, Moore, and Bergmann, *J. Org. Chem.*, 1946, **11**, 664). There is evidence that the sulphonium dichloride functions as an alkylating agent under mild conditions; for example, with cysteine in a bicarbonate buffer at 37° the diacid (II) is formed. In attempts to obtain biological alkylating agents of greater specificity towards neoplastic tissue (cf. Everett, Roberts, and Ross, *J.*, 1953, 2386) several sulphonium di-iodides related to " aromatic nitrogen mustards " have been prepared. It was hoped that the cationic water-soluble nature of the products would confer special biological activity.

(I) $S[CH_2{\cdot}CH_2{\cdot}\overset{+}{S}(CH_2{\cdot}CH_2{\cdot}OH)_2]_2Cl^-{}_2$


$$S(CH_2{\cdot}CH_2{\cdot}S{\cdot}CH_2{\cdot}\overset{NH_2}{\overset{|}{C}}H{\cdot}CO_2H)_2$$
(II)

(III) $p\text{-}R{\cdot}C_6H_4{\cdot}N(CH_2{\cdot}CH_2{\cdot}\overset{+}{S}Me_2)_2I^-{}_2$

$\beta\text{-}C_{10}H_7{\cdot}N(CH_2{\cdot}CHMe{\cdot}\overset{+}{S}Me_2)_2I^-{}_2$ (IV)

The *p*-anisidine (III; R = OMe) and *p*-chloroaniline (III; R = Cl) derivatives were prepared as representative compounds having substituents of opposite polarity. Reaction of the aryldi-2-halogenoethylamine with thiourea gave the corresponding thiuronium salt which on treatment with methyl iodide gave the required sulphonium di-iodides (cf. Walker, *J.*, 1950, 193). These compounds proved to be much less reactive than the parent halogenoethylamines, and so the 2-naphthylamine derivative (IV) and trimethylene-1 : 3-bisdimethylsulphonium di-iodide were also prepared.

All the sulphonium derivatives showed low chemical reactivity when compared with the cytotoxic aryldi-2-halogenoalkylamines, and all were inactive as tumour-growth inhibitors (personal communication from Professor A. Haddow). Significant activity is shown only by bifunctional alkylating agents (Ross, *Adv. Cancer Res.*, 1953, **1**, 397) and hence it was of importance to decide whether the sulphonium compounds suffered fission by water at the *S*-methyl linkage or at the *S*-alkylamine linkage. For the naphthylamine derivative (IV) it was shown that in boiling aqueous acetone the latter occurred, giving *NN*-di-2′-hydroxy-*n*-propyl-2-naphthylamine, whereas on thermal decomposition the former took place with the formation of *NN*-di-2′-methylthiopropyl-2-naphthylamine.

Experimental.—p-*Methoxyphenyliminobis*-(2-*ethylthiuronium chloride*). *NN*-Di-2-chloroethyl-*p*-anisidine (25 g.) (Ross, *J.*, 1949, 183) and thiourea (15 g.) were heated in ethanol (250 ml.) under reflux for 7 hr. After concentration the solution was diluted with ether, giving an oil which solidified when rubbed with dry ether. The *bisthiuronium dichloride* (30 g.) formed prisms, m. p. 204°, from ether–methanol (Found: C, 39·3; H, 6·0; N, 17·4. $C_{13}H_{23}ON_5Cl_2S_2$ requires C, 39·0; H, 5·8; N, 17·5%). Treating the dichloride with an excess of 2N-sodium carbonate gave the free *base*, which formed small prisms, m. p. 84°, from ethyl acetate (Found: C, 47·6; H, 6·4. $C_{13}H_{21}ON_5S_2$ requires C, 47·7; H, 6·5%).

p-*Methoxyphenyliminobis*-(2-*ethyl*-SS-*dimethylsulphonium iodide*). The thiuronium salt (30 g.) was dissolved in warm 2N-sodium hydroxide (400 ml.) and after addition of methyl iodide (10 ml.) to the cooled solution the mixture was shaken for 3 hr. An ethereal extract was washed with 2N-sodium hydroxide and then water and finally dried (K_2CO_3). On evaporation *NN*-di-2-methylthioethyl-*p*-anisidine (20 g.) which formed a ***picrate***, prisms, m. p. 112—114°, from ethanol (Found: C, 45·8; H, 5·1; N, 11·4. $C_{19}H_{24}O_8N_4S_2$ requires C, 45·6; H, 4·8; N, 11·2%) was obtained. A solution of the methylthio-compound (20 g.) and methyl iodide (10 ml.) in methanol (150 ml.) was kept at room temperature for 20 hr. Dilution with dry ether gave an oil which solidified when rubbed with acetone. The ***bis-sulphonium di-iodide*** formed prisms, m. p. 172—173°, from ethanol (Found: C, 32·4; H, 4·9. $C_{15}H_{27}ONI_2S_2$ requires C, 32·4; H, 4·9 %).

p-*Chlorophenyliminobis*-(2-*ethyl*-SS-*dimethylsulphonium iodide*). Since the corresponding 2-chloroethyl compound was not sufficiently reactive the following were prepared starting from *NN*-di-2-bromoethyl-*p*-chloroaniline: S-p-*Chlorophenyliminobis*-(2-*ethylthiuronium bromide*), prisms, m. p. 194°, from ethanol–chloroform (Found: C, 29·2; H, 4·1. $C_{12}H_{20}N_5ClBr_2S_2$ requires C, 29·2; H, 4·1%), and the corresponding free ***base***, prisms, m. p. 96°, from aqueous acetone (Found: C, 43·8; H, 5·3. $C_{12}H_{18}N_5ClS_2$ requires C, 43·4; H, 5·5%); *NN*-di-2-methylthioethyl-*p*-chloroaniline, characterised as its ***picrate***, prisms, m. p. 114—116°, from ethanol (Found: C, 42·8; H, 4·4. $C_{18}H_{21}O_7N_4ClS_2$ requires C, 42·8; H, 4·2%); S-p-*chlorophenyliminobis*-(2-*ethyl*-SS-*dimethylsulphonium iodide*), prisms, m. p. 128·5—131°, from ether–methanol (Found: C, 29·8; H, 4·5; N, 2·6. $C_{14}H_{24}NClI_2S_2$ requires C, 30·0; H, 4·3; N, 2·5%), and the corresponding p-*chloroaniline dipicrate*, prisms, m. p. 159—160°, from water (Found: C, 40·4; H, 3·7. $C_{26}H_{28}O_{14}N_7ClS_2$ requires C, 41·0; H, 3·7%).

β-*Naphthyliminobis*-[2-(1-*methylethyl*)-SS-*dimethylsulphonium iodide*]. *NN*-Di-2-chloropropyl-β-naphthylamine (Everett and Ross, *J.*, 1949, 1972) was converted into NN-*di*-2-*methylthiopropyl*-β-*naphthylamine picrate*, prisms, m. p. 112°, from ethanol (Found: C, 52·8; H, 5·4; N, 10·1. $C_{24}H_{28}O_7N_4S_2$ requires C, 52·5; H, 5·1; N, 10·2%), and thence into the ***bis-sulphonium iodide***, a hygroscopic solid, m. p. 50—60° (decomp.) (Found: C, 39·3; H, 5·5; N, 2·2; S, 10·1. $C_{20}H_{31}NI_2S_2$ requires C, 39·8; H, 5·2; N, 2·3; S, 10·6%).

A solution of the di-iodide (400 mg.) in 50% aqueous acetone (100 ml.) was heated under reflux for 50 hr. The concentrated solution was extracted with ether, giving an oil which formed a ***picrate***, prisms (from benzene), m. p. 164—168°, undepressed on admixture with the picrate of *NN*-di-2-hydroxypropyl-β-naphthylamine (Found: C, 53·7; H, 5·2; N, 11·3. $C_{22}H_{24}O_9N_4$ requires C, 54·1; H, 5·0; N, 11·5%).

The residue obtained when the di-iodide was heated for some time on a water-bath formed a picrate, m. p. 119°, undepressed on admixture with *NN*-di-2-methylthiopropyl-β-naphthylamine picrate.

Trimethylenebis(*dimethylsulphonium iodide*). A mixture of 1 : 3-bismethylthiopropane (9 g.) (Mathias, *Bol. Fac. Filosofia, Cienc., Letras, Univ. Sao Paulo Quimica*, 1942, No. 1, 75; *Chem. Abs.*, 1946, **40**, 2793), methyl iodide (9 ml.), and methyl alcohol (10 ml.) was kept at room temperature for 24 hr. The ***bis-sulphonium iodide*** which separated from the solution formed prisms, m. p. 155° (decomp.), from methanol (Found: C, 20·4; H, 4·6. $C_7H_{18}I_2S_2$ requires C, 20·0; H, 4·3%).

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2-*Alkylthio*-4 : 5-*dihydroglyoxalinium Salts.*

By Walter Wilson.

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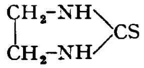
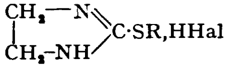
4 : 5-Dihydroglyoxalines are readily prepared by treating tetrahydro-2-thioglyoxaline (I) with alkyl halides, which give the *S*-alkyl compounds (as II) (Schacht, *Arch. Pharm.*, 1897, **235**, 445, and many later papers; cf. Knott and Morgan, U.S.P. 2,514,650; Aspinall and Bianco, *J. Amer. Chem. Soc.*, 1951, **73**, 602; Easton, Hlynsky, and Foster, *ibid.*, p. 3507; Baer and Lockwood, *ibid.*, 1954, **76**, 1162). The base formed from tetrahydro-2-thioglyoxaline, formaldehyde, and piperidine gives a dihydrochloride (Jones and Turner, *J.*, 1950, 1515), and is therefore probably the 2-substituted compound (as II; R =

$CH_2{\cdot}NC_5H_{10}$). We have prepared a series of 2-alkylthio-4 : 5-dihydroglyoxalinium salts (II) and corresponding bis-compounds (see Table) from halogen compounds. These salts and the corresponding picrates and bases may be useful for characterisation of alkyl halides and dihalides (cf. the *S*-alkylthiuronium compounds; Brown and Campbell, *J.*, 1937, 1699; Levy and Campbell, *J.*, 1939, 1442).

(I) 

 (II)

The pK_a values (see Table) fall in the range 8·4—9·6 (Baer and Lockwood, *loc. cit.*, give 9·0 for 2-*n*-butylthiodihydroglyoxaline). The strength of the second basic group in the bis-compounds shows the expected depression, less so as the distance between the basic centres increases. 2-Alkylthiodihydroglyoxalines are much weaker bases than guanidines (pK_a 13·4—13·7 in water; Albert, Goldacre, and Philips, *J.*, 1948, 2240; Angyal and Warburton, *J.*, 1951, 2492), and are appreciably weaker than closely related amidines or dihydroglyoxalines [acetamidine, pK_a 12·52; benzamidine 11·6 in water, Albert, Goldacre, and Philips, *loc. cit.*; 2-diphenylyldihydroglyoxaline, pK_a 9·29 in 50% ethanol, Cymerman-Craig, Parker, and Woodhouse, *J.*, 1953, 3050; 2-diphenylmethyldihydroglyoxaline pK_a 9·64 in 50% ethanol (present work)].

2-Benzylthiodihydroglyoxaline is stable, and with hot alkali forms toluene-ω-thiol only slowly. In contrast, *S*-benzyl*iso*thiourea decomposes when warmed, and instantaneously gives toluene-ω-thiol with hot 2N-alkali; *N*- and *NN'*-substituted *S*-alkyl*iso*thioureas behave similarly, affording thiols and cyanamides or carbodi-imides and their further transformation products (Arndt, *Annalen*, 1911, **384**, 331; *Ber.*, 1921, **54**, 2236; Rhône-Poulenc, Brit. Pat., 649,634; *Chem. Abs.*, 1951, **45**, 8040; Will *et al.*, *Ber.*, 1882, **15**, 338, 1312; Werner, *J.*, 1890, 303). 2-Alkylthiodihydroglyoxalines could not readily undergo elimination reactions of this type, because the product would be a highly strained (and unknown) cyclic carbodi-imide; the relatively slow reaction of 2-alkylthiodihydroglyoxalines with alkalis is possibly hydrolytic.

The reaction of *S*-alkyl*iso*thiuronium and 2-alkylthiodihydroglyoxalinium salts with strongly basic amines (Aspinall and Bianco, *loc. cit.*; Philips and Clarke, *J. Amer. Chem. Soc.*, 1923, **45**, 1755) does not occur with the amine hydrochlorides; the strong acid probably reduces the nucleophilic activity of the amine (cf. Lythgoe, *Quart. Rev.*, 1949, **3**, 197); acetic acid does not have this effect.

In tetrahydrothioglyoxaline itself, the sulphur is less labile than in thiourea, as shown by reactions with heavy-metal compounds (Experimental section). With mercuric oxide it affords tetrahydro-2-oxoglyoxaline (Klut, *Arch. Pharm.*, 1902, **240**, 677); substituted thioureas generally afford cyanamides or carbodi-imides, in addition to ureas, with lead or mercuric oxides (cf., *e.g.*, Khorana, *Chem. Rev.*, 1953, **53**, 145; Lecher and Gubernator, *J. Amer. Chem. Soc.*, 1953, **75**, 1087).

Experimental.—SS'-*Decamethylenebis*-(2-*thio*-4 : 5-*dihydroglyoxalinium bromide*). Tetrahydro-2-thioglyoxaline (*Org. Synth.*, 1946, **26**, 34) (4·08 g.), propanol (50 c.c.), and 1 : 10-dibromodecane (6·0 g.) were refluxed for 6 hr., then cooled, and a little ether was added. The product (7·6 g.; m. p. 173—175°) was recrystallised from ethanol, giving the *dibromide*, m. p. 174—176° (see Table). The other compounds listed were prepared similarly, being crystallised from ethanol, ethanol–ether, or aqueous ethanol. The pK_a values were determined electrometrically in 50% aqueous ethanol at 20—25° by titration of the salts with potassium hydroxide solution. Results were not obtained in some cases because of difficult solubilities.

Reactions of 2-*benzylthio*-4 : 5-*dihydroglyoxalinium chloride*. The chloride was refluxed with methylammonium or ammonium chloride in water; no thiol was formed. After addition of sodium acetate or hydroxide, toluene-ω-thiol was rapidly formed. The chloride also rapidly gave the thiol when warmed with ammonia, ammonium acetate, or methylamine solution, but only slowly with trimethylamine or sodium acetate solution. *S*-Benzylthiuronium chloride behaved similarly. *S*-Methyl compounds were less reactive than *S*-benzyl compounds in most reactions.

Reactions of tetrahydro-2-thioglyoxaline. Tschugaeff's reagent (Ph_2CCl_2) for CS groups (*Ber.*, 1902, 35, 2483) gave an intense blue colour, changing to green, then brown. Similar colours were obtained with thiourea. Hot aqueous silver nitrate gave a slight turbidity with the glyoxaline, *2-Alkylthio-4 : 5-dihydroglyoxalinium halides and* SS′-*alkylenebis-(2-thio-4 : 5-dihydroglyoxalinium) dihalides.*

Halide used	Yield (%)	M. p.	p$K_{a,1}$	p$K_{a,2}$	Formula	Found (%)		Calc. (%)	
						C	H	C	H
Methyl iodide	98	140—141° [1]	8·9	—	$C_4H_8N_2S,HI$	20·0	4·0	19·7	3·7
n-Hexyl bromide	90 [2]	54—55 [2]	—	—	*$C_9H_{18}N_2S$ (base)	58·0	9·7	58·1	9·7
n-Hexadecyl iodide	41	83·5—84 [3]	—	—	*$C_{19}H_{38}N_2S,HI$	50·7	8·8	50·3	8·65
1 : 2-Dibromoethane ...	90	275—276 [4] †	8·97	6·15	*$C_8H_{14}N_4S_2,2HBr$	24·6	4·2	24·5	4·1
1 : 3-Dibromopropane ...	87	221—222 [5]	9·57	8·03	$C_9H_{16}N_4S_2,2HBr$	26·95	4·5	26·6	4·5
1 : 4-Dibromobutane ...	93	205	9·33	8·09	*$C_{10}H_{18}N_4S_2,2HBr$	28·1	4·7	28·6	4·75
1 : 10-Dibromodecane ...	76	174—176	—	—	*$C_{16}H_{30}N_4S_2,2HBr$	38·1	6·5	38·1	6·35
2-Diethylaminoethyl chloride hydrochloride	77	172 [6]	—	—	$C_9H_{19}N_3S,2HCl$	39·75	7·8	39·4	7·7
Benzyl chloride	88	169—171 [7]	8·43	—	$C_{10}H_{12}N_2S,HCl$	52·5	5·7	52·5	5·7
p-Nitrobenzyl bromide	85	150—151 [8] 174—176	—	—	*$C_{10}H_{11}O_2N_3S,HBr$	N, 12·6		N, 13·2	
o-Xylylene dibromide [9]	86	200—201	8·88	7·53	*$C_{14}H_{18}N_4S_2,2HBr$	35·1	4·75	35·9	4·3
4 : 4′-Bischloromethyldiphenylmethane [10] ...	88	219	—	—	*$C_{21}H_{24}N_4S_2,2HCl$	53·85	6·15	53·7	5·6

* New compound. † With decomp.

[1] Free base, m. p. 100—102°, very soluble in water, extracted by ether; *picrate*, m. p. 177·5—178°, bright yellow prisms from ethanol (Found : C, 34·75; H, 3·3. $C_4H_8N_2S,C_6H_3O_7N_3$ requires C, 34·8; H, 3·2%). For the iodide Schacht (*loc. cit.*) gives m. p. 145° and Aspinall and Bianco (*loc. cit.*), m. p. 142°. [2] Hydrobromide not crystalline; product isolated as base, and recryst. from light petroleum (b. p. 60—80°). [3] Hydrobromide probably has m. p. 105° (Imazu and Takada, quoted by *Chem. Abs.*, 1950, **44**, 7775). [4] Schacht, and Knott and Morgan (*locc. cit.*), give no m. p.; Knott and Morgan give m. p. 203° for the base. [5] Knott and Morgan (*loc. cit.*) give m. p. 224°. [6] Polymorphic change at *ca.* 140°. [7] Polymorphic change at *ca.* 146°; Forrest and Walker (*J.*, 1949, 2002) give m. p. 145—145·5°; Aspinall and Bianco (*loc. cit.*) give m. p. 172° (cf. Baer and Lockwood, *loc. cit.*). The base was stable and formed large tablets or needles [from light petroleum (b. p. 60—80°)], m. p. 69° [Found : C, 62·45; H, 6·45%; *M* (Rast), 172. Calc. for $C_{10}H_{12}N_2S$: C, 62·45; H, 6·3%; *M*, 192]; Easton, Hlynsky, and Foster (*loc. cit.*) give m. p. 68—70°. *Picrate*, needles, m. p. 162°, from ethanol (Found : N, 16·9. $C_{10}H_{12}N_2S,C_6H_3O_7N_3$ requires N, 16·1%). [8] Base, m. p. 158°, hydrochloride, m. p. 191° (Easton, Hlynsky, and Foster, *loc. cit.*). [9] Perkin, *J.*, 1888, **53**, 5; Atkinson and Thorpe, *J.*, 1907, **91**, 1687. [10] Reichstein and Oppenauer, *Helv. Chim. Acta*, 1933, **16**, 1373.

and a black precipitate with thiourea. With ammoniacal silver nitrate, the precipitates were white and black respectively. Warm aqueous sodium plumbite gave a black precipitate with thiourea, but none with the glyoxaline.

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Vapour Pressures of Some Unsaturated Hydrocarbons containing Six Carbon Atoms.

By G. A. McD. Cummings and E. McLaughlin.

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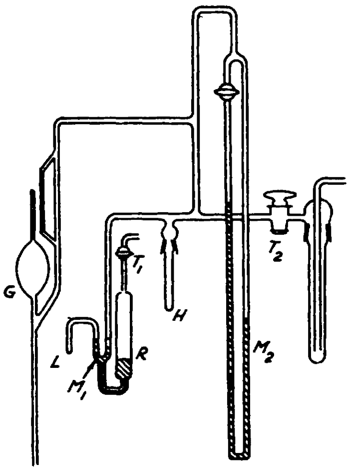
The vapour pressures of hexa-1 : 5-diene, 2 : 3-dimethylbuta-1 : 3-diene, and 2 : 3-dimethylbut-2-ene were determined for the range 0—40°, to provide data for the evaluation of diffusion coefficients (Cummings, McLaughlin, and Ubbelohde, to be published). Heats of vaporisation and molar entropies of vaporisation at the boiling point were derived from these data.

Materials.—Hexa-1 : 5-diene (b. p. 59·2° ± 0·1°/750·8 mm., n_D^{20} 1·4042), 2 : 3-dimethylbuta-1 : 3-diene (b. p. 68·4° ± 0·1°/757·0 mm., n_D^{20} 1·4391), and 2 : 3-dimethylbut-2-ene (b. p. 74·1° ± 0·1°/781·0 mm., n_D^{20} 1·4122) were prepared and purified as previously described (Cummings, McCoubrey, and Ubbelohde, *J.*, 1952, 2725), special care being taken to prevent the formation of peroxides (Howard *et al.*, *J. Res. Nat. Bur. Stand.*, 1947, **38**, 365).

Apparatus and Technique.—The vapour pressures were measured by the static method in the apparatus illustrated, which was made of 1-cm. bore Pyrex tubing and could be evacuated by a two-stage mercury diffusion pump backed by a rotary pump. Before each run, the limb *L* was baked out under vacuum, a coal-gas flame being used. A sample of the hydrocarbon was introduced into the tube *H* where it was degassed by repeated melting and freezing under vacuum. It was then allowed to distil from *H* and the middle fraction was collected in *L* and frozen in liquid air, and the whole system pumped out to better than 10^{-3} mm., as read on the McLeod gauge *G*. A slight amount of air was allowed to leak into the reservoir *R* through a capillary leak and tap T_1, thus forcing the mercury in *R* to rise in the manometer M_1. Subsequently the manometer M_1, the reservoir *R*, and the limb *L* were immersed in a water thermostat accurate to ±0·02°. Temperatures were read to ±0·02° on a mercury-in-glass (N.P.L.) thermometer, 0—40°.



The liquid in *L* was allowed 1—2 hr. to reach temperature equilibrium, the exact time being determined by the reproducibility of the subsequent readings. The mercury in the limbs of the manometer M_1 was then levelled by admitting air through a capillary leak, or by pumping out, *via* T_1 or T_2. The small difference Δh_1 in level in the manometer M_1 was read on a Pye cathetometer to ±0·05 mm. The difference in level dh_2 of the manometer M_2 was also read to ±0·05 mm., and Δh_1 and Δh_2 summed to give the required vapour pressure at the temperature of measurement. As the highest temperature of measurement was approximately 40°, approximate levelling of the mercury column in M_1 rendered a temperature correction to Δh_1 unnecessary, as any such correction was well within the limits of accuracy of the temperature control. Readings were taken as the temperature of the thermostat was raised and as it was lowered, the latter readings being discontinued when condensation of the hydrocarbon distorted the mercury meniscus in M_1. The average precision was ±0·2 mm. Results are given in Table 1.

TABLE 1.

2 : 3-Dimethylbuta-1 : 3-diene				2 : 3-Dimethylbut-2-ene				Hexa-1 : 5-diene			
Temp.	V. p., mm.	Temp.	V. p., mm.	Temp.	V. p., mm.	Temp.	V. p., mm.	Temp.	V. p., mm.	Temp.	V. p., mm.
0·04°	46·0	17·24°	106·8	12·98°	78·3	24·89°	132·2	0·04°	71·9	16·52°	156·5
12·00	83·7	19·86	120·4	13·99	81·9	29·83	162·8	12·96	133·3	17·83	164·9
13·46	89·6	25·74	156·2	15·94	89·4	34·93	199·8	13·90	138·9	31·00	282·6
15·42	98·4	31·35	197·8	16·99	93·6	39·88	242·4	14·83	144·8	38·22	370·3
16·96	105·9	68·4	757·0	19·04	102·6	74·1	781·0	15·64	149·9	59·2	750·8

The data were extrapolated to the boiling points and the vapour pressure–temperature curves fitted to the logarithmic equation $\log_{10} p = A - B/(t + C)$ (cf. Thomson, *Chem. Rev.*, 1946, **38**, 1) where *p* is the pressure in mm. and *t* the temperature. Table 2 gives the constants *A*, *B*, and *C* for the three compounds, and also the heats of vaporisation and molar entropies of vaporisation, at saturation pressure, at the normal boiling point. These values, calculated from the vapour pressure data, were obtained from the equation

$$\Delta S_{\text{vap.}} = \frac{\Delta H_{\text{vap.}}}{T} = \frac{2{\cdot}303\boldsymbol{R}TB}{(t + C)^2} \cdot \frac{P\Delta V}{\boldsymbol{R}T}$$

where *T* is the boiling point (°K) at 760 mm. Perfect gas laws were assumed and $P\Delta V/(\boldsymbol{R}T)$ was taken as unity.

TABLE 2.

Compound	*A*	*B*	*C*	$\Delta H_{\text{vap.}}$(cal./mole)	$\Delta S_{\text{vap.}}$(cal./deg. mole)
Hexa-1 : 5-diene	6·6119	1032	217·0	6830	20·5
2 : 3-Dimethylbuta-1 : 3-diene	7·2017	1346	243·0	7410	21·7
2 : 3-Dimethylbut-2-ene	7·2550	1430	253·7	7340	21·2

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