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PROMOTED DIMERIZATION OF α-METHYLSTYRENE BY 3,5-DIMETHOXY-SUBSTITUENTS

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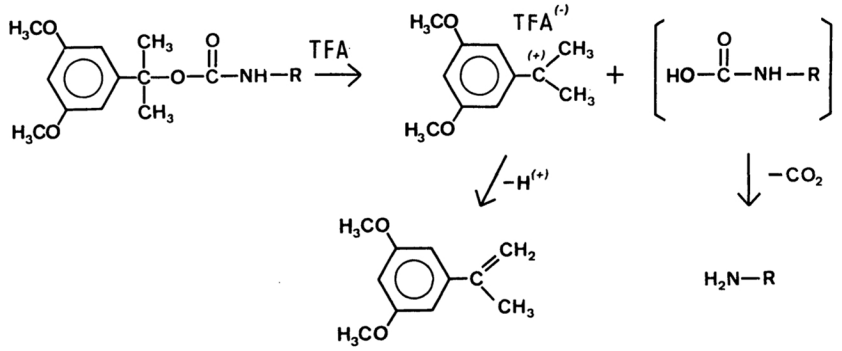
3,5-Dimethoxy-α-methylstyrene, which originates from acidic cleavage of the 3,5-dimethoxy-α,α-dimethyl-benzyl-oxycarbonyl residue, an amino protecting group in peptide synthesis, easily dimerizes in solution to 1,3,3-trimethyl-1-(3,5-dimethoxy)-phenyl-5,7-dimethoxyindan in the presence of trifluoroacetic acid.

The dimerization of styrene [1-4] and α-methylstyrene [4-7] has been investigated by using different acidic catalysts. According to the reaction conditions isomeric dimers in various amounts were found as main products beside oligomers and polymers. Two principal types of dimers were detected: a linear dimer of 1,3-diphenyl-1-butene structure and a cyclic dimer of the 3-methyl-1-phenylindan type.

The reaction of 3,5-dimethoxy-α-methylstyrene under acidic conditiones has not yet been investigated. We obtained a dimer of this compound in a reaction, in which 3,5-dimethoxy-α-methylstyrene was generated by acidic cleavage of the 3,5-dimethoxy-α,α-dimethyl-benzyl-oxycarbonyl (Ddz) group [8], a well suited amino protecting group for peptide synthesis. The Ddz-group is usually removed by 5 % trifluoroacetic acid (TFA) in dichloromethane (v/v, tenfold excess of the acid) within 15-30 minutes corresponding to the following scheme (1) :



1 : Cleavage by trifluoroacetic acid of the Ddz-amino protecting group (R = peptide)

On neutralisation by N-methylmorpholine, evaporation of the solution i.vac. and treatment with methanol, a dimer of 3,5-dimethoxy-α-methylstyrene crystallizes rapidly. The structure of this product was determined as 1,3,3-trimethyl-1-(3,5-dimethoxy)-phenyl-5,7-dimethoxyindan (TDInd) by ^{1}H-NMR-spectrum, mass spectrum and elemental analysis.

^{1}H-NMR spectral data :

ppm 1.03 (s, 3H, $C\underline{H}_3$), 1.30 (s, 3H, $C\underline{H}_3$), 1.75 (s, 3H, $C\underline{H}_3$), 2.16 (d, 1H, AB-system, J_{AB} = 13 Hz, $C\underline{H}_2$, H_A), 2.33 (d, 1H, AB-system, J_{AB} = 13 Hz, $C\underline{H}_2$, H_B), 3.69 (s, 3H, C_6H_2-$OC\underline{H}_3$), 3.72 (s, 6H, C_6H_3-$OC\underline{H}_3$), 3.83 (s, 3H, C_6H_2-$OC\underline{H}_3$), 6.21 - 6.49 (m, 5H, $C_6\underline{H}_2$ and $C_6\underline{H}_3$) .

Mass spectral data :

m/e : I % 356 : 50 (molpeak), 341 : 100, 326 : 1, 311 : 1.5, 219 : 23, 205 : 5, 203 : 10, 189 : 3, 178^{++}: 7, 170.5^{++}: 2, 163^{++}: 6 .

Elemental analysis :

Fig.1 shows the 60 MHz-^{1}H-NMR-spectrum of the product, which is corresponding to the recently reported ^{1}H-NMR-spectrum of 1,3,3-trimethyl-1-phenylindan [7] in the non aromatic part.

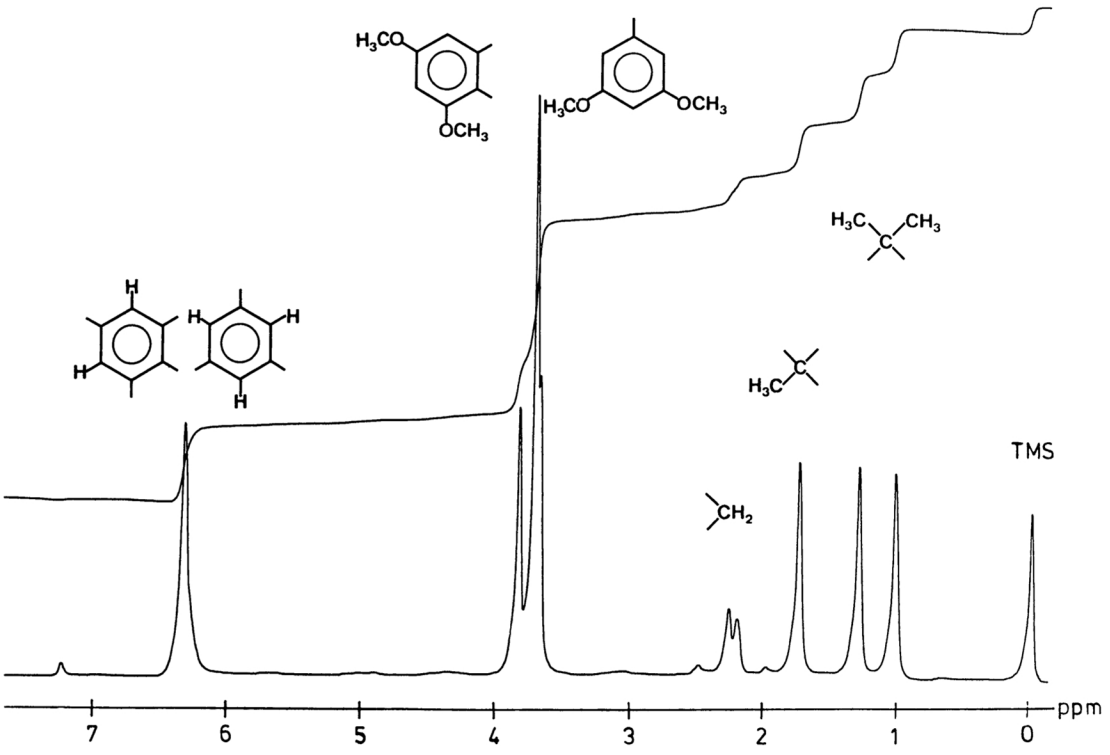
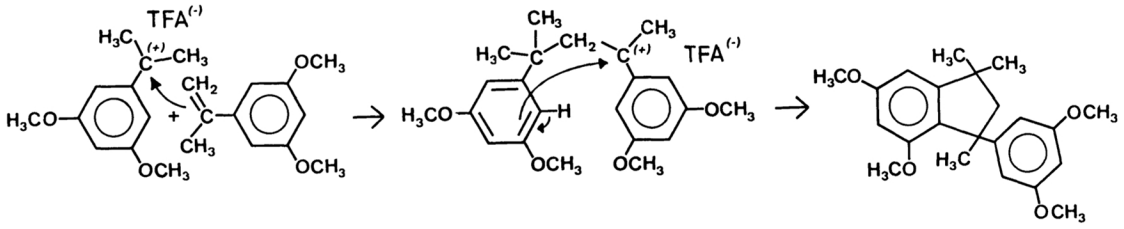


Fig.1 : 6o MHz-^{1}H-NMR-spectrum of 1,3,3-trimethyl-1-(3,5-dimethoxy)-phenyl-5,7-dimethoxyindan ($CDCl_3$, TMS)

The yields of of the cyclic dimer from cleavage of the Ddz-group in peptides like Ddz-Ile-Gly-OEt and Ddz-Gly-Ile-Gly-OEt by 5 % - solution of TFA varied from 40 to 60 %, based upon crystallized products and those obtained from gel chromatography on Sephadex LH 20/ methanol after peptide synthesis. 3,5-Dimethoxy-α-methylstyrene was isolated in yields up to 50 % together with the cyclic dimer TDInd corresponding to 90 % of the starting material, Ddz-peptide. Oligomers, polymers and dimers with other structure than TDInd could not be detected. The formation of trace amounts however cannot be excluded. Most probably therefore, the former published tetramembered cyclic structure has to be revised [8]. The facility of the cyclic dimer formation is favoured by the positive inductive and mesomeric effects of

the methoxy groups. The reaction scheme for the formation of TDInd can be written as follows (2) :



2 : Formation of 1,3,3-trimethyl-1-(3,5-dimethoxy)-phenyl-5,7-dimethoxyindan

The intermediate linear dimeric carbenium ion can attack the adjacent aromatic system in an electrophilic aromatic substitution favoured by the ortho- and para-positioned methoxy groups. The asymmetric configuration of the carbon in position 3 of the indan system was not determined.

References

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