AROMATIC ETHERS WITH THE INSECT JUVENILE HORMONE ACTIVITY*

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A simple preparation of phenoxyalkyloxolanes *VIII*—*XIV* by alkylation of *p*-substituted phenols *I*—*IV* with bromoalkyloxolanes *V*—*VII* has been described.

In the literature, numerous morphogenetically active mixed ethers have been reported, containing phenyl and epoxidated terpenoid groupings[1,2]. In view of the juvenile activity of those juvenile hormone analogues in which the oxirane ring of the parent hormone is replaced by the more stable oxolane ring[3,4], attention has been now paid to the preparation** of some alkyl aryl ethers containing an oxolane ring in the aliphatic portion of the molecule instead of the oxirane ring. Some of these ethers have been so far reported in a Czechoslovak Patent Application only[5].

The present bioanalogues have been prepared by alkylation of 4-chlorophenol (*I*), 4-methylphenol (*II*), 4-ethylphenol (*III*) or 4-methoxycarbonylphenol (*IV*) with 1-bromo-3-methyl-5-(2-oxolanyl)pentane[3] (*V*), 1-bromo-3-methyl-5-(2-oxolanyl)-2--pentene[3] (*VI*) or 2-bromo-4-(2-oxolanyl)butane[4] (*VII*).

EXPERIMENTAL

Column chromatography was performed on the Pitra[6] silica gel (produced by Service Laboratories of this Institute; particle size, 60—120 micron) purified by extraction with 1 : 1 chloroform–methanol, activated at 120°C for 24 h, and partially deactivated by the addition of 12% water, or on neutral alumina (Brockmann activity II; Reanal, Hungary). Thin-layer chromatography was carried out on silica gel G (Merck, German Federal Republic). The homogeneity of substances was checked by gas chromatography on a Pye Argon Chromatograph with ionisation detection (^{90}Sr) and a column packed with 10% LAC-6R-860 on Chromosorb W, or, on a Perkin Elmer F 11 apparatus and a column packed with 3% QF 1 on Diatomite CQ or with 3% SE 30 on silanised Chromosorb G. IR spectra were taken in tetrachloromethane on UR 10 and UR 20 spectrophotometers (Carl Zeiss, Jena, German Democratic Republic).

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** The biological activity of the present substances will be reported elsewhere.

1-Chloro-4-[3-methyl-5-(2-oxolanyl)pentyloxy]benzene (*VIII*)

To a stirred suspension of 70% sodium hydride (0·34 g; 10 mmol) in dry 1,2-dimethoxyethane (10 ml) there was added dropwise under argon over 15 min a solution of 4-chlorophenol (*III*; 0·95 g; 7·40 mmol) in 1,2-dimethoxyethane (6 ml) and the stirring continued for 1 h at room temperature. 1-Bromo-3-methyl-5-(2-oxolanyl)pentane[3] (*V*; 1·74 g; 7·40 mmol) in 1,2-dimethoxyethane (4 ml) was the added dropwise over 5 min and the mixture stirred at room temperature for 30 min, at 65—70°C for 12 h, and at 100°C for 12·5 h. The cold mixture was then treated under cooling with ethanol to decompose excess sodium hydride, poured into water, and extracted with ether. The extract was washed with 5% ice-cold aqueous sodium hydroxide (twice) and water till neutral, dried over anhydrous magnesium sulfate, and evaporated under diminished pressure. The residue (1·83 g) was chromatographed on a column of silica gel (190 g) in 98 : 2 light petroleum–ethyl acetate. The appropriate fractions (as determined by thin-layer chromatography on silica gel G in 9 : 1 light petroleum–ethyl acetate) were pooled and distilled to afford 0·74 g (37%) of compound *VIII* boiling at the bath temperature of 150—157°C/0·006 Torr along with 0·87 g of a less pure product. For $C_6H_{23}ClO_2$ (282·8) calculated: 67·95% C, 8·20% H, 12·54% Cl; found: 68·23% C, 8·34% H, 12·20% Cl. IR spectrum (cm^{-1}): 1598, 1580, 1494, 1245, 1065, 1040, and 828.

TABLE I

Preparation and Properties of Phenoxyalkyloxolanes *IX*—*XIV*

Compound	Formula (m.w.)	Phenol *a* mmol	K_2CO_3 *b* mmol	Bromide *c* mmol
IX	$C_{16}H_{21}ClO_2$ (280·8)	*III*	24	*I* 20
X	$C_{17}H_{24}O_2$ (260·4)	*IV*	12	*I* 10
XI	$C_{18}H_{24}O_4$ (304·4)	*V*	20	*I* 20
XII	$C_{14}H_{19}ClO_2$ (254·8)	*III*	30	*II* 20
XIII	$C_{26}H_{24}O_2$ (248·4)	*VI*	30	*II* 20
XIV	$C_{16}H_{22}O_4$ (278·3)	*V*	30	*II* 20

[a] The boiling point data refer to bath temperature and the pressure of 0·005 Torr; [b] IR spectrum (cm^{-1}): 1669, 1595, 1578, 1492, 1237, 1025, and 827; [c] performed in 10 ml of acetone; the two fractions exhibited a different ratio of isomers; IR spectrum (cm^{-1}): 1612, 1583, 1511, 1239, 1070, 1025, and 823; [d] the product was not distilled; [e] IR spectrum (cm^{-1}): 1720, 1672, 1607,

Preparation of Oxolanes *IX*—*XIV* (general procedure)

To a solution of the phenols *III*—*VI* (*a* mmol) in dry acetone (15 ml) there was added anhydrous potassium carbonate (*b* mmol) and a solution of the bromide *VI* or *VII* (*c* mmol) in dry acetone (5 ml). The reaction mixture was stirred for *t* hours at room temperature and then for *T* hours at the reflux temperature. The reaction course was checked by thin-layer chromatography on silica gel G. As soon as the starting bromide disappeared or when the composition of the reaction mixture remained constant, the mixture was cooled down and the salts filtered off and washed with ether. The filtrate and washings were combined and evaporated under diminished pressure. The above salts were dissolved in water and the aqueous solution extracted with ether. This extract was combined with the residue previously dissolved in ether. The ethereal solutions were washed with 4% ice-cold aqueous sodium hydroxide and water till neutral, dried over anhydrous magnesium sulfate, and evaporated under diminished pressure. The residue was purified by chromatography on a column of silica gel (or alumina, in the case of the oxolane *XIII*). Fractions identical according to thin-layer chromatography on silica gel G were pooled and distilled under diminished pressure to afford the following compounds (for preparative details, properties, and analyses see Table I): 1-chloro-4-[3-methyl-5-(oxolanyl)-2-pentenyloxy]-benzene (*IX*), 1-methyl-4-[3-methyl-5-(2-oxolanyl)-2-pentenyloxy]benzene (*X*), methyl 4-[3-me-

(*Continued*)

t, h	*T*, h	Calculated/Found			B.p., °C[a]	Yield, %
		% C	% H	% Cl		
2·5	12	68·44	7·54	12·63	142—152[b]	62·3
		68·75	7·59	12·59		
2	8	78·42	9·29	—	135—142[c]	18·0
		78·57	9·26	—	146—152[c]	55·3
1	8	71·02	7·95	—	—	71·3[d,e]
		71·00	7·91	—		
1·5	13	66·00	7·52	13·92	148—160[f]	37·3
		65·78	7·47	14·23		
0·5	33	77·37	9·74	—	114—129[g]	51·9
		77·75	9·75	—		
0·5	26	69·04	7·97	—	—	46·3[d,h]
		69·17	7·81	—		

1 580, 1 510, 1 280, 1 248; [f] along with 47·6% of a substance of a lower purity; IR spectrum (cm^{-1}): 1 598, 1 581, 1 493, 1 244, 1 193, 1 055, 1 030, 824; [g] IR spectrum (cm^{-1}): 1 612, 1 583, 1 513, 1 250, 1 240, 1 060, 1 035, 828; [h] IR spectrum (cm^{-1}): 1 723, 1 607, 1 581, 1 511, 1 280, 1 253, 1 056, 1 027, 848.

thyl-5-(2-oxolanyl)-2-pentenyloxy]benzoate (*XI*), 1-chloro-4-[1-methyl-3-(2-oxolanyl)propoxy]-benzene (*XII*), 1-ethyl-4-[1-methyl-3-(2-oxolanyl)propoxy]benzene (*XIII*), and methyl 4-[1-methyl-3-(2-oxolanyl)propoxy]benzoate (*XIV*).

Elemental analyses were performed in the Analytical Department (Dr J. Horáček, Head) of this Institute by Mrs V. Rusová, Mrs E. Šípová, and Mr V. Štěrba. The IR spectra were measured by Mr P. Formánek and interpreted by Dr J. Smolíková. The technical assistance was provided by Mrs V. Kalvodová.

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