

Method A. 19-Nortestosterone 17 β -Geranate (1). A soln of geranoyl chloride (3.08 g, 0.0165 mole) in CHCl_3 (30 ml) was dropped at room temp for 10 min into a stirred soln of 19-nortestosterone (4.11 g, 0.015 mole) and dry pyridine (1.5 g, 0.019 mole) in CHCl_3 (70 ml). The mixt was stirred overnight, dild with CHCl_3 (200 ml), and washed (2% HCl , H_2O) until neutral. After drying (MgSO_4), the solvent was evapd, and the residue was chromatographed on neutral, activity grade I alumina. Elution with C_6H_6 and $\text{C}_6\text{H}_6\text{-Me}_2\text{CO}$ gave 2.42 g of pure 1.

Method B. 19-Nortestosterone 17 β -trans,trans- and cis,trans-Homofarnesate (7). Trans,trans- and cis,trans-homofarnesic acid² (2.7 g, 0.01 mole) and 19-nortestosterone (1 g, 0.0036 mole) were heated under N_2 for 3 hr at 200°. After cooling, the reaction mixt was taken up in Et_2O (100 ml) and washed repeatedly with 5% Na_2CO_3 . The organic layer was washed (H_2O) until neutral and dried (MgSO_4), and the solvent was evapd. The residue was chromatographed as described in method A to give 1.57 g of pure 7.

Method C. 19-Nortestosterone 17 β -trans,trans- and cis-trans-Farnesylacetate (9). Farnesylacetic anhydride¹ (3.06 g, 0.006 mole) was added dropwise at room temp for 10 min to a soln of 19-nortestosterone (0.8 g, 0.003 mole) in dry pyridine (3 ml). The

mixt was stirred overnight, dild with Et_2O (30 ml), and washed (1% NaOH , 2% HCl , H_2O) until neutral. Evapn of the solvent and chromatog as described in method A furnished 1.2 g of pure 9.

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New Compounds

Terpene Compounds as Drugs. 14. Terpenyl Carbamates as Central Nervous System Depressants

Giovanna Minoli,* Ernesta Marazzi-Uberti, and Silvano Casadio

Research Laboratories of Istituto De Angeli, 20139 Milan, Italy.
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The well-known anticonvulsant properties of several carbamate esters, together with our interest in the terpene field, have led us to synthesize a number of terpenyl carbamates (Table I) for a pharmacological evaluation of their CNS activity.

All the compounds were tested orally for CNS activity in mice, using meprobamate as reference standard. As can be seen from Table II, which reports the most interesting results, all the compounds caused CNS depression, which appeared as decrease in spontaneous motility¹ and body muscle tonus, motor incoordination, and loss of righting reflex. The most active compound was 1, which in addition exhibited a marked anticonvulsant action against maximal electroshock (MES) and pentylenetetrazole (Met) seizures.² This effect, however, was less lasting than that of meprobamate. Unlike the standard, the new substances failed to potentiate the hexobarbital-induced sleep, as well as to prevent aggressive behavior induced by L-dopa.³ None of the compounds showed central analgetic activity (tail-pinch test).⁴

Table I. Terpenyl Carbamates. ROCONH_2

Compd	R	Yield, %	Bp (mm) or mp, °C	Formula ^a
1	Prenyl	62 ^b	45–46	$\text{C}_{10}\text{H}_{17}\text{NO}_2$
2	Homoprenyl	76.8 ^c	69–70	$\text{C}_{11}\text{H}_{19}\text{NO}_2$
3	Citronellyl	63 ^d	122–123 (0.5)	$\text{C}_{11}\text{H}_{21}\text{NO}_2$
4 ^e	Geranyl	68.2 ^d	110–117 (0.02)	$\text{C}_{15}\text{H}_{25}\text{NO}_2$
5	Neryl	53.8 ^d	110–120 (0.06)	$\text{C}_{15}\text{H}_{25}\text{NO}_2$
6	Farnesyl	46.1 ^d	144–145 (0.03)	$\text{C}_{15}\text{H}_{27}\text{NO}_2$

^aAll compds were analyzed for C, H, and N; the analytical values were within $\pm 0.4\%$ of the theoretical values. ^bRecrystd from petroleum ether (bp 40–70°). ^cRecrystd from cyclohexane. ^dOnce distd. ^eThiele, *et al.*,⁵ report bp 112–115° (0.01 mm).

Table II. Pharmacological Results

Compd	Approx LD_{50} , mg/kg po	Anticonvulsant act.		Spontaneous motility decrease, ED_{50} , mg/kg po
		Met, ^a ED_{50} , mg/kg po	MES, ^b ED_{50} , mg/kg po	
1	>800	87	90	288
2	>800	400	207	261
3	>800	460	230	395
4	>800	530	>800	>400
5	>800	365	570	291
6	>800	285	435	207
Meprobamate	750	62	182	203

^a125 mg/kg ip. ^bEar electrodes, 10 mA, 0.2 sec.

Experimental Section†

General Procedure. Phenyl chloroformate (15.65 g, 0.1 mole) was added over 20 min to a stirred soln of the appropriate alcohol (0.1 mole) in dry pyridine (50 ml) at 5–10°. After 2 hr stirring at room temp, the mixt was poured into ice H_2O and extd (Et_2O). The Et_2O soln of the carbonate ester was washed (H_2O , 5% HCl , satd NaHCO_3 , H_2O), dried (Na_2SO_4), and then added dropwise with stirring to liquid NH_3 . After 2 hr the excess NH_3 was allowed to evaporate at room temp, and the residue was taken up in Et_2O , washed (1 N NaOH , satd NaCl), and dried (Na_2SO_4). Removal of the solvent afforded the crude product, which was purified as shown in Table I.

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†Melting points were taken on a Büchi capillary melting point apparatus and are corrected; boiling points are uncorrected. Ir and nmr spectra were consistent with the assigned structures.