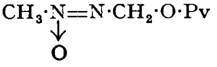
807. *Macrozamin. Part III.* Azoxymethane and Some Simple Analogues.*

By B. W. LANGLEY, B. LYTHGOE, and L. S. RAYNER.

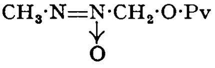
The formerly unknown primary aliphatic azoxy-compounds can be obtained by oxidising the corresponding azo-compounds with perbenzoic acid. Spectroscopic and chemical properties of azoxymethane and some of its symmetrically substituted analogues are described and compared with those of macrozamin.

EVIDENCE outlined in Part II * led us to formulate macrozamin, the toxic β-primeveroside of *Macrozamia* species, as a substituted azoxymethane of the structure (I*a* or *b*). Primary azoxy-compounds were hitherto unknown; their synthesis and examination have now been effected as a step towards synthesis of the natural compound, and also as a means of confirming our structural conclusions and of deciding between the two structures.

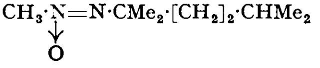
With one exception the classical methods for synthesising aromatic azoxy-compounds are not well fitted for use with aliphatic compounds unless purely tertiary representatives are required, although recently, by condensing *N*-methylhydroxylamine and 2 : 5-dimethyl-2-nitrosohexane, Aston and Jenkins obtained material which was considered to be the mixed primary-tertiary compound (II) (*Nature*, 1951, **167**, 863). The only method which promised to be at all general was that involving oxidation of azo-compounds. Its first use in the aliphatic series was recorded by Aston and Parker (*J. Amer. Chem. Soc.*, 1934, **56**, 1387) who prepared the tertiary compound (III; R = CO_2Et) by use of hydrogen peroxide in acetic acid as the oxidant; this was extended by us (Part II, *loc. cit.*) to the preparation of the secondary representative azoxy*cyclo*hexane, using nitric acid as the oxidant. Attempts have now been made to extend the scope of the method to simpler primary and secondary compounds.


$\mathrm{CH_3{\cdot}\underset{\substack{\downarrow\\ O}}{N}{=}N{\cdot}CH_2{\cdot}O{\cdot}Pv}$

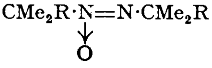
(I*a*)


$\mathrm{CH_3{\cdot}N{=}\underset{\substack{\downarrow\\ O}}{N}{\cdot}CH_2{\cdot}O{\cdot}Pv}$

(I*b*)


$\mathrm{CH_3{\cdot}\underset{\substack{\downarrow\\ O}}{N}{=}N{\cdot}CMe_2{\cdot}[CH_2]_2{\cdot}CHMe_2}$

(II)

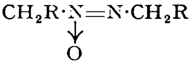

$\mathrm{CMe_2R{\cdot}\underset{\substack{\downarrow\\ O}}{N}{=}N{\cdot}CMe_2R}$

(III)

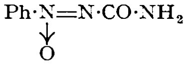
(Pv = $C_6H_{10}O_4{\cdot}O{\cdot}C_5H_9O_4$)

Neither hydrogen peroxide in acetic acid nor nitric acid oxidised 2-azopropane or 1-azo-*n*-heptane to the azoxy-compounds; apparently acid-catalysed isomerisation to hydrazones took place before oxidation. This was overcome by using the relatively weakly acidic aromatic per-acids as oxidising agents; the best and most rapid-acting was perbenzoic acid, which converted azo*cyclo*hexane quantitatively into azoxy*cyclo*hexane.

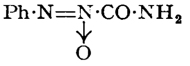
This reagent yielded azoxymethane (IV; R = H) from azomethane, 1-azoxypropane (IV; R = Et) from 1-azopropane, 2-azoxypropane (III; R = H) from 2-azopropane, and ω-azoxy-*p*-chlorotoluene (IV; R = $CH_2{\cdot}C_6H_4Cl$-*p*) from ω-azo-*p*-chlorotoluene. [1-Azopropane and ω-azo-*p*-chlorotoluene were prepared by reducing the corresponding azines to hydrazo-compounds, in the former case catalytically, in the latter with sodium amalgam and alcohol, and oxidising the hydrazo-compounds with mercuric oxide in ether.] Alone among the azo-compounds tested, ethyl azoformate was not oxidised by perbenzoic acid, but this was not unexpected since the inhibiting effect of an adjacent carbonyl group was apparent from Angeli's finding that phenylazoformamide and hydrogen peroxide in acetic acid give only (V) and no (VI) (*Atti R. Accad. Lincei*, 1917, **26**, i, 210).


$\mathrm{CH_2R{\cdot}\underset{\substack{\downarrow\\ O}}{N}{=}N{\cdot}CH_2R}$

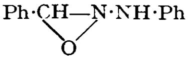
(IV)


$\mathrm{Ph{\cdot}\underset{\substack{\downarrow\\ O}}{N}{=}N{\cdot}CO{\cdot}NH_2}$

(V)


$\mathrm{Ph{\cdot}N{=}\underset{\substack{\downarrow\\ O}}{N}{\cdot}CO{\cdot}NH_2}$

(VI)



(VII)

The compound which Kijner (*J. Russ. Phys. Chem. Soc.*, 1899, **31**, 872) obtained by treating *N*-bromomenthylamine with silver oxide, and described as menthone menthyl-

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* Part II, *J.*, 1951, 2309.

hydrazone, was oxidised by perbenzoic acid to 3-azoxy-*p*-menthane; so at first it was thought that oxidation of hydrazones might provide a valuable alternative route to azoxy-compounds. Consequently the compound which Bergmann, Ulpts, and Witte (*Ber.*, 1923, **56**, 679) obtained by the action of perbenzoic acid on benzaldehyde phenylhydrazone, and to which they assigned the structure (VII), was re-examined. Its properties convinced us that, whatever its structure, it was not the expected azoxy-compound, and this in turn threw doubt on the nature of Kijner's "menthone menthylhydrazone." The latter's ultra-violet spectrum resembled closely those of authentic azo-compounds (Fig. 1), and its infra-red absorption spectrum showed no bands in the 6μ region corresponding to a $C{=}N$ group. It must therefore be reformulated as 3-azo-*p*-menthane, a structure consistent with its formation and oxidation and hydrolysis products.

Of the new azoxy-compounds ω-azoxy-*p*-chlorotoluene was solid, the others were colourless liquids of relatively high boiling points for their molecular size; azoxymethane had b. p. 98° (cf. azomethane, b. p. 1·5°), and was completely miscible with water, but the azopropanes were immiscible. The ultra-violet spectra of the new primary compounds resembled those of the secondary and tertiary compounds qualitatively, showing a maximum at short wave-lenths and an inflection. As shown in Table 1 the positions of these features depend characteristically upon the size and tertiary, secondary, or primary nature of the attached groups. The extinction curves of azoxymethane and macrozamin correspond very closely (Fig. 2).

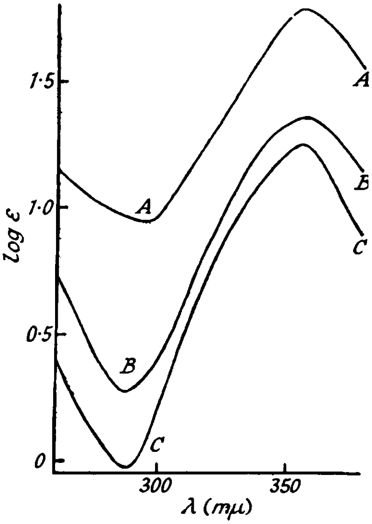


FIG. 1. *Ultra-violet light absorption of Kijner's compound* (*A*), *azocyclohexane* (*B*), *and 2-azopropane* (*C*) *in alcohol.*

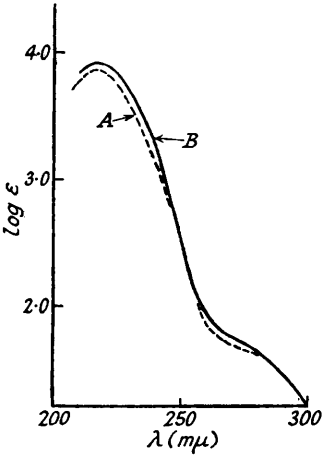


FIG. 2. *Light absorption of azoxymethane* (*A*) *and macrozamin* (*B*) *in alcohol.*

TABLE 1. *Light absorption of azoxy-compounds in alcohol.*

	Maximum		Inflection	
Compound	λ(mμ)	log ε	λ(mμ)	log ε
2-Azoxy-2 : 5-dimethylhexane [a]	223	3·75	287	1·58
2-Azoxypropane	220·5	3·84	278	1·72
1-Azoxypropane	217	3·86	277	1·75
Azoxymethane	217	3·86	274	1·64
Macrozamin [a]	217	3·92	273	1·72

[a] Part II, *loc. cit.*

In Part II, the strong bands at 1531 and 1546 cm.$^{-1}$ in the infra-red spectra of macrozamin and its hexa-acetate were provisionally identified as due to the asymmetric stretching of the azoxy-group; the correlation was not completely certain because for the synthetic compounds then available the corresponding frequency was much lower (*ca.* 1500 cm.$^{-1}$). The data obtained from the new compounds remove this uncertainty and enable the identification of a further band, due to symmetric stretching of the azoxy-group, in the spectra of macrozamin and its hexa-acetate. The spectrum of azoxymethane is very simple in the 4—8-μ region, consisting of four very strong absorption bands at 1342, 1382, 1439, and 1527 cm.$^{-1}$; the bands at 1382 and 1439 cm.$^{-1}$ clearly correspond to C–H deformation modes. Those at 1342 and 1527 cm.$^{-1}$ are assigned respectively to symmetric and asymmetric stretching modes of the azoxy-group; the corresponding vibrations of the electronically similar nitro-group in nitromethane cause bands at 1379 and 1570 cm.$^{-1}$ (Smith, Pan, and Nielsen, *J. Chem. Phys.*, 1950, **18**, 706). The relevant frequencies for other azoxy-compounds vary in a characteristic way with the size and primary, secondary, or tertiary nature of the attached groups (see Table 2), so that although the values for the tertiary compounds investigated in Part II differ by up to 60 cm.$^{-1}$ from those of hexa-acetyl macrozamin, those of azoxymethane and hexa-acetyl macrozamin are almost identical. These results reinforce those from the ultra-violet spectra and leave little doubt, not merely that macrozamin contains an azoxy-group, but that it is a substituted azoxymethane.

TABLE 2. *Characteristic frequencies of the azoxy-group.*

Compound	State	Symmetric stretching (cm.$^{-1}$)	Asymmetric stretching (cm.$^{-1}$)
2-Azoxy-2 : 5-dimethylhexane	Liquid	1285 s	1495 vs
Azoxy*cyclo*hexane	,,	1285 s	1495 vs
2-Azoxypropane	,,	1295 vs	1500 vs
1-Azoxypropane	,,	1316 s	1506 vs
Azoxymethane	,,	1342 vs	1527 vs
Hexa-acetyl macrozamin	Nujol mull	1344 s	1531 s

Chemical examination of the primary and secondary azoxy-compounds was limited to the effect of acids, alkalis, and reducing agents; these are characteristic reagents for macrozamin and also for aliphatic nitro-compounds. Since azoxy-compounds are, formally, the nitrogen analogues of nitro-compounds, some similarity between the two classes was expected.

Azoxy*cyclo*hexane was not reduced by lithium aluminium hydride in boiling ether, although this reagent reduced azoxybenzene to azobenzene, and 2-nitrobutane to 2-aminobutane (Nystrom and Brown, *J. Amer. Chem. Soc.*, 1948, **70**, 3739). ω-Azoxy-*p*-chlorotoluene was reduced to ω-azo-*p*-chlorotoluene by magnesium and methanol, but some further reduction to the hydrazo-compound also took place. Azoxymethane and 1-azoxypropane were reduced smoothly to the corresponding hydrazo-compounds by stannous chloride in hydrochloric acid. Like that of macrozamin, catalytic reduction of the primary and secondary azoxy-compounds at room temperature required the presence of a mineral acid, but the course of the reduction of the synthetic compounds was different in that, with one exception, only 2 mols. of hydrogen were absorbed, the link between the two nitrogen atoms being preserved intact and a *NN'*-dialkylhydrazine formed. The exceptional compound was ω-azoxy-*p*-chlorotoluene, which absorbed 11 mols. of hydrogen, giving hexahydrobenzylamine. It is thus clear that constitutional factors may determine a reductive fission of the linked nitrogen atoms, and the fission which occurs with macrozamin is clearly due to the presence of the primeverosyloxy-substituent, but the way in which its effect is exercised remains obscure.

It had been expected that the primary azoxy-compounds might contain readily ionisable C–H links adjacent to the quatercovalent nitrogen atom, but azoxymethane did not behave as a pseudo-acid when titrated with alkali, and ω-azoxy-*p*-chlorotoluene, where the effects of phenyl and azoxy-groups should reinforce each other in promoting ionisation, was insoluble in dilute aqueous alkali. Azoxymethane and 1-azoxypropane were decomposed by hot concentrated aqueous alkali with the formation of volatile bases. It was of interest that from azoxymethane, but not from 1-azoxypropane, some cyanide ion was formed under these conditions; nitromethane also gives cyanide ion on treatment with alkali, presumably by decomposition of methazonic acid (Dunstan and Dymond, *J.*, 1891, **59**, 430). The similar behaviour of azoxymethane may be related to the formation of cyanide ion from macrozamin (Part II, *loc. cit.*), for which, however, very much milder alkaline conditions suffice.

Possibly the most interesting reactions of the primary and secondary azoxy-compounds were those with hot aqueous hydrochloric acid. The secondary compounds reacted principally thus :

$$R_2CH{\cdot}\underset{\overset{\downarrow}{O}}{N}{=}N{\cdot}CHR_2 + H_2O \longrightarrow 2R_2CO + NH_2{\cdot}NH_2$$

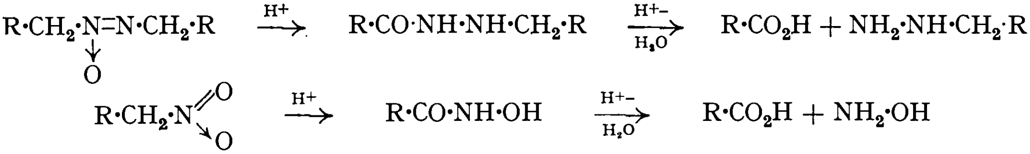
Azoxy*cyclo*hexane gave hydrazine (0·6 mol.) together with *cyclo*hexanone and dodecahydrotriphenylene; it was shown that, although the latter is not formed from interaction of hydrochloric acid and *cyclo*hexanone alone, it is produced in comparatively high yield when hydrazine is present. 2-Azoxypropane also gave hydrazine (0·6 mol.) but the acetone formed simultaneously was destroyed.

Closely related to these decompositions is that which α-azoxy*iso*butyric acid (III; $R = CO_2H$) undergoes in hot water; it was noticed but not further investigated by Aston and Parker (*loc. cit.*). Quantitative determinations showed that it proceeds in approximate accordance with the expression :

$$2(HO_2C{\cdot}CMe_2{\cdot})_2(N_2O) + H_2O \longrightarrow CHMe_2{\cdot}CO_2H + 3Me_2CO + 3CO_2 + N_2H_4 + N_2.$$

In view of the ready decarboxylation of α-nitro- and α-azo-acids, the nature and proportions of the products of the above reaction suggest two simultaneous reactions of about equal speed involving initial loss of, respectively, one and two molecules of carbon dioxide. It is however unlikely that the expected azoxy-compounds were actually formed as intermediates, since 2-azoxypropane would certainly have survived the prevailing conditions.

The primary azoxy-compounds were converted by hot hydrochloric acid into carboxylic acids and monosubstituted hydrazines; thus azoxymethane gave formic acid and methylhydrazine (0·9 mol.), and 1-azoxypropane gave propionic acid and *n*-propylhydrazine (0·9 mol.). Prolonged treatment of ω-azoxy-*p*-chlorotoluene gave *p*-chlorobenzoic acid and *p*-chlorobenzylhydrazine, but briefer treatment gave largely *N*-*p*-chlorobenzoyl-*N'*-*p*-chlorobenzylhydrazine, the structure of which was shown by hydrolysis. Clearly the reaction takes place in two steps, the first an acid-catalysed isomerisation to a *N*-acyl-*N'*-alkylhydrazine, which is then hydrolysed, rapidly if the acyl group is of the Alk·CO type, but more slowly if it is of the Ar·CO type. The reaction is closely similar to that undergone by primary aliphatic nitro-compounds in 85% sulphuric acid (Lippincott and Mass, *Ind. Eng. Chem.*, 1939, **31**, 118) :

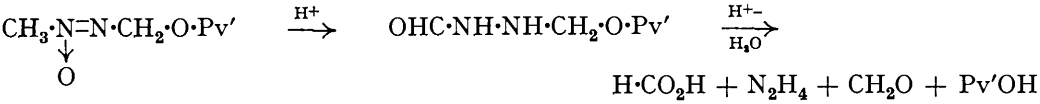


$$R{\cdot}CH_2{\cdot}\underset{\overset{\downarrow}{O}}{N}{=}N{\cdot}CH_2{\cdot}R \xrightarrow{H^+} R{\cdot}CO{\cdot}NH{\cdot}NH{\cdot}CH_2{\cdot}R \xrightarrow[H_2O]{H^+-} R{\cdot}CO_2H + NH_2{\cdot}NH{\cdot}CH_2{\cdot}R$$

$$R{\cdot}CH_2{\cdot}N\substack{/\!\!/O \\ \searrow O} \xrightarrow{H^+} R{\cdot}CO{\cdot}NH{\cdot}OH \xrightarrow[H_2O]{H^+-} R{\cdot}CO_2H + NH_2{\cdot}OH$$

both reactions have as driving force the tendency of highly oxidised nitrogen systems to achieve a lower oxidation level by oxidising adjacent methylene or methine groups.

Azoxymethane was converted into formic acid and methylhydrazine at room temperature by ethereal hydrogen chloride, and formylhydrazine was similarly hydrolysed to hydrazine, the small amounts of water necessary for these changes gaining entry through the calcium chloride guard-tube of an apparatus with ground joints. Consequently, a logical interpretation can be given of the behaviour of macrozamin towards hydrochloric acid under two different sets of conditions. The reaction with hot aqueous acid, which gives the component sugars, methanol, formaldehyde, and nitrogen, is initiated by hydrolysis of the molecule at the glycosidic link. When the hexa-acetate is treated with ethereal hydrogen chloride, the products identified are hydrazine and formaldehyde (Part II); clearly water is then present in such low concentration that the hydrolysis at the glycosidic link is suppressed and, instead, oxidation–reduction of the azoxymethane part of the molecule takes place, giving a sensitive intermediate which is gradually hydrolysed as the necessary water is absorbed :



$$\mathrm{CH_3{\cdot}}\underset{\substack{\downarrow\\ \mathrm{O}}}{\mathrm{N}}\mathrm{{=}N{\cdot}CH_2{\cdot}O{\cdot}Pv'} \xrightarrow{\mathrm{H^+}} \mathrm{OHC{\cdot}NH{\cdot}NH{\cdot}CH_2{\cdot}O{\cdot}Pv'} \xrightarrow[\mathrm{H_2O}]{\mathrm{H^+-}} \mathrm{H{\cdot}CO_2H + N_2H_4 + CH_2O + Pv'OH}$$

$[\mathrm{Pv'} = {\cdot}\mathrm{C_6H_7O(OAc)_3{\cdot}O{\cdot}C_5H_6O(OAc)_3}]$

The production of hydrazine rather than methylhydrazine, and of formaldehyde, shows that it is the methyl, not the methylene group of the aglycone which has been oxidised. From this, it would clearly be possible to decide between the two structures (I*a* and *b*) for macrozamin, provided the exact course of the acid-catalysed isomerisation of primary azoxy-compounds were known.

We regard it as very probable that the correct structure is (I*a*), since we believe such isomerisations are structurally specific, and that oxidation occurs at the methylene group adjacent to the quatercovalent and more highly oxidised nitrogen atom of the azoxy-group, and not at that adjacent to the tervalent nitrogen atom. However, a direct verification of this view is perhaps desirable, because acid hydrolysis of secondary azoxy-compounds is accompanied by the equal oxidation of both the adjacent methine groups. For this verification the preparation, structural determination, and hydrolysis of isomeric pairs of unsymmetrically substituted primary azoxy-compounds are clearly necessary, and appropriate experiments are in progress.

EXPERIMENTAL

Azoxymethane.—A conventional vacuum trap, the inlet tube of which was equipped with a tap, was connected through a delivery tube of bore not less than 8 mm. to a flask (1 l.) provided with a wide-bore spiral condenser protected by an efficient calcium chloride tube. The flask contained perbenzoic acid (30 g.) in dry ether (20 c.c.), and initially the delivery tube from the trap was raised above the surface of the solution. The trap and condenser were cooled in acetone–carbon dioxide, and the flask in ice, and azomethane (10 g.; Thiele, *Ber*, 1909, **42**, 2578), dried by passage over calcium chloride, was distilled through the inlet tube into the trap. The delivery tube was then lowered just below the surface of the liquid in the flask, and the inlet tube was connected to a source of dry nitrogen, which was admitted through the tap at such a rate that *ca.* 2 bubbles per second emerged from the delivery tube. The trap was allowed to warm slowly, so that the azomethane was transferred during ½ hour to the flask. The nitrogen current was continued for a further ½ hour, the condenser rinsed into the flask with a little dry ether, and the flask then removed from its cooling-bath, disconnected from the rest of the apparatus, and connected at once to a vacuum line through a series of traps cooled in liquid nitrogen. The volatile contents of the reaction flask were transferred to the traps during 24 hours at 1 mm. pressure, and the ethereal distillate so obtained, after drying ($CaSO_4$), was fractionally distilled with the aid of a short but efficient column (Dixon, *J. Soc. Chem. Ind.*, 1949, **68**, 299), giving *azoxymethane* (7 g.), b. p. 98°/760 mm., n_D^{17} 1·4300 [Found : C, 32·7; H, 8·3%; *M* (Regnault bulb), 71. $C_2H_6ON_2$ requires C, 32·4; H, 8·1%; *M*, 74]. The combustion was carried out in a current of air as the use of oxygen with azoxymethane and the azoxypropanes led to explosions. Nitrogen determinations by the Dumas method gave low and inconsistent values for azoxymethane.

NN′-*Di*-n-*propylhydrazine.*—Freshly distilled propaldazine in alcohol (5 vols.) was hydrogenated in contact with Adams's platinic oxide at room temperature and 5 atm.; 12 hours were required for the uptake of 2 mols. of hydrogen. Concentrated hydrochloric acid was then added, the catalyst filtered off, and the solution evaporated under reduced pressure. Repeated recrystallisation of the residue from alcohol gave the base *dihydrochloride* (30%) which evolved hydrogen chloride when heated and had m. p. *ca.* 160° (decomp.) (Found : C, 38·2; H, 9·4; N, 14·8. $C_6H_{18}N_2Cl_2$ requires C, 38·1; H, 9·5; N, 14·8%). The *bis*-3 : 5-*dinitrobenzoyl* derivative formed crystals (from acetic acid), m. p. 200° (Found : C, 47·5; H, 4·0; N, 16·8. $C_{20}H_{20}O_{10}N_6$ requires C, 47·6; H, 4·0; N, 16·7%).

1-*Azopropane.*—The above dihydrochloride (10 g.) was added to a solution of sodium hydroxide (10 g.) in water (20 c.c.), and the mixture extracted with ether (4 × 10 c.c.). The ethereal extract was washed with a little water and then shaken with mercuric oxide (13 g.) for 1 hour, dried (Na_2SO_4), and filtered. Fractional distillation of the filtrate in nitrogen gave 1-*azopropane* (3·8 g.) as a pale yellow liquid, b. p. 104°, n_D^{20} 1·4060 (Found : N, 24·4. $C_6H_{14}N_2$ requires N, 24·6%).

1-*Azoxypropane*.—A solution of 1-azopropane (10 g.) in dry methylene dichloride (20 c.c.) was cooled to 0° and perbenzoic acid (14 g.) in methylene dichloride (40 c.c.) added during 1 hour; the reaction was vigorous and benzoic acid separated from solution. After it had been kept for a further ½ hour the solution was treated with excess of 10% aqueous potassium iodide, followed at once by an excess of aqueous sodium thiosulphate. The methylene dichloride layer was separated, washed with N-sodium hydroxide, then with water, dried, and fractionally distilled under reduced pressure (Dixon column; *loc. cit.*). 1-*Azoxypropane* (7·9 g.) was obtained with b. p. 67°/20 mm., d^{20} 0·902, n_D^{20} 1·4365 (Found : C, 55·2; H, 10·5; N, 21·4. $C_6H_{14}ON_2$ requires C, 55·4; H, 10·8; N, 21·5%).

2-*Azoxypropane*.—2-Azopropane (5·4 g.; Lochte, Bailey, and Noyes, *J. Amer. Chem. Soc.*, 1922, **44**, 2556) was oxidised in methylene dichloride as described for 1-azopropane. Fractional distillation gave 2-*azoxypropane* (3·6 g.), b. p. 38°/14 mm. (Found : C, 54·9; H, 10·6; N, 21·5%).

NN'-*Di*-p-*chlorobenzylhydrazine*.—To *p*-chlorobenzaldazine (22·8 g.) in boiling alcohol (690 c.c.) 4% sodium amalgam (690 g.) was added during 3 hours and the mixture heated under reflux for a further 4 hours and then filtered. The filtrate was concentrated under reduced pressure in nitrogen to *ca.* 150 c.c., poured into cold water (1·5 l.), and extracted with ether (3 × 250 c.c.). The ethereal extract was shaken with 2N-hydrochloric acid (110 c.c.) at 0°, giving a thick white precipitate which was collected and recrystallised from alcohol. The base *hydrochloride* (16 g.) was obtained as needles, m. p. 215—216° (decomp.) (Found : C, 53·2; H, 5·5; N, 9·2; Cl', 11·2. $C_{14}H_{15}N_2Cl_3$ requires C, 53·0; H, 4·7; N, 8·8; Cl', 11·2%).

ω-*Azo*-p-*chlorotoluene*.—The above hydrochloride (4 g.), 10% aqueous sodium hydroxide (40 c.c.), and ether (50 c.c.) were shaken together until all the solid had dissolved. The ethereal layer was removed, the alkaline layer extracted with more ether, and the combined ethereal layers were washed with a little water, dried briefly, and then shaken for 6 hours with mercuric oxide (4 g.). The mixture was filtered, the filtrate evaporated to dryness, and the residue crystallised from a little alcohol, giving ω-*azo*-p-*chlorotoluene* (2·7 g.), m. p. 89—90° (Found : C, 60·7; H, 4·5; N, 10·4. $C_{14}H_{12}N_2Cl_2$ requires C, 60·2; H, 4·3; N, 10·0%).

ω-*Azoxy*-p-*chlorotoluene*.—The azo-compound (2·46 g.) in chloroform (10 c.c.) was added slowly to a stirred and cooled solution of perbenzoic acid (1·33 g.) in chloroform (23 c.c.), the solution kept at 0° overnight, and then freed from perbenzoic and benzoic acids in the usual manner and evaporated. Crystallisation of the residue from alcohol gave ω-*azoxy*-p-*chlorotoluene* (2·5 g.) as needles, m. p. 103° (Found : C, 57·1; H, 4·2; N, 9·8. $C_{14}H_{12}ON_2Cl_2$ requires C, 57·0; H, 4·1; N, 9·5%). Light absorption in alcohol : max. at 218 mμ, ε 27,700.

Reduction of ω-*Azoxy*-p-*chlorotoluene with Magnesium and Methanol*.—The azoxy-compound (0·3 g.), magnesium turnings (0·5 g.), and dry methanol (20 c.c.) were heated together under reflux till all the magnesium had dissolved (2 hours). The cooled mixture was diluted with water and extracted with ether. Evaporation of the ethereal extract gave an oil which was dissolved in methanol, whereupon it slowly deposited ω-azo-*p*-chlorotoluene, m. p. 89—90°, undepressed on admixture with authentic material. A portion of the mother-liquor reduced mercuric oxide, showing the presence of a hydrazine derivative, so the rest was treated with hydrogen chloride, *NN'*-di-*p*-chlorobenzylhydrazine being obtained as the hydrochloride, m. p. 211—212° (decomp.).

Reduction of Azoxymethane with Stannous Chloride.—A solution of stannous chloride dihydrate (1 g.) in cold 12N-hydrochloric acid (2 c.c.), and azoxymethane (280 mg.), were kept together overnight, then diluted with water (30 c.c.), and freed from tin by hydrogen sulphide. Evaporation of the filtered solution gave crystalline *NN'*-dimethylhydrazine dihydrochloride, which was identified by conversion into the dibenzoyl derivative, m. p. 87°, undepressed on admixture with authentic material.

Catalytic Reduction of Azoxy-compounds.—(*a*) 1-Azoxypropane (1·18 g.) in methanol (10 c.c.) was added to pre-reduced Adams's platinic oxide (48 mg.) in methanol (30 c.c.), and the mixture shaken at room temperature and pressure with hydrogen, but none was absorbed. Addition of hydrochloric acid (1 c.c.; *d* 1·16) caused rapid absorption of 2 mols. of hydrogen; the filtered solution gave on evaporation a crystalline solid (1·61 g.) identified as *NN'*-di-1-propylhydrazine dihydrochloride by conversion into the bis-3 : 5-dinitrobenzoyl derivative, m. p. 200°.

(*b*) The following reductions, each involving absorption of 2 mols. of hydrogen, were carried out as described above. Azoxymethane gave *NN'*-dimethylhydrazine, identified as the dibenzoyl derivative, m. p. 87°. 2-Azoxypropane gave *NN'*-di-2-propylhydrazine (4-phenylthiosemicarbazide, m. p. 128°; Lochte *et al.*, *loc. cit.*, record m. p. 128°). Azoxy*cyclo*hexane gave *NN'*-di*cyclo*hexylhydrazine [*benzoyl* derivative, m. p. 101—102°, from alcohol (Found: C, 76·4; H, 9·5; N, 9·5. $C_{19}H_{28}ON_2$ requires C, 76·0; H, 9·3; N, 9·3%)].

(*c*) ω-Azoxy-*p*-chlorotoluene (150 mg.) was reduced in the presence of platinic oxide (80 mg.), alcohol (20 c.c.), and hydrochloric acid (0·2 c.c.; *d* 1·16). Reduction stopped when 11 mols. of hydrogen had been absorbed; the filtered solution was evaporated under reduced pressure to small volume and then treated with ether, giving a crystalline hydrochloride (145 mg.), m. p. 249—251°. The benzoyl derivative, crystallised from *n*-heptane, had m. p. 101—102° (Found: C, 77·6; H, 8·9; N, 6·1. Calc. for $C_{14}H_{19}ON$: C, 77·4; H, 8·8; N, 6·4%). The reduction product was thus hexahydrobenzylamine; Demjanow (*J. Russ. Phys. Chem. Soc.*, 1904, **36**, 166) records m. p. *ca.* 254° for the hydrochloride, and Skita (*Ber.*, 1923, **56**, 1014) gives m. p. 98° for the benzoyl derivative.

Reaction of Primary Azoxy-compounds with Hydrochloric Acid.—(*a*) 1-Azoxypropane (2 g.) and 8N-hydrochloric acid (40 c.c.) were heated together under reflux for 1 hour, the mixture being then homogeneous. The cooled solution was extracted with ether, evaporation of the ether yielding propionic acid, identified as the piperazine salt, m. p. 122—123°, and as the phenylhydrazide, m. p. 156—157°. The acidic aqueous layer was evaporated, giving *n*-propylhydrazine hydrochloride, which was identified by conversion into the *NN'*-dibenzoyl derivative, m. p. 127—128°. Stollé and Reichert (*J. pr. Chem.*, 1929, **122**, 344) give m. p. 128° for this compound (Found: N, 9·9. Calc. for $C_{17}H_{18}O_2N_2$: N, 9·9%). In a parallel experiment the *n*-propylhydrazine was determined iodimetrically (Found: 0·9 mol.).

(*b*) Azoxymethane and 8N-hydrochloric acid were heated together at 75° for 1 hour in a sealed tube, and the products isolated as described above. The formic acid was identified by reduction to formaldehyde which was detected by the reaction with chromotropic acid; the methylhydrazine was characterised as its *NN'*-dibenzoyl derivative, m. p. 141°. Iodimetric determination showed that 0·9 mol. of methylhydrazine was formed.

(*c*) (By Mr. J. N. BROUGH.) ω-Azoxy-*p*-chlorotoluene (1 g.), 12N-hydrochloric acid (24 c.c.) and alcohol (12 c.c.) were boiled together under reflux. After ¾ hour the mixture became homogeneous and then deposited colourless crystals, the amount of which decreased slowly as heating progressed. After 13 hours the reaction was terminated, the cooled mixture extracted with ether, and the ether evaporated, giving *p*-chlorobenzoic acid (410 mg.) which after sublimation had m. p. 235°, undepressed on admixture with authentic material. The aqueous acidic layer was filtered, giving a crystalline residue (226 mg.), m. p. *ca.* 212° (decomp.) (Found: C, 50·9; H, 4·0; N, 8·4; Cl, 31·6. $C_{14}H_{12}ON_2Cl_2,HCl$ requires C, 50·7; H, 3·9; N, 8·4; Cl, 32·1%). When hydrolysed under reflux for 72 hours with concentrated hydrochloric acid and a little alcohol it gave *p*-chlorobenzoic acid (80%) and *p*-chlorobenzylhydrazine (70%); this compound is thus the *hydrochloride* of *N*-chlorobenzoyl-*N'*-*p*-chlorobenzylhydrazine. The free *base* had m. p. 148° (Found: C, 57·2; H, 4·4; N, 9·6. $C_{14}H_{12}ON_2Cl_2$ requires C, 57·0; H, 4·1; N, 9·5%).

Evaporation of the acid filtrate described above gave colourless crystals (371 mg.), m. p. *ca.* 160°, very soluble in water. The Schotten–Baumann method gave NN'-*dibenzoyl*-N-p-*chlorobenzylhydrazine*, m. p. 183—184° (Found: C, 69·3; H, 4·8; N, 7·6. $C_{21}H_{17}O_2N_2Cl$ requires C, 69·1; H, 4·7; N, 7·7%). A second portion of the *p*-chlorobenzylhydrazine was treated with phenyl *iso*thiocyanate, giving 2-p-*chlorobenzyl*-4-*phenylthiosemicarbazide*, m. p. 116—117°, from alcohol (Found: C, 57·6; H, 4·9; N, 14·6. $C_{14}H_{14}N_3SCl$ requires C, 57·6; H, 4·8; N, 14·4%). For comparison the same compound was also obtained by reducing *p*-chlorobenzaldehyde hydrazone with sodium amalgam and alcohol, and treating the resulting base with phenyl *iso*thiocyanate.

Reaction of Secondary Azoxy-compounds with Hydrochloric Acid.—(*a*) Azoxy*cyclo*hexane (500 mg.) and 8N-hydrochloric acid (10 c.c.) were heated together under reflux for 4 hours and the cooled solution was filtered. The residue was washed with ether, evaporation of the ether giving *cyclo*hexanone, identified as the 2 : 4-dinitrophenylhydrazone, m. p. 162°. The ether-insoluble material was recrystallised from light petroleum (b. p. 100—120°), giving dodecahydrotriphenylene (110 mg.), m. p. 232°. The acidic filtrate from the hydrolysis was shown by titration to contain 0·6 mol. of hydrazine. Evaporation of the main portion under reduced pressure, and treatment with sulphuric acid gave hydrazine sulphate, m. p. 252° (decomp.).

(*b*) 2-Azoxypropane (0·2 g.) and 12N-hydrochloric acid (2 c.c.) were heated in a sealed tube at 100° for 20 hours and then cooled. The crystalline precipitate was identified as hydrazine hydrochloride by converting it into the sulphate. No acetone could be detected in the solution.

*Hydrolysis of α-Azoxy*iso*butyric Acid.*—The acid used was prepared according to Aston and Parker (*loc. cit.*). It was recrystallised from water and dried in a vacuum immediately before use. (*a*) A solution of the acid (100 mg.) in water was heated under reflux for 10 minutes and then titrated with 0·05N-sodium hydroxide (methyl-red) (Found: 0·49 equiv. of acid). The neutral solution was concentrated and treated with *S*-benzylthiuronium chloride, giving *S*-benzylthiuronium *iso*butyrate, m. p. 141—142°.

(*b*) The azoxy-acid (70 mg.) and water (5 c.c.) were heated in a sealed tube at 100° for 1 hour, then cooled and treated with a saturated solution of 2 : 4-dinitrophenylhydrazine in 2N-hydrochloric acid (50 c.c.). The acetone 2 : 4-dinitrophenylhydrazone (111 mg.), m. p. 126°, was collected and dried to constant weight in a vacuum (Found: 1·49 mols. of acetone).

(*c*) The nitrogen evolved when a solution of the azoxy-acid in water was heated in a current of air-free carbon dioxide was collected over 50% potassium hydroxide solution in a nitrometer (Found: N_2, 0·46 mol.).

(*d*) When the azoxy-acid and water were heated together gas was evolved containing carbon dioxide, and hydrazine was detected after the reaction was over by conversion into the sulphate, and was determined iodimetrically (Found: N_2H_4, 0·52 mol.).

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