

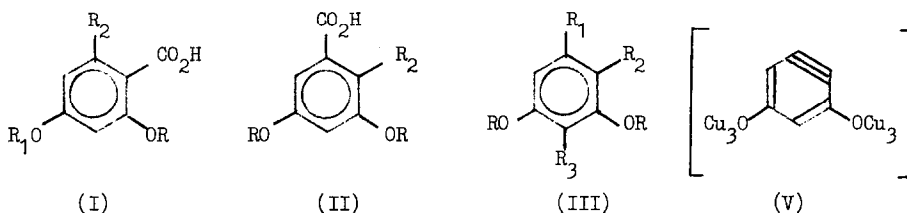
A NOVEL SYNTHESIS OF HOMOLOGOUS ORSELLINIC ACIDS AND 5-ALKYLRESORCINOLS

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We report a novel synthesis of homologous orsellinic acids (I; $R = R_1 = H$, $R_2 = C_nH_{2n+1}$), the monomethyl ethers (I; $R = H$, $R_1 = CH_3$, $R_2 = C_nH_{2n+1}$), the dimethyl ethers (I; $R = R_1 = CH_3$, $R_2 = C_nH_{2n+1}$) or the parent 5-alkylresorcinols and their dimethylethers, by the use of aromatic rather than acyclic intermediates¹ and precursors,² modelled on the biosynthetic pathway, which can lead to a number of products.



Addition of 2,4-dimethoxyfluorobenzene or 3,5-dimethoxyfluorobenzene to an excess of ethereal alkyllithium followed by carbonation of the reaction mixture by discharge onto solid carbon dioxide³ gave either the dimethylorsellinic acid or 2,6-dimethoxy-3-fluorobenzoic acid as summarised in Table I (the reaction proceeded best with $R > CH_3$)

Table I

<u>Fluoro Compound</u>	<u>Alkyllithium</u>	<u>Product (I)</u>	<u>Parent Natural Substance</u>
3,5-dimethoxyfluorobenzene	$n-CH_3Li$	$R=R_1=R_2=CH_3$	orsellinic acid
"	$n-C_3H_7Li$	$R=R_1=CH_3$, $R_2=n-C_3H_7$	divaric acid ⁴
"	$n-C_5H_{11}Li$	$R=R_1=CH_3$, $R_2=n-C_5H_{11}$	olivitol carboxylic acid ⁵
"	$n-C_7H_{15}Li$	$R=R_1=CH_3$, $R_2=n-C_7H_{15}$	spherolpherol carboxylic acid ⁶
"	$n-C_{15}H_{31}Li$	$R=R_1=CH_3$, $R_2=n-C_{15}H_{31}$	- ⁷
2,4-dimethoxyfluorobenzene	C_2H_5Li	$R=CH_3$, $R_1=H$, $R_2=F$, $R_3=CH_2H$	-
		2,6-dimethoxy-3-fluorobenzoic acid	

Traces of the isomeric acids II ($R = CH_3$, $R_2 = C_nH_{2n+1}$, $n = 1, 3, 5, 7, 15$), having a

characteristic low R_f value in preparative TLC, were present. The dimethylorsellinic acids had the required elementary analyses and possessed the predicted ^1H NMR spectra with τ values (C_6D_6) at τ -0.43 (1H, CO_2H), 3.83, 3.67 (2H, HAr, 2 doublets, J 2.5 cps, meta), 6.8, 6.67 (6H, OCH_3 , S), 7.13 (2H, CH_2Ar , t), 8.73 ($(\text{CH}_2)_n$, S), 9.13 (CH_3 , t). 2,6-Dimethoxy-3-fluorobenzoic acid showed the expected splitting of the proton signal of the OCH_3 group by the fluorine atom and the presence of two ortho aromatic protons.

The vicinal elimination of LiF , aryne formation (V) and alkyllithium addition by way of III ($R = \text{Me}$, $R_3 = \text{H}$, $R_2 = \text{Li}$, $R_1 = \text{F}$) can only occur with 3,5-dimethoxyfluorobenzene due to the substitution of lithium predominantly at o or o/p positions to the methoxy groups indicating the participation of only the more stable⁸ orthoaryne.

Decomposition of alkyllithiated mixtures from 3,5-dimethoxyfluorobenzene with water produced the corresponding 5-alkylresorcinol dimethyl ether identical with that obtained by copper-catalysed/quinoline decarboxylation of the dimethylorsellinic acid.

Smooth demethylation of the latter with boron trichloride⁹ gave the monomethyl compounds (I; $R = \text{H}$, $R_1 = \text{CH}_3$, $R_2 = \text{C}_n\text{H}_{2n+1}$, $n = 1, 3, 5, 7, 15$). Boron tribromide¹⁰ at a low temperature gave the orsellinic acids having the expected ^1H NMR spectra (C_6D_6) with τ values at -2.52 (broad S, 2H, $\text{OH}\dots\text{CO}_2\text{H}$) and 0-5 (concentration and solvent-dependent, broad S, 1H, HOAr).

References

- 1 A. Sonn and J. Burkhard, Chem. Ber., 1928, 61B, 2479.
- 2 T.M. Harris and R.L. Carney, J. Amer. Chem. Soc., 1967, 89, 6734.
- 3 A.A. Durrani and J.H.P. Tyman, Chem. and Ind., 1972, 762.
- 4 T. Asahina and H. Akagi, Chem. Ber., 1935, 68B, 1130.
- 5 T. Asahina and M. Yasue, Chem. Ber., 1937, 70B, 206.
- 6 A. Hasimoto, J. Pharm. Soc. Japan, 1938, 58, 776.
- 7 This substance has not yet been detected in natural sources, J.H.P. Tyman, J. Chem. Soc., Perkin I, 1973, 1639.
- 8 D.L. Wilhite and J.L. Whitten, J. Amer. Chem. Soc., 1971, 93, 2858.
- 9 F.M. Dean, J. Goodchild, L.E. Houghton, J.A. Martin, R.B. Morton, B. Parton, A.W. Price and N. Somvichien, Tetrahedron Letters, 1966, 4153.
- 10 J.F.W. McOmie, M.L. Watts and D.E. West, Tetrahedron, 1968, 24, 2289.