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CHAIN EXTENSION OF SUGAR-ACID ESTERS WITH SULPHOXIDES

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A number of sulphur-containing sugar derivatives are known having moderate activity against virus and other microorganisms, and as part of work directed to the preparation of some analgous sugars containing sulphur residues we have investigated the reactions of various sulphoxides with sugar derivatives.

Since carbanion formation occurs readily with sulphoxides, we considered that an analogous reaction to the Claisen reaction (1) should permit the synthesis of β-ketosulphoxides from esters - ①

① $$R.CO.OR' + R''\overset{\ominus}{C}HSOCH_2R'' \longrightarrow \overset{\ominus}{O}R' + R.COCR''H.SOCH_2R''$$

and the application of this reaction to suitably protected glyconic or glycuronic acid esters should lead to chain extension with formation of interesting new sugars. Further, since it is possible to cleave sulphoxides readily, with, eg. Raney nickel (2) or aluminium amalgm (3), a variety of sulphur-free chain-extended sugars should also become accessible ②

② $$RCO.CR''H.SOCH_2R'' \xrightarrow{H} RCOCH_2R''$$

Preliminary experiments using simple esters and carbanions produced from dimethyl-or dibutyl-sulphoxides showed that rapid reaction occurs to give, generally solid, β-ketosulphoxides, the structures of which were confirmed by cleavage to give known ketones.

Thus ethyl benzoate was converted to acetophenone or valerophenone respectively by the action of sodio-dimethyl sulphoxide or sodio dibutylsulphoxide; in analogous reactions ethyl phenylacetate gave benzyl methyl ketone and benzyl butylketone.

Application to sugars was investigated, and again reaction was confirmed by the conversion of intermediate sulphur compounds to known materials. For example methyl 1,2;3,4-di-*O*-isopropylidene *α*-*D*-galacturonate with dimethyl sulphoxide gave finally 1,2;3,4-di-*O*-isopropylidene-7-deoxy*α*-*D*-galactohepto-6-ulose, whilst methyl methyl-2,3-*O*-isopropylidene-*D*-lyxuronate and methyl 1,2-*O*-isopropylidene-3-*O*-benzyl*α*-*D*-xyluronate were converted respectively to methyl 2,3-*O*-isopropylidene-6-deoxy-*D*-lyxohexo-5-ulose and 1,2-*O*-isopropylidene-3-*O*-benzyl-6-deoxy*α*-*D*-xylohexo-5-ulose.

Examination of the reaction of lactones with the reagent was made. γ-Butyrolactone reacted readily with sodio-dimethyl sulphoxide to give, after desulphurisation, 5-hydroxy-pentan-2-one. The action upon sugar lactones is being examined.

Since a variety of dialkyl and diaralkyl sulphoxides are available or readily synthesised, this method should prove capable of considerable variation and a range of poly-deoxy sugars should become available for investigation.

The following is a typical experiment.

Preparation of methyl-octyl ketone - (a) All operations were carried out where appropriate under dry nitrogen. Sodium hydride (1.15g), obtained from the oil suspension by repeated washing witn petrol-ether, was dissolved in dimethyl sulphoxide (15 ml.) and to the solution was added dry methyl nonoate with ice-cooling. The mixture was allowed to reach room temperature, warmed for 5 min. at 25°C., and then left overnight at room temperature. From the reaction mixture was obtained 2-keto-decyl methyl sulphoxide m.63-64° (from ethyl acetate), showing moderate or strong bands in the infra red at 1710,* 1698*, 1470, 1370, 1235,$\overset{1025}{/}$and 718 cm^{-1}. Found : C, 60.38, 60.80; H, 9.66, 9.75; S, 14.36, 14.87: $C_{11}H_{22}O_2S$ requires C, 60.55; H, 10.09; S, 14.68%.

(b) The β-ketosulphoxide was dissolved in 65% aqueous ethanol. Aluminium foil was activated with mercuric chloride and the solution of sulphoxide was added immediately. The solution was kept slightly warmed for several hours, the reduced product was separated, and fractionally distilled, to give methyl octyl ketone (5.3g.), b.104-108°C./17 mm., n_D^{21} 1.4252, band at 1703 cm^{-1} in the infra red.

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*A number of these compounds have shown split carbonyl bands, with the higher band as a shoulder.

References

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Some examples of chain extension

Ester	Sulphoxide[a]	Desulphurised product[b]
Ethyl benzoate	DMSO	Acetophenone b.200°, n_D^{20} 1.5352.
Ethyl benzoate	DBSO	Valerophenone b 125°/15 mm., n_D^{20} 1.5344
Ethyl phenylacetate	DMSO	Benzyl methyl ketone b.100°/15 mm. n_D^{20} 1.5166
Ethyl phenylacetate	DBSO	Benzyl butyl ketone b.140°/18 mm.
Methyl nonoate	DMSO	Octyl methyl ketone b.106/17 mm., n_D^{21} 1.4252
Methyl oleate	DMSO	Methyl heptadecenyl ketone b.60/1 mm. Semi-carbazone m. 98-90°. (4)
Methyl 1,2;3,4-di-O- isopropylidene α-D-galacturonate	DMSO	1,2;3,4-di-O-isopropylidene-7-deoxyα-D-*galacto*-hepto-6-ulose b.125°/0.12 mm. $[\alpha]_D^{19}$ -133° (CHCl$_3$)
Methyl methyl 2,3-O-isopropylidene -D-lyxuronate	DMSO	Methyl 2,3-O-isopropylidene-6-deoxy-D-*xylo*-hexo-5-ulose b.80°/0.04 mm. $[\alpha]_D^{23}$ -17° (EtOH).
Methyl 1,2-O-isopropylidene-3--O-benzylα-D-xyluronate	DMSO	1,2-O-isopropylidine-3-O-benzyl-6-deoxy-D-*xylo*hexo-5-ulose m.50-52°; $[\alpha]_D^{25}$ -88°(c.1.4 CHCl$_3$)

[a] DMSO = dimethyl sulphoxide. DBSO = dibutyl sulphoxide [b] Identity confirmed by comparison, where appropriate, with spectra, gas-liquid chromatography, thin layer chromatography, 2,4-dinitrophenylhydrazones or other derivatives.