610. *The Preparation of Some Cytotoxic Epoxides.*

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The preparation of certain diepoxy-compounds possessing a cytotoxic action, as measured by their activity against the transplantable Walker rat carcinoma, and of certain related compounds, is described.

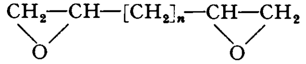
It has been clearly recognised that cytotoxic activity in the di(halogenoalkyl)amines, as measured by the inhibition of the Walker rat carcinoma 256, is limited to compounds possessing at least two halogenoalkyl chains (cf. Haddow, Kon, and Ross, *Nature*, 1948, **162**, 824; Ross, *J.*, 1949 183 and later papers). These reactive centres are capable of acting as alkylating agents (cf. also Fruton, Stein, and Bergmann, *J. Org. Chem.*, 1946, **11**, 559) and the further suggestion has recently been made by Goldacre, Loveless, and Ross (*Nature*, 1949, **163**, 667) that these compounds may act as cross-linking agents, by reacting at two points with reactive centres forming part of the same, or of two adjacent, protein fibres. A study of many types of compounds which could show this behaviour is being undertaken in these Laboratories.

Epoxides are well known to act as cross-linking agents and are used as such in the textile industry. The epoxide ring is readily opened and the compound can then react with nucleophilic reagents in a manner similar to that of the carbonium ions derived from the halogenoalkylamines (cf. Hammett, " Physical Organic Chemistry," New York, 1940, p. 301); a study of their reactivity towards such reagents has already been made (Ross, *J.*, 1950, 2257), whilst the results of biological tests will be described elsewhere. It may be noted, however, that no monoepoxide has been found to be cytotoxic in the intact animal, whereas several diepoxides are highly active. The preparation of a number of these compounds is described in the present communication.

The method of preparation used was the oxidation of the appropriate olefin or diolefin with perbenzoic acid (Prileshajew, *Ber.*, 1909, **42**, 4811); this appeared to be preferable for small-scale work to the use of peracetic acid, although the latter should present advantages for large-scale work (for a discussion of the subject see Swern, *Chem. Reviews*, 1949, **45**, 1).

The simplest compound, and one of considerable biological potency, prepared in the course of this work is 1 : 2-3 : 4-diepoxybutane. This has long been known, but the published method of preparation is tedious and does not easily afford a pure product (Przybytek, *Ber.*, 1884, **17**, 1092); it has now been prepared by the epoxidation of the commercially available butadiene monoepoxide. Substitution in the carbon chain of diepoxybutane leads to inactive or less active compounds. Of greater interest are the compounds obtained by the insertion of successive CH_2 groups between the oxiran rings, of the general structure (I), amongst which may also be included di-(2 : 3-epoxypropyl) ether in which the oxiran groups are separated by CH_2-O-CH_2; most of these are highly active.

(I.)



$$CH_2-CH-[CH_2]_n-CH-CH_2 \quad (\text{each } CH_2-CH \text{ bridged by } O)$$

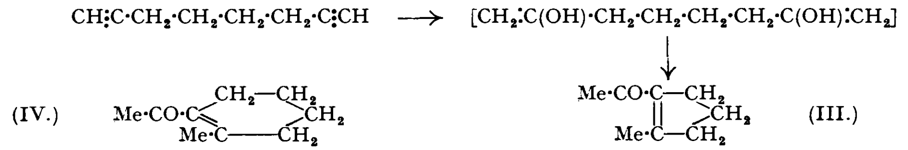
Of these, 1 : 2-5 : 6-diepoxyhexane (I; $n = 2$) has already been obtained, but not isolated, by Böseken (*Rec. Trav. chim.*, 1926, **45**, 838) by epoxidation of diallyl. We find that this compound, b. p. 187—188°, is readily formed in this reaction together with a new monoepoxide. The diepoxide has also been obtained by a similar method by Dr. L. F. Wiggins (private communication; cf. Wiggins and Wood, *Nature*, 1949, **164**, 402). A product boiling some 8° too low, but doubtless consisting mainly of the diepoxide, has been prepared by Przybytek (*Ber.*, 1885, **18**, 1350) by the action of potassium hydroxide on dichlorohexylene glycol. The material of b. p. 153° prepared from epichlorohydrin and sodium by Bigot (*Ann. Chim.*, 1891, **22**, 433) must, on the other hand, possess a different structure; Bigot himself found that only one epoxide grouping could be detected in his product by the action of acids, a finding confirmed in these Laboratories by Dr. Ross on a specimen kindly supplied by Professor J. B. Speakman. The true diepoxide prepared from diallyl has two functional oxiran-oxygen atoms, as expected.

The preparation of diepoxides with longer straight chains involved the preparation of the corresponding diolefins, some of which are new. It had been hoped to prepare 1 : 6-heptadiene from diallylcarbinol, originally obtained by Saitzew (*Annalen*, 1877, **185**, 129) from allyl iodide, ethyl formate, and zinc. We find that the same product is formed from allyl chloride, provided that a little of the bromide is added to start the reaction; the bromide alone reacts too vigorously. The carbinol readily affords the chloride, but all attempts to reduce this were unsuccessful. The corresponding bromide could not be completely purified and gave a very poor yield of hydrocarbon on treatment with lithium aluminium hydride. All attempts to oxidise the carbinol to the unknown ketone, in the hope of reducing the latter, were unsuccessful. The required hydrocarbons were eventually prepared from the appropriate diacetylenes.

In the preliminary experiments the more readily available octa-1 : 7-diyne was employed (Bader, Cross, Heilbron, and Jones, *J.*, 1949, 619; Lespieau and Deluchat, *Compt. rend.*, 1926, **183**, 889). Partial reduction of acetylenes to the ethylenes is generally carried out in the presence of a palladium catalyst (cf. Campbell and Eby, *J. Amer. Chem. Soc.*, 1941, **63**, 216; Bourguel, *Bull. Soc. chim.*, 1927, **41**, 1443; 1929, **45**, 1067); but in the present instance it was found impossible to arrest the reaction at the desired stage and some monoethylenic compound was produced. Sodium in liquid ammonia, on the other hand, caused the hydrogenation of only one of the triple bonds, doubtless because the monoacetylenic products so formed again combine with sodium to produce insoluble solid complexes. The addition of a large amount of ammonium sulphate (Henne and Greenlee, *J. Amer. Chem. Soc.*, 1943, **65**, 2020) obviates this difficulty and all the diacetylenes used in this work could be successfully reduced by this method. Hepta-1 : 6-diene had already been obtained by Henne and Greenlee; the compounds with 8 and 9 carbon atoms appear to be new, whilst the preparation of deca-1 : 9-diene from allylmagnesium bromide and tetramethylene iodide has been described by von Braun, Deutsch, and Schmatloch (*Ber.*, 1912, **45**, 1246).

The acetylenic hydrocarbons prepared from sodium acetylide and the appropriate polymethylene dibromide by the method of Lespieau and Deluchat (*loc. cit.*; Lespieau and Journaud, *Compt. rend.*, 1929, **188**, 1410) are not quite pure as a general rule and afford analytical figures adding up to 90—96% only, a fact already noted by the French authors. To effect purification we adopted the method described by Johnson and McEwen (*J. Amer. Chem. Soc.*, 1926, **48**, 469), in which the acetylenic hydrocarbon is regenerated by means of dilute hydrochloric acid from its crystalline addition product with mercuric iodide. Pure acetylenic hydrocarbons, giving perfect analytical values, could be obtained in this way, but it was noticed that a sweet-smelling high-boiling fraction was also formed and sometimes constituted the sole product. It was found to be a ketone formed by the addition of the elements of water to the acetylene, namely $C_7H_{10}O$, $C_8H_{12}O$, and $C_9H_{14}O$ respectively (deca-1 : 9-diyne was not purified in this way).

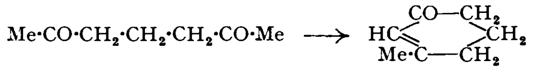
The C_8 ketone was obtained in quantity and investigation showed that it approximated in properties to the known tetrahydroacetophenone, but, although the semicarbazones had the same melting point, they were distinct, whilst the 2 : 4-dinitrophenylhydrazones had widely differing melting points. The ketone, which readily took up two atoms of hydrogen to form a saturated ketone $C_8H_{14}O$, was identified as 1-acetyl-2-methyl*cyclo*pentene (III), a compound originally prepared by the dehydration of octane-2 : 7-dione (Colman and Perkin, *J.*, 1890, **57**, 242). It is evident that the unsaturated ketone is formed by an analogous mechanism in the present instance, namely by the addition of two molecules of water to the diacetylene, followed by the elimination of one molecule of water with ring formation :



$$CH{:}C{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}C{:}CH \longrightarrow [CH_2{:}C(OH){\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}C(OH){:}CH_2]$$

(IV.) $Me{\cdot}CO{\cdot}C{<}\overset{CH_2-CH_2}{\underset{Me{\cdot}C-\!\!-\!\!-CH_2}{}}{>}CH_2$ (III.) $\overset{Me{\cdot}CO{\cdot}C-CH_2}{\underset{Me{\cdot}C-CH_2}{\|}}{>}CH_2$

In agreement with this, the C_9 ketone formed from nona-1 : 8-diyne appears to be (IV), judging from the melting point of the semicarbazone. On the other hand, the C_7 ketone formed from hepta-1 : 6-diyne has been identified as 3-methyl*cyclo*hex-2-en-1-one (V), which was obtained from heptane-2 : 6-dione by Harries (*Ber.*, 1914, **47**, 790) ; cyclisation involves the first, and not the third, carbon atom of the chain :



$$Me{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}Me \longrightarrow HC{<}\overset{CO-CH_2}{\underset{Me{\cdot}C-\!\!-CH_2}{}}{>}CH_2 \quad (V.)$$

EXPERIMENTAL.

M. p.s and b. p.s are uncorrected. The titration of oxiran groups was carried out as described by Ross (*J.*, 1950, 2257) ; branched-chain compounds generally gave low values.

Epoxidation of Olefins.—To a titrated ice-cold solution of perbenzoic acid in chloroform (*Org. Synth.*, 1932, Coll. Vol. I, p. 422, John Wiley and Sons, New York) was added 90% of the theoretical amount of the olefin in chloroform solution, and the mixture kept in a refrigerator for 7—14 days. The progress of the reaction could be followed iodometrically. The solution was washed with sodium carbonate solution, then water, dried, and evaporated using a column. The residue was fractionated from a modified Claisen flask. The properties of the epoxides prepared are listed in the Table.

Compound.	B. p., etc.	Formula.	Found, C, %.	Found, H, %.	Calc., C, %.	Calc., H, %.	Oxiran-O, %.
1 : 2-3 : 4-Diepoxybutane	140°	—	—	—	—	—	96
1 : 2-4 : 5-Diepoxypentane	160°	—	—	—	—	—	90[1]
1 : 2-3 : 4-*Diepoxy-2-methylbutane* (*isoprene diepoxide*)	55°/20 mm.	$C_5H_8O_2$	59·0	7·5	60·0	8·1	94
1 : 2-*Epoxyhex-5-ene*	119—121°	$C_6H_{10}O$	73·1	10·5	73·4	10·3	100
1 : 2-5 : 6-Diepoxyhexane	187—188°, d_4^{24} 1·0028, n_D 1·4373	—	—	—	—	—	98
2 : 3-4 : 5-Diepoxyhexane	175—177°	—	—	—	—	—	75[2]
1 : 2-3 : 4-*Diepoxy-2 : 3-dimethylbutane*	150—155°	$C_6H_{10}O_2$	61·2	8·9	63·2	8·8	82[3]
1 : 2-6 : 7-*Diepoxyheptane*	104—105°/ 31 mm.	$C_7H_{12}O_2$	65·9	9·7	65·6	9·4	90
1 : 2-7 : 8-*Diepoxyoctane*	120°/28 mm.	$C_8H_{14}O_2$	68·3	10·0	67·6	9·9	96
1 : 2-5 : 6-*Diepoxy-2 : 5-dimethylhexane*	88°/20 mm.	$C_8H_{14}O_2$	67·7	10·2	67·6	9·9	—
1 : 2-*Epoxynon-8-ene*	98°/32 mm.	$C_9H_{16}O$	77·1	11·5	77·1	11·5	100
1 : 2-8 : 9-*Diepoxynonane*	138°/33 mm.	$C_9H_{16}O_2$	68·9	10·3	69·2	10·3	96·5
1 : 2-9 : 10-*Diepoxydecane*	150°/30 mm.	$C_{10}H_{18}O_2$	70·0	10·8	70·6	10·7	97
2 : 3-6 : 7-*Diepoxy-2 : 6-dimethyloctane* (*dihydromyrcene diepoxide*)	110—113°/ 13 mm.	$C_{10}H_{18}O_2$	70·8	10·7	70·6	10·7	81
Methyl di-(2 : 3-*epoxypropyl*)*acetate* (1 : 2-6 : 7-*diepoxyheptane*-3-*carboxylate*)	162—165°/ 20 mm.	$C_9H_{14}O_4$	58·4	7·6	58·0	7·6	96[4]
Ethyl di-(2 : 3-epoxypropyl)malonate (1 : 2-6 : 7-diepoxyheptane-3 : 3-dicarboxylate)	160°/5 mm.	$C_{13}H_{20}O_6$	56·6	7·2	57·3	7·4	—[5]
3 : 4-*Epoxy*-1-(1 : 2-*epoxyethyl*)cyclo*hexane*	110—113°/ 20 mm.	$C_8H_{12}O_2$	68·4	8·7	68·6	8·6	97[6]
Divinylbenzene diepoxide	100—104°/ 0·5 mm.	$C_{10}H_{10}O_2$	70·1	6·5	74·0	6·2	81[7]
1 : 2-3 : 4-*Diepoxy*-1 : 4-*diphenylbutane*	Plates, m. p. 165—167°	$C_{16}H_{14}O_2$	80·6	6·2	80·6	5·9	25

[1] Prepared by a similar method by Paul and Tschelitcheff (*Bull. Soc. chim.*, 1948, 896). [2] By epoxidation of di*iso*propenyl; previously obtained by Duden and Lemme (*Ber.*, 1902, **35**, 1342) by a different method. [3] Not obtained pure. [4] By epoxidation of methyl diallylacetate. [5] By epoxidation of ethyl diallylmalonate. [6] By epoxidation of commercial dibutadiene (vinyl*cyclo*hexene). [7] Crude preparation, obtained by epoxidation of commercial divinylbenzene.

Isoprene Diepoxide.—Pummerer and Reindel (*Ber.*, 1933, **66**, 337) state that isoprene only forms a monoepoxide. When 10 g. of the hydrocarbon were kept with 400 c.c. of a 10% solution of perbenzoic acid in chloroform for 14 days at 0° a high fraction, b. p. 55°/20 mm. (3 g.), was isolated in addition to the monoepoxide; titration gave a diepoxide content of 94% and the other analytical figures were also in agreement.

Penta-1 : 4-*diene*.—This was prepared essentially as described by Elsner and Wallsgrove (*J. Inst. Petroleum*, 1949, **35**, 304), but with allyl bromide in place of the chloride (cf. Kistiakowsky, Ruhoff, Smith, and Vaughan, *J. Amer. Chem. Soc.*, 1936, **58**, 146). An experiment was also made to see whether this diene could be prepared by the dehydration of pentamethylene glycol with phthalic anhydride and toluenesulphonic acid (Waldmann and Petru, *Chem. Ber.*, 1950, **83**, 287). The sole product, however, was tetrahydropyran, b. p. 86·5—87·5°, d_4^{24} 0·8731, n_D 1·4187. This compound has already been obtained by the dehydration of pentamethylene glycol under rather different conditions (Demjanow, *J. Russ. Phys. Chem. Soc.*, 1890, **22**, 389).

Diallyl carbinol.—A mixture of 80 c.c. of ethyl formate and 170 c.c. of allyl bromide was added in small portions to 130 g. of zinc wool, and the reaction started by warming. It may become violent and even explosive. When it was complete water was added to the viscous black mass, and the mixture distilled, the carbinol being recovered from the distillate.

In later experiments allyl chloride (163 c.c.) was substituted for the bromide, but a little bromide was added to the first portion of the chloride and ethyl formate to start the reaction; once started, it proceeded quietly. Steam-distillation was found to be superfluous and the reaction mixture, consisting largely of a viscous grey mass, was decomposed by the addition of dilute hydrochloric acid and extracted with ether. It was also found that the amount of zinc used (this is not stated by the Russian authors) can be reduced to one-half. The yield of carbinol, b. p. 49—51°/16 mm., was 30%. It was characterised by the 3 : 5-*dinitrobenzoate*, silky needles (from pentane), m. p. 62—63° (Found : C, 55·0; H, 4·7. $C_{14}H_{14}O_6N_2$ requires C, 54·9; H, 4·6%). The chloride was prepared by adding dropwise 8 c.c. of thionyl chloride to a well-cooled solution of 13 c.c. of the carbinol in 14 c.c. of dimethylaniline with constant shaking. After 3½ hours ice and hydrochloric acid were added and the chloride was extracted with ether; it had b. p. 50°/20 mm. (yield 50%) (Found : C, 65·9; H, 8·3. Calc. for $C_7H_{11}Cl$: C, 65·8; H, 8·5%). It did not form an epoxide with perbenzoic acid. The bromide was prepared by treating an ice-cold solution of the carbinol in 5 volumes of dry benzene with a slight excess of phosphorus tribromide and working-up as above. The yield of fraction, b. p. 66·5—67·5°/25 mm., was 40%, but analyses suggest that it was not pure (Found : C, 57·8; H, 7·9. Calc. for $C_7H_{11}Br$: C, 48·0; H, 6·3%).

Reduction. 15·2 G. of powdered lithium aluminium hydride were suspended in 100 c.c. of tetrahydrofuran and 14 g. of the above chloride gradually dropped into the stirred suspension, the solvent being kept gently boiling. After 2 hours' further boiling the mixture was left overnight, then cooled, and cautiously decomposed by addition of a mixture of water and tetrahydrofuran, then more water, and finally dilute sulphuric acid. The mixture was extracted with pentane, and the extract repeatedly shaken with water to remove tetrahydrofuran. It was dried and evaporated through a column, and the residue fractionated but it contained practically no low-boiling constituents, whilst most of the chloride was recovered.

The bromide was used in later experiments and the amount of lithium aluminium hydride reduced to one-quarter. A very small amount of hydrocarbon fraction boiling at about 90° was obtained but could not be completely purified.

Hepta-1 : 6-*diyne*.—Sodium acetylide was prepared in liquid ammonia solution and treated with trimethylene dibromide following the directions of Bader *et al.* (*loc. cit.*) for the higher homologue. The yield of acetylenic derivative was poor, sometimes nil, and the compound impure. It was treated with mercuric iodide solution (Johnson and McEwen, *loc. cit.*), the gummy precipitate was collected, purified by trituration with alcohol and then ether (it was not sufficiently soluble to recrystallise as recommended for monoacetylenic derivatives), and treated with dilute hydrochloric acid (1 : 3) in a current of steam. The oil recovered from the distillate by extraction with ether consisted solely of ketonic material, characterised as the semicarbazone, m. p. 199° (Found : C, 57·4; H, 7·7. Calc. for $C_8H_{13}ON_3$: C, 57·5; H, 7·8%), not depressed on admixture of the semicarbazone of 3-methyl*cyclo*hex-2-en-1-one. The 2 : 4-*dinitrophenylhydrazone* of the latter is also a suitable derivative for characterising the ketone; it forms crimson needles, m. p. 174—175°, from ethanol (Found : N, 19·4. $C_{13}H_{14}O_4N_4$ requires N, 19·3%).

Later batches of the diyne, purified by repeated distillation under reduced pressure, had b. p. 30°/26 mm. and so obtained were sufficiently pure for the next step (Found : C, 89·7; H, 9·2. Calc. for C_7H_8 : C, 91·3; H, 8·7%); it resinifies extensively when distilled under atmospheric pressure.

Hepta-1 : 6-*diene*.—Reduction of the diyne with sodium in liquid ammonia and ammonium sulphate (Henne and Greenlee, *loc. cit.*) gave 30% of the pure diene, b. p. 90° (Found : C, 87·8; H, 12·9. Calc. for C_7H_{12} : C, 87·4; H, 12·6%).

Octa-1 : 7-*diyne*.—This was prepared in good yield as described by Bader *et al.* (*loc. cit.*) but various batches gave unsatisfactory figures on analysis. A specimen of the diyne regenerated from the mercuric iodide complex as described above had b. p. 136—138° (Found : C, 90·3; H, 9·5. Calc. for C_8H_{10} : C, 90·5; H, 9·5%). There was also a small high-boiling fraction; on another occasion this constituted the sole product of the reaction; it gave a semicarbazone, sparingly soluble prisms, m. p. 220—221°, from ethanol (Found : C, 59·5; H, 8·3. Calc. for $C_9H_{15}ON_3$: C, 59·7; H, 8·3%), the m. p. being depressed by the semicarbazone of tetrahydroacetophenone. The 2 : 4-*dinitrophenylhydrazone* formed crimson needles, m. p. 174°, from ethanol (Found : N, 18·2. $C_{14}H_{16}O_4N_4$ requires N, 18·4%). The 2 : 4-*dinitrophenylhydrazone* of tetrahydroacetophenone prepared for comparison was similar in appearance but much less soluble, m. p. 204° (Found : N, 18·8%). The ketone regenerated from the semicarbazone had b. p. 90°/30 mm., d_4^{24} 0·9506, n_D 1·4868, $[R_L]_D$ 37·56 (Found : C, 77·4; H, 9·9. Calc. for $C_8H_{12}O$: C, 77·4; H, 9·7%); it also formed a somewhat soluble oxime, m. p. 85°. The ketone was reduced to the saturated ketone, which had a strong camphoraceous odour, b. p. 165—166°, d_4^{24} 0·8967, n_D 1·4411, d_{24}^{24} 0·8996. These constants are in reasonable agreement with those given by Colman and Perkin (*loc. cit.*) as the properties of 2-acetyl-1-methyl*cyclo*pentane. This compound was further characterised by the *semicarbazone* forming somewhat soluble plates (from methanol), m. p. 145° (Found : C, 59·0; H, 9·5. $C_9H_{17}ON_3$ requires C, 59·0; H, 9·3%), and the 2 : 4-*dinitrophenylhydrazone*, orange needles (from ethanol), m. p. 109° (Found : N, 18·8. $C_{14}H_{18}O_4N_4$ requires N, 18·3%).

Octa-1 : 7-*diene*.—The octadiyne (10·6 g.), dissolved in 40 c.c. of ethyl acetate, was shaken in an atmosphere of hydrogen with 0·7 g. of 0·5% palladised calcium carbonate. After some 4 hours the uptake of hydrogen appeared to slow down considerably, rather more than the theoretical amount (2 moles) of hydrogen having been absorbed. The hydrocarbon isolated at this point no longer gave the characteristic reaction of acetylenes. The fraction of b. p. 122—124° (after distillation from metallic sodium) gave analytical figures indicating that reduction had proceeded beyond the required stage (Found : C, 85·1, 85·3; H, 14·4, 13·9. Calc. for C_8H_{14} : C, 87·2; H, 12·8%).

13·8 G. of sodium were dissolved in 600 c.c. of liquid ammonia cooled in alcohol–solid carbon dioxide, 10·6 G. of the diyne were added during 40 minutes with rapid stirring, the stirring continued for another 2 hours, and the solvent allowed to evaporate off. Aqueous ammonia was then added and the reaction product isolated by means of ether. On fractionation the bulk of the product boiled at 127—129° and there were two other fractions (b. p. 129—131° and 131—135°). The first fraction was analysed (Found : C, 88·1; H, 10·9%). A repetition of the reduction gave similar material (Found : C, 88·9; H, 11·9%), in approximate agreement with the formula C_8H_{12} (Calc. : C, 88·8; H, 11·2%).

Finally, the pure regenerated octadiyne (25 g.) dissolved in 5 volumes of dry ether was added to rapidly stirred liquid ammonia (240 c.c.) and 145 g. of ammonium sulphate, cooled as above. Sodium (26·5 g.) was added in small pieces until the blue colour persisted for some time (Henne and Greenlee, *loc. cit.*). *Octa*-1 : 7-*diene* (16 g.) was isolated as above and boiled sharply at 116° after distillation from sodium, and had $d_4^{21\cdot4}$ 0·7293, n_D 1·4215, $[R_L]_D$ 38·35 (Found : C, 86·8; H, 13·3. C_8H_{14} requires C, 87·2, H, 12·8%).

Nona-1 : 8-*diyne*.—This was obtained from sodium acetylide and pentamethylene dibromide exactly as the lower homologue (yield, 40 g. from 90 g. of dibromide). The *diyne* regenerated from the mercuric iodide complex had b. p. 68—69·5°/29 mm., $d_4^{24\cdot4}$ 0·8230, n_D 1·4500, $[R_L]_D$ 39·24 (Found : C, 89·8; H, 10·3. C_9H_{12} requires C, 89·9; H, 10·1%). A ketonic by-product was also produced in the regeneration of the diyne, affording a semicarbazone, plates m. p. 207—208° (Found : C, 61·4; H, 9·3. Calc. for $C_{10}H_{17}ON_3$: C, 61·5; H, 8·8%). The semicarbazone of 1-methyl-2-acetyl*cyclo*hexene is stated to melt at 207—208° (Meerwein and Schäfer, *J. pr. Chem.*, 1922, **104**, 304).

Nona-1 : 8-*diene*.—Reduction of the above diyne by the method of Henne and Greenlee (*loc. cit.*) afforded an excellent yield of the *diene*, b. p. 140°, $d_4^{24\cdot4}$ 0·7395, n_D 1·4275, $[R_L]_D$ 43·18 (Found : C, 87·2; H, 13·5. C_9H_{16} requires C, 87·0; H, 13·0%). Catalytic reduction gave a mixture giving analytical values in better agreement with the formula C_9H_{18} (Found : C, 85·4, 85·3; H, 14·0, 14·9%).

An attempt was also made to prepare nona-1 : 8-diene by the reduction of *s*-diallylacetone, prepared in poor yield by the hydrolysis of ethyl diallylacetonedicarboxylate (Volhard, *Annalen*, 1892, **267**, 86; Schroeter, *Ber.*, 1916, **49**, 2697). It was converted into the *semicarbazone* (mentioned but not described or analysed by Auwers and Moosbrugger, *Annalen*, 1912, **387**, 194), plates, m. p. 93—94° (from methanol) (Found : N, 21·2. $C_{10}H_{17}ON_3$ requires N, 21·5%). Three portions of 4·1 g. of the semicarbazone were heated in sealed tubes, each with 1·3 c.c. of hydrazine hydrate and 20 c.c. of a 5% solution of sodium in ethanol for 8 hours at 180°. On working up, 7 g. of the diene, b. p. 146°, were obtained (Found : C, 86·8; H, 13·4. C_9H_{16} requires C, 87·0; H, 13·0%).

Deca-1 : 9-*diyne*.—58 G. of hexamethylene dibromide gave 22 g. of the *diyne*, which was sufficiently pure for the next step after two fractionations under reduced pressure, b. p. 78—80°/29 mm. (Found : C, 89·0; H, 10·6. $C_{10}H_{14}$ requires C, 89·5; H, 10·5%), $d_4^{24\cdot3}$ 0·8288, n_D 1·4528, $[R_L]_D$ 43·75.

Deca-1 : 9-*diene*.—The reduction of the diyne by the method of Henne and Greenlee gave a good yield of *diene* (18 g. from 22 g. of diyne), but the product still gave the reaction of an acetylene with ammoniacal silver nitrate; after a second treatment it was pure, having b. p. 165°, $d_4^{25\cdot0}$ 0·7484, n_D 1·4300, $[R_L]_D$ 47·72 (Found : C, 87·2; H, 13·1. $C_{10}H_{18}$ requires C, 86·9; H, 13·1%). The boiling point is 5° lower than that quoted by von Braun, Deutsch, and Schmatloch (*loc. cit.*) and as these authors did not determine the physical properties of their diene, the identity of the two preparations cannot be regarded as proved.

Di-(2 : 3-*epoxypropyl*) *Ether*.—This compound was originally prepared from epi-iodohydrin by a laborious process giving poor yields (Nef, *Annalen*, 1904, **335**, 238). It was more easily obtained by the epoxidation of diallyl ether.

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