

NATURAL AND SYNTHETIC MATERIALS
WITH THE INSECT HORMONE ACTIVITY. XV.*

THE SYNTHESIS OF GERANYLATED AROMATIC SULFUR
CONTAINING COMPOUND

J.KAHOVCOVÁ, Z.ARNOLD and F.ŠORM

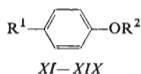
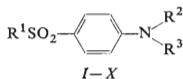
*Institute of Organic Chemistry and Biochemistry,
Czechoslovak Academy of Sciences, Prague 6*

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A series of sulfur containing derivatives of N-geranylaniline and O-geranylphenol were prepared.

In a preceding communication¹ of this series we described the preparation of substituted phenyl geranyl ethers and related substances. This study was now extended to sulfur containing compounds.

The derivatives which we describe in this paper are derived from two basic types, *i.e.* N-geranylaniline (*I-X*) and O-geranylphenol (*XI-XIX*, Table I). The sulfur-containing groups are the sulfo group, methylmercapto group, and some other related groups. In the case of anilines digeranylated derivatives were also obtained in some instances.



The introduction of the geranyl residue into the above mentioned compounds was carried out generally by a standard procedure². In order to attain a higher biological activity the obtained substances were submitted to some additional reactions, for example the addition of gaseous hydrogen chloride³, reaction with perphthalic acid⁴ and addition of ethanol^{1,5}.

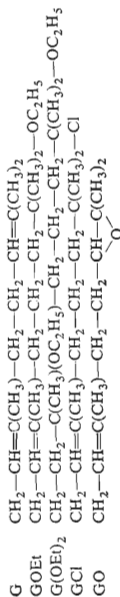
* Part XIV: This Journal 38, 261 (1973).

TABLE I
Derivatives of N-Geranyl-aniline (I-X) and O-Geranyl-phenol (XI-XIX)

Compound (method ^a)	R ¹	R ² (R ³)	Conditions °C/h (yield, %)	Formula (M. w.)	Calculated/Found			
					% C	% H	% N	
I (A)	(C ₂ H ₅) ₂ N	H (G)	70/8 ^b (55.0)	C ₂₀ H ₃₂ N ₂ O ₂ S (364.5)	65.91 66.05	8.85 8.84	7.69 7.83	—
II (C)	(C ₂ H ₅) ₂ N	H (GOEt)	20/1.5 ^c (49.0)	C ₂₂ H ₃₈ N ₂ O ₃ S (410.6)	64.36 64.11	9.33 9.59	—	7.78 7.29
III (D)	(C ₂ H ₅) ₂ N	H (GCl)	a, d (59.2)	C ₂₀ H ₃₃ ClN ₂ O ₂ S (401.0)	59.90 59.84	8.22 8.29	6.99 7.04	—
IV (A)	(C ₂ H ₅) ₂ N	G (G)	70/8 ^b (26.6)	C ₃₀ H ₄₈ N ₂ O ₂ S (500.7)	71.96 72.26	9.66 9.91	5.59 5.74	—
V (A)	F	H (G)	20/20 ^e (61.6)	C ₁₆ H ₂₂ FNO ₂ S ^f (311.4)	61.76 61.38	7.04 7.03	4.49 4.25	10.28 10.06
VI (D)	F	H (GCl)	a, d (54.0)	C ₁₆ H ₂₃ ClFNO ₂ S (347.8)	55.23 55.54	6.66 6.81	4.02 4.06	—
VII (A)	CH ₃	H (G)	20/3 ^d (39.0)	C ₁₇ H ₂₅ NO ₂ S (307.4)	66.41 66.35	8.19 7.95	4.55 4.94	10.42 10.39
VIII (A)	CH ₃	G (G)	20/3 ^d (45.1)	C ₂₇ H ₄₁ NO ₂ S (443.6)	73.10 72.76	9.32 9.60	3.16 3.01	7.21 7.26
IX (D)	CH ₃	GCl (GCl)	a, d (44.0)	C ₂₇ H ₄₃ Cl ₂ NO ₂ S (516.6)	62.78 62.93	8.39 8.70	—	—
X ^a	CH ₃ O	H (G)	20/0.5 ^g (67.0)	C ₁₇ H ₂₅ NO ₃ S (323.4)	63.14 63.48	7.79 7.76	4.33 3.60	9.89 9.68
XI (B)	CH ₃ S	G	20/0.5 ^h (90.5)	C ₁₇ H ₂₄ OS (276.4)	73.86 73.94	8.75 8.84	—	11.59 11.46

XII (C)	CH ₃ S	GOEt	20/1.5 ⁱ (41.8)	C ₁₉ H ₃₀ O ₂ S (322.5)	70.75 70.97	9.37 9.32	—	9.94 9.80
XIII (C)	CH ₃ S	G(OEt) ₂	20/1.5 ⁱ (13.6)	C ₂₁ H ₃₆ O ₃ S (368.5)	68.43 68.43	9.84 9.80	—	8.64 8.52
XIV (D)	CH ₃ S	GCl	^{a,d} (53.0)	C ₁₇ H ₂₅ ClOS (312.9)	65.25 65.50	8.05 7.86	—	—
XV (B)	CH ₃ SO	G	20/3 ^j (62.0)	C ₁₇ H ₂₄ O ₂ S (292.4)	69.85 69.50	8.27 8.18	—	10.94 11.41
XVI (B)	CH ₃ SO ₂	G	20/2 ^d (64.0)	C ₁₇ H ₂₄ O ₃ S (308.4)	66.20 66.52	7.84 7.82	—	10.39 10.00
XVII (B)	(C ₂ H ₅) ₂ NSO ₂	G	30/3 ^b (82.5)	C ₂₀ H ₃₁ NO ₃ S (365.5)	65.73 65.53	8.55 8.56	3.83 3.86	8.75 8.72
XVIII (E)	(C ₂ H ₅) ₂ NSO ₂	GO	20/24 ^g (80.0)	C ₂₀ H ₃₁ NO ₄ S (381.5)	62.97 63.33	8.19 8.39	3.67 3.27	—
XIX (C)	(C ₂ H ₅) ₂ NSO ₂	GOEt	20/1.5 ^k (70.2)	C ₂₂ H ₃₇ NO ₄ S (411.6)	64.21 64.34	9.06 9.15	—	7.77 7.41

^aSee Experimental; ^bchromatographed on silica gel, 30% ether in light petroleum; ^cchromatographed on silica gel, 5% ether in benzene; ^dchromatographed on silica gel, 75% ether in light petroleum; ^echromatographed on silica gel, 20% ether in light petroleum; ^f% F calculated 6.16% found 6.16%; ^gchromatographed on silica gel, 50% ether in light petroleum; ^hchromatographed on silica gel, 5% ether in light petroleum; ⁱchromatographed on silica gel, benzene-ether (50:1); ^jchromatographed on silica gel, 10% ether in light petroleum; ^kchromatographed on silica gel, 5% acetone in benzene.



EXPERIMENTAL

The compounds prepared were purified by column chromatography on silica gel containing 8% weight of water. With the exception of compound *XI* all other were obtained as oils.

N,N-Diethyl-4-(3,7-dimethylocta-2,6-dienylamino)benzenesulfonamide (*I*) and N,N-diethyl-4-[bis-(3,7-dimethylocta-2,6-dienyl)amino]benzenesulfonamide (*IV*) (Method *A*)

A mixture of 0,65 g (0.003 mol) of N,N-diethyl-4-aminobenzenesulfonamide⁶, 0.4 g (0.003 mol) of anhydrous potassium carbonate, and 0.98 g (0.0045 mol) of geranyl bromide⁷ in 5 ml of dimethylformamide was heated at 70–80°C under stirring for 8 h. After cooling, dilution with water and extraction with ether the organic extract was washed with water and dried. After evaporation of the solvent under reduced pressure the residue was chromatographed on silica gel (30% of ether in light petroleum). Yield 0.6 g (55%) of compound *I* and 0.4 g (26.6%) of compound *IV*. In a similar manner compound *V* was prepared from *p*-aminobenzenesulfonyl fluoride⁸ and compound *VII* and *VIII* from 4-(methylsulfonyl)aniline⁹.

4-(3,7-Dimethylocta-2,6-dienyloxy)-1-(methylthio)benzene (*XI*) (Method *B*)

A mixture of 1.4 g (0.01 mol) of 4-(methylthio)phenol (m.p. 81–82°C), 0.4 g (0.01 mol) of NaOH, and 3.3 g (0.015 mol) of geranyl bromide in 10 ml of dimethylformamide was stirred at room temperature for 30 min and then partitioned between water and ether. After the washing of the ethereal layer with a 10% NaOH and water, it was dried and evaporated under reduced pressure. The residue was separated on a silica gel column from which it was eluted with 5% ether in light petroleum. Chromatographically homogeneous fractions gave 2.5 g (90.5%) of compound *XI*, m.p. about 25°C. From 4-(methylsulphonyl)phenol¹⁰, 4-(methylsulphonyl)phenol¹⁰, and N,N-diethyl-4-hydroxybenzenesulfonamide¹¹ substances *XV*–*XVII* were prepared in a similar manner.

N,N-Diethyl-4-(7-ethoxy-3,7-dimethyloct-2-enylamino)benzenesulfonamide (*II*) (Method *C*)

A mixture of 0.36 g (0.001 mol) of compound *I*, 0.32 g (0.001 mol) of mercuric acetate, and 4 ml of ethanol was stirred at 20–25°C for 90 minutes. After the addition of 1 ml of 3*M*-NaOH and a solution of 0.02 g (0.00054 mol) of sodium borohydride in 1 ml of 3*M*-NaOH the mixture was stirred for 2 h, diluted with water and extracted with light petroleum. The extract was washed with water, dried over magnesium sulfate, evaporated under reduced pressure, and the residue chromatographed on silica gel with 5% ether in benzene. Chromatographically pure fractions gave 0.2 g (49%) of compound *II*. In the same manner substances *XII*, *XIII* and *XIX* were also obtained.

N,N-Diethyl-4-(7-chloro-3,7-dimethyloct-2-enylamino)benzenesulfonamide (*III*) (Method *D*)

A solution of 0.2 g of compound *I* in a minimum amount of ether was saturated under cooling with hydrogen chloride gas and then allowed to stand at room temperature for one hour. The reaction mixture was partitioned between ether and water, the ethereal layer was washed with 10% NaHCO₃ and water, dried, and evaporated under reduced pressure. The residue was chromatographed on a silica gel column (75% ether in light petroleum). Yield 0.13 g (59.2%) of compound *III*. Substances *VI*, *IX*, and *XIV* were obtained in a similar manner.

N,N-Diethyl-4-(6,7-epoxy-3,7-dimethyloct-2-enyloxy)benzenesulfonamide (XVIII) (Method E)

A mixture of 1.1 g (0.003 mol) of compound XVII and 4.7 ml (0.0033 mol) of mono-perphthalic acid in ether (127 mg/ml) was allowed to stand at room temperature for 24 h. After separation of the precipitated phthalic acid by filtration and the partitioning of the reaction mixture between ether and 10% NaHCO₃ the ethereal layer was washed with water, dried, and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (50% ether in light petroleum), yielding 0.92 g (80%) of compound XVIII.

Methyl 4-(3,7-dimethylocta-2,6-dienylamino)benzenesulfonate (X)

Substance V (1 g; 0.003 mol) was mixed with 7.5 ml (0.003 mol) of a solution of 0.5 g of sodium in 50 ml of methanol and stirred for 30 min. The reaction mixture was partitioned between ether and 10% NaHCO₃. The ethereal layer was washed with water, dried, and evaporated under reduced pressure. The residue was separated by column chromatography with 50% ether in light petroleum. The yield of compound X was 0.65 g (67%).

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