

NATURAL AND SYNTHETIC MATERIALS WITH INSECT
HORMONE ACTIVITY. XVI.*

THE SYNTHESIS OF DERIVATIVES OF OXYGEN
HETEROCYCLES CONTAINING N-GERANYLANILINE MOIETY

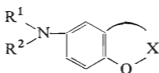
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In connection with the study of compounds with a potential juvenile hormone activity a series of compounds was prepared, derived by fusion of a five- or six-membered heterocyclic ring, containing one or two oxygen atoms, to N-geranylaniline.

The high biological activity of O-geranyl-3,4-methylenedioxyphenol prompted us to prepare now a series of five and six-membered oxygen heterocycles containing N-geranyl or N,N-digeranylaniline in the molecule (Table I, I–XI). Some of them had a remarkable activity, especially toward *Triatoma infestans*, the carrier of the pandemic Chagas illness.



For the attachment of a geranyl group onto a nitrogen atom the standard procedure was made use of which we described earlier¹. The obtained substances were then submitted to hydrogenation in order to affect their biological property. In some cases their unsaturated carbon atom chain was oxidized with monophtalic acid².

EXPERIMENTAL

All prepared substances were purified by column chromatography on silica gel containing 8 weight % of water. The final products were oils.

4-(3,7-Dimethyl-2,6-octadienylamino)-1,2-methylenedioxybenzene (I) and 4-[Bis(3,7-dimethyl-2,6-octadienylamino)-1,2-methylenedioxybenzene (II) (Method A)

A mixture of 2.7 g (0.02 mol) 4-amino-1,2-methylenedioxybenzene³, 2.8 g (0.02 mol) anhydrous potassium carbonate, and 4.3 g (0.02 mol) geranyl bromide⁴ in 10 ml of dimethylformamide was

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heated at 70°C for 8 h under stirring. After cooling it was diluted with water and extracted with ether. The ethereal layer was washed with water and dried. After removing the solvent under reduced pressure the residue was chromatographed on silica gel (10% of ether in light petroleum, v/v). Yield 2.1 g (38.4%) of compound *I* and 2.5 g (30%) of compound *II*. In the same manner

TABLE I

Derivatives of Oxygen Heterocycles Containing an N-Geranyl- and N,N-Digeranylaniline Residue

Compound (method) ^a	X	R ¹ (R ²)	Conditions °C/h (yield, %)	Formula (m.w.)	Calculated/Found		
					% C	% H	% N
<i>I</i> (A)	—O—CH ₂	G (H)	70/8 ^b (38.4)	C ₁₇ H ₂₃ NO ₂ (273.3)	74.69 74.57	8.48 8.48	5.12 5.19
<i>II</i> (A)	—O—CH ₂ —	G (G)	70/8 ^b (30.0)	C ₂₇ H ₃₉ NO ₂ (409.6)	79.17 78.91	9.60 9.69	3.42 3.05
<i>III</i> (B)	—O—CH ₂ —	GO (H)	— ^{a,c} (53.0)	C ₁₇ H ₂₃ NO ₃ (289.3)	70.56 70.58	8.01 7.99	4.84 5.10
<i>IV</i> (C)	—O—CH ₂ —	GH (H)	— ^a (44.2)	C ₁₇ H ₂₇ NO ₂ (277.4)	73.60 73.94	9.81 9.70	5.04 4.60
<i>V</i> (A)	—CH ₂ —CH ₂ —	G (G)	20/21 ^d (39.2)	C ₂₈ H ₄₁ NO (407.6)	82.49 82.22	10.13 9.93	3.43 3.17
<i>VI</i> (A)	—CH=C—COOCH ₃ 	G (H)	20/0.5 ^d (44.5)	C ₂₀ H ₂₅ NO ₃ (327.4)	73.36 73.58	7.98 8.19	4.28 4.52
<i>VII</i> (A)	—CH=C—COOCH ₃ 	G (G)	20/0.5 ^d (29.3)	C ₃₀ H ₄₁ NO ₃ (463.6)	77.71 77.85	8.91 8.80	3.02 3.27
<i>VIII</i> (A)	—CH ₂ —O—CH ₂	G (H)	70/8 ^d (37.7)	C ₁₈ H ₂₅ NO ₂ (287.3)	75.22 75.21	8.77 8.82	4.87 4.71
<i>IX</i> (A)	—CH ₂ —O—CH ₂ —	G (G)	70/8 ^d (32.8)	C ₂₈ H ₄₁ NO ₂ (423.6)	79.38 79.58	9.76 9.63	3.31 3.02
<i>X</i> (A)	—O—CH ₂ —CH ₂ —	G (H)	70/8 ^d (32.2)	C ₁₈ H ₂₅ NO ₂ (287.3)	75.22 75.61	8.77 8.89	4.87 5.08
<i>XI</i> (A)	—O—CH ₂ —CH ₂	G (G)	70/8 ^d (34.6)	C ₂₈ H ₄₁ NO ₂ (423.6)	79.38 79.07	9.76 9.72	3.31 3.13

G CH₂—CH=C(CH₃)—CH₂—CH₂—CH=C(CH₃)₂; GO CH₂—CH=C(CH₃)—CH₂—
—CH₂—CH—C(CH₃)₂; GH CH₂—CH₂—CH(CH₃)—CH₂—CH₂—CH₂—CH(CH₃)₂

^a See Experimental; ^b chromatographed on silica gel, 10% ether in light petroleum; ^c chromatographed on silica gel, 50% ether in light petroleum; ^d chromatographed on silica gel, 20% ether in light petroleum.

substance *V* was prepared from 5-amino-2,3-dihydrobenzofuran⁵, substances *VI* and *VII* from 5-aminobenzofuran-2-carboxylic acid⁵, substances *VIII* and *IX* from 5-aminobenzo-1,3-dioxan⁶, and compounds *X* and *XI* from 5-aminobenzo-1,4-dioxan⁷.

4-(6,7-Epoxy-3,7-dimethyl-2-octenylamino)-1,2-methylenedioxybenzene (*III*) (Method *B*)

A mixture of 0.6 g (0.0022 mol) of compound *I* and 2.2 g (0.011 mol) of trifluoroacetic anhydride in ether was allowed to stand for one hour at room temperature. After partitioning of the reaction mixture between ether and a saturated solution of NaHCO₃ the ethereal layer was washed, dried, and evaporated under reduced pressure. The residue was mixed with 15 ml of monoperphthalic acid in ether (27 mg/ml) and after 7 h standing at room temperature the separated phthalic acid was filtered off and the reaction mixture partitioned between ether and a 10% NaHCO₃ solution. The ethereal layer was washed with water, dried, and evaporated under reduced pressure. The residue, dissolved in a minimum amount of ethanol, was added with 2 ml of 10% NaOH solution and allowed to stand at room temperature for 2 days. Then the pH of the mixture was adjusted to 6–7, ethanol was evaporated, the mixture was partitioned between ether and water, and the ethereal layer dried and evaporated. The residue was chromatographed on silica gel with a 50% ether in light petroleum mixture. Yield 0.34 g (53%) of substance *III*.

4-(3,7-Dimethyloctylamino)-1,2-methylenedioxybenzene (*IV*) (Method *C*)

Substance *I* (0.27 g) in ethyl acetate was hydrogenated in the presence of 50 mg of PtO₂ at room temperature and normal pressure. The catalyst was filtered off and the solvent evaporated. The residue was extracted with dry ether, the solution washed with water and dried over MgSO₄. Vacuum distillation of the residue gave 0.12 g (44%) of compound *IV* boiling at 180°C/0.5 Torr (bath temperature).

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