

GERMAZONE, A NOVEL TRICYCLIC SESQUITERPENE KETONE
IN THE ESSENTIAL OIL FROM GERANIUM MACRORRHIZUM L.

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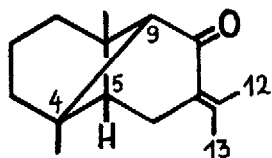
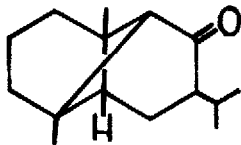
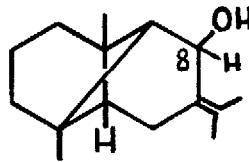
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A novel unsaturated ketone, germazone, 1, ($[\alpha]_D = 0^\circ$, m.p. 36-38^o, semicarbazone m.p. 126-128^o) was isolated via repeated chromatography on silica as a minor component in the liquid part of the Bulgarian essential oil from *Geranium macrorrhizum* L. leaves (Zdravetz oil)¹. The carbonyl group in 1 is conjugated ($\lambda_{\text{max}}^{\text{EtOH}}$ 254 nm, ϵ 9500, i.r. 1680 cm^{-1}) with a tetrasubstituted double bond (1610 cm^{-1}). Catalytic hydrogenation of 1 (20% Pd/C in methanol, 1 mole of H₂) led to the saturated ketone 2 - negative reaction with tetranitromethane, doublet for isopropyl group (1370 - 1385 cm^{-1}) and absorption band for saturated ketone (1705 cm^{-1}). Germazone contains, therefore, only one double bond, the isopropylidene one, conjugated with the carbonyl group, both functions being substituents of a six-membered ring. The ketone 1 has no methylene group adjacent to the carbonyl since it fails to form a benzylidene derivative. This conclusion is supported by the lack of a maximum or inflection in the i.r. spectrum in the 1410 - 1415 cm^{-1} region. The failure of 1 to form an enolacetate also points towards either the absence of an α -hydrogen atom or the presence of a nonenolizable one (bridgehead hydrogen). Reduction of 1 with LiAlH₄ afforded the unsaturated alcohol germazol, 3, m.p. 101-103^o, $[\alpha]_D = 0^\circ$, which on oxidation with aqueous chromic acid in ether yielded the initial ketone 1. Elemental analysis and the mass-spectrum indicated C₁₅H₂₄O

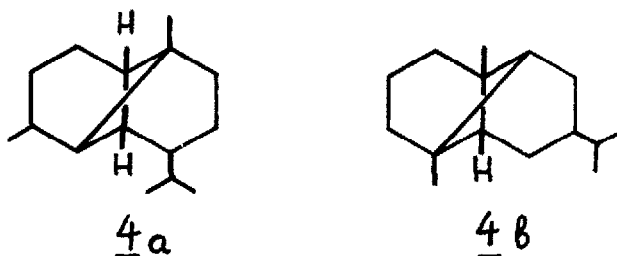
for 2. Germazol, as well as 2 and 3 have therefore a tricyclic carbon skeleton.

On the basis of these results and the n.m.r. spectra of both 1 and 3 was ascribed to germazone structure 1.

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The n.m.r. spectrum of germazone (100 MHz, CDCl_3) shows a common signal for two tertiary methyl groups (0.82δ , s, 6H). The Dreiding model of 1 shows the presence of a plane of symmetry intersecting C-5 and C-9 as well as the C-2 methylene group, which is corroborated by the absence of optical activity despite the presence of the asymmetric C-5 and C-9 carbon atoms. Both methyl groups at C-4 and C-10 are symmetric with respect to the carbonyl function thus giving rise to a common n.m.r. singlet. With the alcohol 3 this symmetry is destroyed and the one methyl deshielded by the hydroxyl oxygen atom absorbs at 0.98δ (s, 3H), while the other resonates at 0.75δ (s, 3H). The methylene protons of 1 give a sharp multiplet at 1.68δ (6H) in which are easily discernible two doublets arising from protons at a dihedral angle of about 60° ($J = 2$ Hz). The C-13 methyl group protons in 1 appear as a sharp signal at 1.84δ (s, 3H), while those of the C-12 methyl group resonate as a triplet at 2.28δ (t, $J = 1.8$ Hz, 3H), the splitting being caused by the transoid homoallylic coupling with the methylene protons at C-6. In 3 the C-12 methyl group absorbs as a sharp unresolved multiplet because of the simultaneous interaction with the C-6 protons (transoid) and the C-8 proton (cisoid). Irradiation of the C-8 proton leaves only the transoid homoallylic coupling between C-12 and C-6 protons thus converting the C-12 multiplet into a triplet ($J = 1.8$ Hz) analogous to the one in germazone. The doublet at 2.44δ ($J = 6$ Hz, H) in the n.m.r. spectrum of 1 is due to the C-9 proton which is coupled with the proton at C-5. Both these methine protons lie in the plane of symmetry and form a

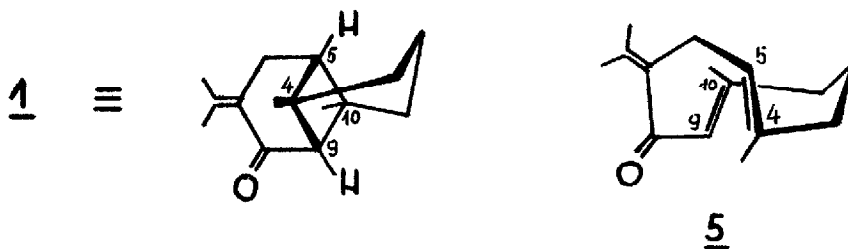
"W"-system of 4 σ -bonds interacting in the same way ($J = 6$ Hz) as the analogous protons of the cyclobutane ring in bicyclo(2.1.1)hexane². The same C-9 proton in 2 appears as a pair of doublets at 1.95δ and 2.01δ ($J = 6$ Hz) which on irradiation of C-8 proton (4.6 , m, $W_{1/2} = 8$ Hz, H) produces a doublet at 1.98δ ($J = 6$ Hz) analogously to the signal of the proton at C-9 in 1. The sextet due to the proton at C-5 in 1 (2.03δ , $J = 3$ Hz, H) arises as a result of coupling with the C-9 proton and the adjacent C-6 methylene protons. Each peak of the sextet is subjected to additional fine splitting (J ca. 0.5 Hz) from long range coupling with other protons. The n.m.r. spectra of both 1 and 2 contain also a broad signal ($W_{1/2} = 7$ Hz, 2H) at 2.51δ and 2.45δ respectively, which arises from the C-6 methylene protons adjacent to the double bond. The broadening of the signal is caused by the simultaneous interaction of C-6 protons with the C-5 methine proton and transoid - cisoid homoallylic coupling with the protons of both isopropylidene methyls.



The known tricyclic cis-decalin sesquiterpenes with a C-4 - C-9 cyclobutane ring as for example ylangene, copaene and others³ have substituents situated as in cadinane (4a). As far as we know, analogous tricyclic cis-decalin sesquiterpenes with substituents as in selinane (4b) have not yet been reported. Germazone is the first representative of this theoretically expected group of sesquiterpenes with a novel carbon skeleton.

The high germacrone content of zdravetz oil⁴ makes the link between germacrone and the isolated from the same oil germazone quite plausible. In this connection isogermacrone⁴ is a very likely germazone precursor since it

possesses two endocyclic trans double bonds in suitable position for ring formation. As can be seen from 5 twisting the isogermacrone molecule easily



brings together both double bonds thus rendering cyclobutane formation between C-5 - C-10 and C-4 - C-9 quite feasible.

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