153. *Action of Diazomethane on Hydroxy-compounds and of Diazomethane Derivatives on Phenanthraquinone.*

By Alexander Schönberg and Ahmed Mustafa.

Certain hydroxy-compounds are stable towards *ethereal* diazomethane solutions, but are readily methylated if methyl alcohol is added. This stability of *o*-hydroxy-ketones is explained by chelation (I). The effect of methyl alcohol is ascribed to its opening of the chelate ring system (VI), thus rendering the *o*-hydroxy-group free. Furthermore, it is believed that diazomethane reacts with the lower alcohols to give the powerful methylating agent $CH_2{:}N{\cdot}NH{\cdot}OR$ or $CH_3{\cdot}N{:}N{\cdot}OR$.

By treatment of 4 : 4′-dihydroxy-$\alpha\beta$-diethylstilbene (stilboestrol) with ethereal diazomethane solution in the presence of *n*-propyl alcohol, its di-*n*-propyl ether was obtained.

1-Benzoyl-2-naphthol (IV) and 6-hydroxy*meso*benzanthrone (V) react with ethereal diazomethane solutions, probably owing to lack of chelation in these substances.

The action of diphenyl-, phenylmethyl-, and phenyl-diazomethane on phenanthraquinone yields methylenedioxy-derivatives of type (VIII) which give phenanthraquinone when treated with sulphuric acid.

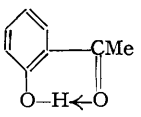
Chrysoquinone reacts in a similar manner (cf. X).

It has been pointed out that certain *o*-hydroxy-compounds are not methylated by an ethereal solution of diazomethane, *e.g.*, alizarin 2-methyl ether (Herzig and Klimosch, *Monatsh.*, 1909, **30**, 535), the benzopyrone derivative (II) (Shah, Virkar, and Venkataraman, *J. Indian Chem. Soc.*, 1942, **19**, 135), *o*-hydroxyacetophenone (Schönberg and Ismail, *J.*, 1944, 367), and 9 : 10-dihydroxynaphthacene-11 : 12-quinone (Schönberg and Moubasher, *J.*, 1944, 336). This stability is also shown by *o*-hydroxybenzophenone, 1-hydroxy-, 1 : 5-dihydroxy-, and 1 : 4-dihydroxy-anthraquinone, and by the 4-methyl ether of resacetophenone. On the other hand, we find that 1-benzoyl-2-naphthol (IV) and 6-hydroxy*meso*benzanthrone (V) react readily with diazomethane in ethereal solution.

The generally accepted reason (*e.g.*, Sidgwick and Callow, *J.*, 1924, **125**, 527; Perkin and Storey, *J.*, 1928, 233) for the stability of *o*-hydroxy-ketones and related substances towards diazomethane is the formation of a chelated ring system (*e. g.*, I), so the different behaviour of 1-benzoyl-2-naphthol may be ascribed to the large contribution to its resonance structure made by (IV). This *o*-quinonoid structure hinders the formation of a chelated ring, as there is no double bond between C_1 and C_2 (fixation of double bonds), and is in agreement with the yellow colour of the substance. A similar explanation accounts for the methylation of 6-hydroxy*meso*-benzanthrone (V) by diazomethane in ethereal solution.

In agreement with the theory of chelation is the fact that *p*-hydroxyacetophenone and *p* : *p*′-dihydroxybenzophenone react with ethereal diazomethane, in contrast to *o*-hydroxy-acetophenone and -benzophenone; also 2-hydroxy-1-methylanthraquinone reacts with ethereal diazomethane in spite of the fact that the hydroxy-group is sterically hindered.

Action of Diazomethane in the Presence of Methyl Alcohol.—We have found that *o*-hydroxy-aceto- and -benzo-phenone, the 4-methyl ether of resacetophenone, 1 : 5-dihydroxyanthraquinone, and alizarin 2-methyl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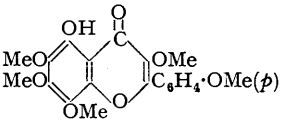
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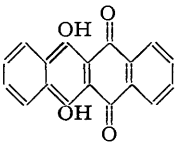
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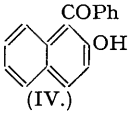
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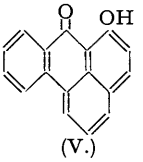
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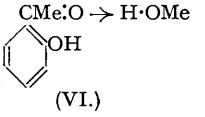
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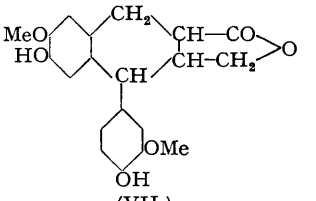

(VII.)

ether,which are stable towards diazomethane in ether, are methylated if methyl alcohol is added to the solution. Further, under the latter conditions, methyl salicylate, conidendrin (VII), and benzophenone oxime are methylated, whereas they are unaffected by ethereal diazomethane (Hölljes and Wagner, *J. Org. Chem.*, 1944, **9**, 40; Brauns, *ibid.*, 1945, **10**, 216; Forster and Dunn, *J.*, 1909, **95**, 425, respectively).

To explain this difference of reactivity caused by the presence of methyl alcohol, it might be assumed that the alcohol reacts with the carbonyl group of the substances concerned to form complexes of the type (VI), in which the phenolic hydroxy-group is free and therefore capable of reacting with diazomethane; but such a theory cannot explain why benzophenone oxime and conidendrin (VII) exhibit this phenomenon or why stilboestrol is only slowly methylated by ethereal diazomethane, but more quickly in the presence of methyl alcohol. The following theory covers the whole field.

It is possible that in methyl-alcoholic solution diazomethane coexists with a compound formed as in (A) (R = Me), which acts as a strong methylating agent. Similarly, for other alcoholic solutions, the corresponding

$$CH_2N_2 + R{\cdot}OH \longrightarrow CH_2{:}N{\cdot}NH{\cdot}OR \text{ or } CH_3{\cdot}N{:}N{\cdot}OR \quad (A)$$

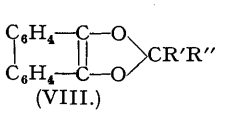
$$CH_3{\cdot}N{:}N{\cdot}OR + Ar{\cdot}OH \longrightarrow Ar{\cdot}OR + CH_3{\cdot}N{:}N{\cdot}OH \longrightarrow N_2 + CH_3{\cdot}OH \quad (B).$$

alkyl group R should be introduced (B). This is indeed the case, for when stilboestrol, dissolved in ether and *n*-propyl alcohol, was treated with ethereal diazomethane, a product was obtained which yielded, after recrystallisation, the pure di-*n*-propyl ether of stilboestrol. The formation of this ether cannot be explained by assuming that the dimethyl ether is first formed by diazomethane and that the two methyl groups are replaced by two *n*-propyl groups by the action of *n*-propyl alcohol, for we found that both stilboestrol and its dimethyl ether are stable towards cold *n*-propyl alcohol.

The schemes (A) and (B) account for the production of diazomethane from nitrosomethylurethane and sodium methoxide in the presence of methyl alcohol, rather than sodium ethoxide in the presence of ethyl alcohol, during methylation of phenols by diazomethane. Since, in the latter case, there is the possibility of the formation of the ethyl ether of the phenol in addition to the methyl ether, it is difficult to separate the ethers.

Action of Diazomethane Derivatives on Phenanthraquinone.—We have investigated the action of diphenyl-, phenylmethyl-, and phenyl-diazomethane on phenanthraquinone. *Methylenedioxy*-derivatives (VIII) were obtained as already described in the case of phenanthraquinone and diazomethane (Arndt, Amende, and Ender, *Monatsh.*, 1932, **59**, 202). It is clear that the products obtained by the action of these diazomethanes are not ethylene oxides (IX), for they are easily hydrolysed to phenanthraquinone by concentrated sulphuric acid at room temperature. Under these conditions, a scission of a C–C link is not probable. A methylenedioxy-derivative has also been obtained by the action of diphenyldiazomethane on 6-bromo-1 : 2-naphthaquinone (Fieser and Hartwell, *J. Amer. Chem. Soc.*, 1935, **57**, 1479).

Diazomethane and diphenyldiazomethane converted chrysoquinone into the corresponding *methylene ethers* of 1 : 2-dihydroxychrysene (X; R = R′ = H and R = R′ = Ph, respectively).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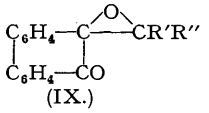
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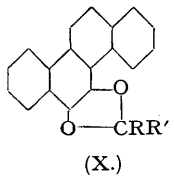
(X.)

Experimental.

The ethereal diazomethane solution was prepared according to *Org: Synth.*, **15**, 3.

Action of Ethereal Diazomethane on p-*Hydroxyacetophenone*,* p : p′-*Dihydroxybenzophenone*,* 2-*Hydroxy*-1-*methylanthraquinone*,* 1-*Benzoyl*-2-*naphthol*,* 6-*Hydroxy*mesobenzanthrone,† 4-*Benzoyl*-1-*naphthol, and* p : p′-*Dihydroxystilbene*.—The hydroxy-compound (1 g.) was dissolved in ether (25 c.c.), the solution cooled in ice, and treated with a cooled ethereal solution of diazomethane (from 4 g. of nitrosomethylurethane). The solvent was evaporated off, and the residue crystallised from alcohol. The resulting methyl or dimethyl ether was identified by m. p. and mixed m. p. with an authentic specimen in each case.

Hydroxy-compounds Unaffected by Ethereal Diazomethane.—Ethereal solutions of 1 g. each of 1-hydroxyanthraquinone,* 1 : 4- and 1 : 5-dihydroxyanthraquinone,* *o*-hydroxybenzophenone,* and resacetophenone 4-methyl ether were treated separately with excess of ethereal diazomethane (from nitrosomethylurethane, 8 g.) as above. The mixtures were left for 48 hours at 0°, and the ether then evaporated, but in every case unchanged starting material was obtained. We confirmed that methyl salicylate (Hölljes and Wagner, *loc. cit.*), benzophenone oxime (Forster and Dunn, *loc. cit.*), and conidendrin (Brauns, *loc. cit.*) also do not react with ethereal diazomethane.

Action of Diazomethane on Hydroxy-compounds in the Presence of Methyl Alcohol.—(*a*) Resacetophenone 4-methyl ether (Adams, *J. Amer. Chem. Soc.*, 1919, **41**, 260) (1 g.) in cold methyl alcohol (about 20 c.c.) was treated with ethereal diazomethane (from nitrosomethylurethane, 8 g.) and the mixture left at 0° for 4 days, during which fresh amounts of the diazomethane solution were added. The solvents were evaporated off, and the oily residue treated with aqueous-alcoholic hydroxylamine hydrochloride. After 4 days at room temperature the mixture was poured into ice-water, and the resulting solid collected and crystallised from ethyl alcohol; it formed colourless crystals, m. p. 127°, not depressed in admixture with resacetophenone oxime dimethyl ether (Sachs and Herold, *Ber.*, 1907, **40**, 2724).

(*b*) Similarly, *o*-methoxybenzophenone was obtained from *o*-hydroxybenzophenone and characterised (m. p. and mixed m. p.) as its oxime.

(*c*) By the same means, alizarin afforded its dimethyl ether (m. p. and mixed m. p.); this was completely insoluble in aqueous sodium hydroxide, whereas in the absence of methyl alcohol the product formed from alizarin was completely soluble in 10% sodium hydroxide, showing that no dimethyl ether was formed.

(*d*) Ethereal diazomethane in the presence of methyl alcohol dimethylated 1 : 5-dihydroxyanthraquinone and converted benzophenone oxime into its *N*-methyl ether and methyl salicylate into its *O*-methyl ether (identified as *o*-methoxybenzoic acid).

(*e*) A suspension of conidendrin (VII) in ether–methyl alcohol was similarly converted by ethereal diazomethane into its dimethyl ether (m. p. not depressed by sample prepared by means of methyl sulphate) (Found : C, 68·3; H, 6·2. Calc. for $C_{22}H_{24}O_6$: C, 68·8; H, 6·2%).

Methylation of 4 : 4′-*Dihydroxy*-αβ-*diethylstilbene* (*Stilboestrol*).—Stilboestrol (0·4 g.), dissolved in dry ether, was treated with an ethereal solution of diazomethane (from 4 g. of nitrosomethylurethane) and kept at 0° for 24 hours. The product was the dimethyl ether (about 0·1 g.); m. p. not depressed on admixture with an authentic specimen (Reid and Wilson, *J. Amer. Chem. Soc.*, 1942, **64**, 1625). When the above experiment was repeated in the presence of methyl alcohol (10 c.c.) the same ether (0·35 g.) was obtained.

n-*Propylation of Stilboestrol*.—Stilboestrol (0·5 g.) was dissolved in a mixture of ether (25 c.c.) and *n*-propyl alcohol (10 c.c.) and the ice-cooled mixture treated with ethereal diazomethane (from nitrosomethylurethane, 8 g.) added in two portions during 48 hours at 0°. The solvents were evaporated off, the residue was dissolved in ether, and the solution extracted with aqueous potassium hydroxide, washed with water, and dried (sodium sulphate). The ether was driven off, and the residue crystallised from ligroin (b. p. 50—60°); m. p. 98°, not depressed by admixture with an authentic specimen of stilboestrol di-*n*-propyl ether (Reid and Wilson, *loc. cit.*) (Found : C, 81·9; H, 9·0. Calc. for $C_{24}H_{32}O_{25}$: C, 81·8; H, 9·1%).

Action of Diazomethane Derivatives on Phenanthraquinone.—(a) *Diphenyldiazomethane*. Phenanthraquinone (0·5 g.), suspended in benzene (20 c.c.), was treated with diphenyldiazomethane (Staudinger and Gaule, *Ber.*, 1916, **49**, 1897) (prepared from benzophenone hydrazone, 1·2 g., and yellow mercuric oxide, 3 g.). The quinone dissolved, and after 24 hours at room temperature, the benzene was evaporated off; the oily residue solidified on washing with cold ethyl alcohol, and crystallised from hot absolute ethyl alcohol in almost colourless crystals, m. p. 166—167° (orange melt). The 9 : 10-(*diphenylmethylenedioxy*)*phenanthrene* (VIII; R′ = R″ = Ph) dissolves readily in cold benzene or hot ethyl alcohol and with difficulty in light petroleum (b. p. 30—50°). When treated with concentrated sulphuric acid it gives a brownish-violet colour, changing after some time into greenish-brown (Found : C, 86·3; H, 5·1. $C_{27}H_{18}O_2$ requires C, 86·6; H, 4·8%).

(b) *Phenyldiazomethane*. 9 : 10-(*Benzylidenedioxy*)*phenanthrene* (VIII; R = H, R″ = Ph) was obtained by the action of phenyldiazomethane (Staudinger and Gaule, *loc. cit.*) on phenanthraquinone. It formed almost colourless crystals, m. p. 121° (orange melt), soluble in benzene, difficultly soluble in light petroleum (b. p. 30—50°), and dissolving in concentrated sulphuric acid to give a green coloration (Found : C, 83·8; H, 4·8. $C_{21}H_{14}O_2$ requires C, 84·6; H, 4·7%).

(c) *Phenylmethyldiazomethane*. 9 : 10-(α-*Phenylethylidenedioxy*)*phenanthrene* (VIII; R′ = Ph, R″ = Me) was similarly obtained by the action of phenylmethyldiazomethane (Staudinger and Gaule, *loc. cit.*); it crystallised in almost colourless crystals from hot ethyl alcohol, m. p. 90° (orange melt), was soluble in benzene, difficultly soluble in light petroleum (b. p. 30—50°), and gave a violet colour with concentrated sulphuric acid (Found : C, 84·3; H, 5·2. $C_{22}H_{16}O_2$ requires C, 84·6; H, 5·1%).

Action of Sulphuric Acid on the Foregoing Three Compounds.—0·5 G. of each of the three methylenedioxyphenanthrenes was mixed with concentrated sulphuric acid (3 c.c.) at room temperature and set aside overnight, during which a green solution was formed. The solution was poured on ice, neutralised with sodium carbonate, and extracted with ether. The ethereal solution was dried (sodium sulphate) and distilled, affording phenanthraquinone (m. p. and mixed m. p.).

Action of Diazomethane Derivatives on 1 : 2-*Chrysoquinone*.—(*a*) Diphenyldiazomethane, under the above conditions, afforded 1 : 2-(*diphenylmethylenedioxy*)*chrysene* (X; R = R′ = Ph), colourless crystals, m. p. 264—265° (red melt) (Found : C, 87·2; H, 4·7. $C_{31}H_{20}O_2$ requires C, 87·7; H, 4·7%), from benzene. (*b*) Excess of ethereal diazomethane was added to a suspension of chrysoquinone in ether, and the mixture kept overnight in the ice-chest. The resulting 1 : 2-*methylenedioxychrysene* separated from benzene–ligroin (b. p. 50—60°) in almost colourless crystals, m. p. 158° (Found : C, 83·3; H, 4·8. $C_{19}H_{12}O_2$ requires C, 83·8; H, 4·4%), giving a reddish-brown colour in sulphuric acid. In both cases the action of sulphuric acid, as in the preceding section, regenerated chrysoquinone.

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