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THE SYNTHESIS OF 1β(H), 6β(Me)-2,2,6-TRIMETHYL-8-ETHYLBICYCLO-[4,3,0]-7-THIANONANE AND THE STRUCTURE OF THE ISOMERIC BICYCLIC-TERPENOID SULFIDES OCCURRING IN PETROLEUM.

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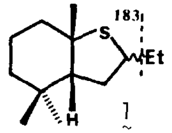
Abstract: The synthesis of the title compound is described. Comparison of ms and nmr data with those of the isomeric bicyclic terpenoid sulfide of petroleum shows that the latter has the structure of 1α(H), 6β(H)-2,2-dimethyl-9-ethylbicyclo-[4,4,0]-8-thiadecane.

In a previous communication from this laboratory[1] the detection and isolation from petroleum of a highly complex mixture of alicyclic sulfides, (along with some sulfoxide derivatives) containing homologous series of novel terpenoid structures were reported. The two predominant classes of the terpenoid sulfides (sulfoxides) comprised a bicyclic and a tetracyclic series each containing an isoprenoid side chain ranging from C_1 to C_{11}. The most abundant components were one of the C_{13} and one of the C_{23} isomers in the bicyclic and tetracyclic series, respectively, for which structures 1 and 2 were considered to be most likely. The bases of these tentative structural assignments were as follows: i) high resolution ms gave for 1 and 2 the elemental formulae $C_{13}H_{24}S$, and $C_{23}H_{40}S$. ii) reduction with Raney nickel afforded the hydrocarbons[2-5], 1a and 2a, as was shown by capillary gc retention time and mass spectral comparisons. iii) the mass spectra of 1 and 2 and all members of their respective homologous series featured a medium intensity parent along with ions m/z = 183 and 319 corresponding to the dealkylated ring structures being the characteristic base peak. These facts taken together clearly established that the sulfur was attached to the C_2 position in the side chain of hydrocarbons 1a and 2a but left the site of attachment of the residual valence of the sulfur ambiguous. Participation of the sulfur in a five membered ring giving 1 and 2 was preferred over possible six membered ring structures on the grounds that the m/z = 123 fragment ion from 1 and 2 and the 191 ion from 2 had significant intensities in the mass spectra. The former fragmentation has been considered to be diagnostic for the presence of the trimethylated A ring of bi- and higher cyclic terpanes and the latter of the tetramethylated AB rings of tri- and higher cyclic terpanes. In order to establish the structure of the $C_{13}H_{24}S$ compound unequivocally, we have synthesized two stereoisomers of 1 according to the procedure outlined in Scheme 1.



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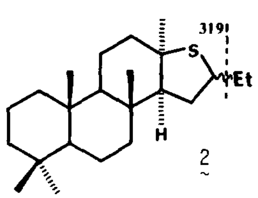

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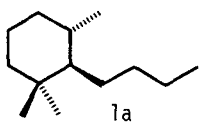
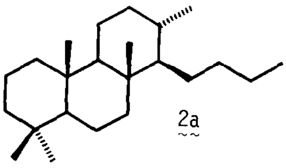
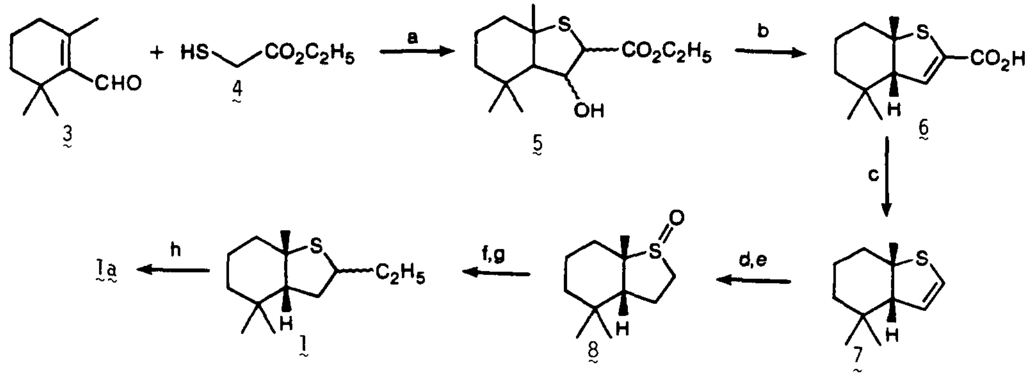


1a



2a

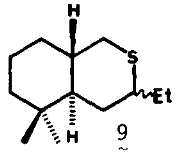


Scheme 1. a) NaOEt (dry, 0.2 eq) (4/3) = 1.2, 25°, Ar, 13 days (80%); b) KOt-Bu/HOt-Bu, 25°, 16 h, (48%); c) 235°, 1/2 h, (91%); d) PtO_2, EtOH, H_2 (1 atm), 5 days (65%); e) $NaIO_4$, EtOH, H_2O (90%); f) n-BuLi, THF, -78°, 1 h, EtBr, -78° to 25°, 1 h (80%); g) $LiAlH_4$, dioxane, reflux 1 h; h) Raney nickel, EtOH, reflux 3 h.

β-Cyclocitral 3 [6] and 2-mercaptoethylacetate 4 slowly condense[7] and cyclize in the presence of sodium ethoxide to afford the alcohol 5 as a mixture of isomers. Treatment of crude 5 with strong base gave, in moderate yield, a solid, the acid 6.[8] This contained the correct skeleton and appeared to be appropriately functionalized for conversion to 1. However, we were unable to convert the carboxyl group of 6 to an alkyl group, presumably because of its β position to the S atom.[9] Typically, a reaction sequence involving this site produced material resulting from rearrangement or polymerization. However, thermal decarboxylation gave the olefin 7 in high yield. Catalytic hydrogenation of the double bond followed by oxidation gave the sulfoxide 8 which could be readily alkylated α to the sulfur atom and reduced to a mixture of two stereoisomers of 1. The spectral properties[10] of the synthetic materials are in accord with structure 1. Reduction of 1 with Raney nickel gives the hydrocarbon 1a. The acidic proton of the sulfoxides of 1 may be exchanged for deuterium (NaH in CD_3SOCD_3/THF, 25°, 3 h) and the sulfoxides reduced ($LiAlD_4$, dioxane, 1 h) to the sulfides. The mass spectra of these sulfides show the incorporation of one atom of deuterium in each isomer. The isomers of 1 have mass spectra and gc retention times quite different from those of the natural material we detected in petroleum. Clearly our earlier hypothesized structure was not correct.

Next, we isolated the C_{13} terpenoid sulfide from a petroleum sample (Lloydminster, Alberta) for nmr analysis. The lower boiling ∿20% of the oil was oxidized with photochemically generated singlet O_2 [11] to convert the sulfides to sulfoxides which were then removed from the mixture by filtration on silica gel. Reduction of the sulfoxides ($LiAlH_4$, dioxane, 1 h) afforded the crude sulfides which were fractionally distilled, chromatographed (silica gel, 15% toluene/hexanes) and rechromatographed by reverse phase chromatography on C_8 bonded silica gel (EtOH/H_2O, 95:5) to yield a sample of 55-60% purity, suitable for ^1H nmr analysis.

The 400 MHz ^1H nmr spectrum of the sample[12] reveals only three methyl groups, two singlets and a triplet along with three one-hydrogen-atom signals assignable to hydrogens on the carbon atoms adjacent to the sulfur, and two one-hydrogen-atom signals assignable to the ring junction protons of structure 9. The remaining signals appear as a complex pattern. The sulfide was



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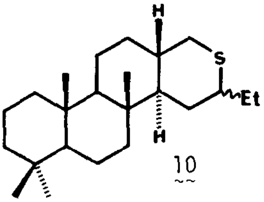
oxidized (HOAc/30% H_2O_2, 25°, 16 h) to the corresponding sulfone. In the ^1H nmr of the sulfone[13] the three signals assigned to the hydrogens on the carbons adjacent to the sulfur shift significantly, while the remaining signals are essentially unchanged. The acidic hydrogens of the sulfone may be exchanged for deuterium (n-BuLi/CD_3SOCD_3, 25°, 16 h). The mass spectra of the deuterated sulfone[13] shows that three atoms of deuterium have been incorporated.

The mass spectrum of the C_{13} terpenoid sulfide with the base peak at M-29 is consistent with the sulfur atom being attached to the second carbon atom of the n-butyl side chain of **1a**. The deuterium exchange experiments and nmr data show three hydrogens on the carbons adjacent to the sulfur and the nmr spectrum reveals the presence of only three methyl groups, the multiplicities of which are satisfied by **9**.

The ms fragmentation pattern of the two different ring systems **1** and **9** show characteristic differences, the main feature is that when the S is present in a six-membered ring, the base peak is $(M-R)^+ = 183$ for the entire series, while in the case of the five-membered ring, it is the $(M-Me)^+$ ion. Therefore we postulate that the entire main homologous series of bicyclic terpenoid sulfides we reported to occur in petroleum have the ring framework of **9** and by inference, the main homologous series of tetracyclic terpenoid sulfides should have an analogous ring structure **10**. The ms fragmentation patterns of the two series are very similar, $(M-R)^+ = 319$ being the characteristic base peak for the entire tetracyclic series. In addition, the C_{23} tetracyclic sulfone incorporated three atoms of deuterium under the same conditions used for the exchange of the acidic hydrogens of the C_{13} sulfone and gives the characteristic m/z = 191 fragment ion of the same relative intensity as the undeuterated C_{23} compound.[14]



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In the homologous series of all head to tail isoprenoid bicyclic sulfides occurring in Alberta bitumens and several conventional petroleums of which **9** is always the most abundant member, the carbon number ranges from 12 to 22. Each member is present in at least two isomeric forms, the first eluting member always being the more abundant. We assign to this major series the 9α(H) stereochemistry leaving the stereochemistry of the minor series unassigned. However, evidence from the distribution of the sulfide-derived hydrocarbons shows that the minor series is not the 9β(H) isomer.

Further studies are in progress.

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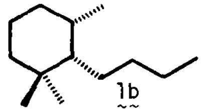
2, **1a** was prepared from α-Ionone·α-Ionone $\xrightarrow[2)Zn/Hg,HCl]{1)H_2,Rd/C}$ **1a** +  **1b** ; **1a**/**1b** = 1/5.

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8. Analytical data for **6**: MS (70 eV) m/z = 226 (M^+, 65%), 211(7), 193(7), 183(10), 170(7), 157(45), 155(25), 144(75), 143(100), 141(82); Exact mass: M^+ = 226.1028, $C_{12}H_{18}SO_2$ = 226.1028, m.p. 127° - 128.5°; IR (cm^{-1}): 3200-2500, 1690, 1590; ^1H NMR (400 MHz, $CDCl_3$): 1.01(3H,s), 1.04(3H,s), 1.18(1H,m), 1.42(1H,m), 1.50(3H,s), 1.52(2H,m), 1.60(1H,m), 2.01 (1H,m), 2.42(1H,d,3.4 Hz), 6.75(1H,d,3.4 Hz),δ(ppm); Irradiation of the signal at δ = 2.42 enhances the signal at δ = 1.50 and vice versa in the N.O.E. difference experiment.
9. C.R. Noller, Chemistry of Organic Compounds, p.316, Saunders (1966).
10. Analytical data for **1**: GCMS (70 eV), (the two isomers have similar MS), m/z = 212 (M^+, 30%), 197(100), 183(35), 169(20), 149(6), 141(11), 129(18), 127(15), 123(31), 109(21); GCMS (70 eV), (Deuterated): m/z = 213 (M^+, 27%), 198(100), 197(2), 184(35), 170(21), 150(70), 142(10), 130(18), 123(29); ^1H NMR (400 MHz, $CDCl_3$, one isomer of **1** as the sulfoxide): 0.92(3H,s), 1.06(3H,s), 1.07(3H,t), 1.24(2H,m), 1.56(3H,s), 1.40-1.70 (5H,m), 1.96 (2H,m), 2.33(2H,m), 3.04(1H,m), δ(ppm).
11. C. Gu, C.S. Foote and M.L. Kacher, *J. Am. Chem. Soc.*, *103*, 5949 (1981).
12. C_{13} sulfide (Lloydminster): GCMS (70 eV): m/z = 212 (M^+, 30%), 197(10), 183(100), 169(8), 149(7), 141(8), 129(5), 127(10), 123(23), 109(19); ^1H NMR (400 MHz, $CDCl_3$), sample integrated to be 55-60% pure: 0.80(3H,s), 0.86(3H,s), 0.96(3H,t), 1.05-1.55 (m), 1.63 (1H,m), 2.02(1H,m), 2.33(1H,dd, $J \simeq 5$ and 5Hz), 2.45(1H, dd, $J \simeq 2$ and 5Hz), 2.58(1H,m); δ(ppm).
13. C_{13} sulfone (Lloydminster): GCMS (70 eV): m/z = 244 (M^+, 10%), 229(10), 227(9), 179(34), 163(25), 137(26), 123(63), 109(73), 95(75), 81(70), 69(100); GCMS (70 eV), (Deuterated): m/z = 247 (M^+, 10%), 232(8), 230(7), 182(32), 166(20), 140(12), 139(14), 125(38), 112(42), 111(42), 97(48), 83(63), 69(100); ^1H NMR (400 MHz, $CDCl_3$): 0.85(3H,s), 0.97(3H,s), 1.09 (3H,t), 1.2-1.6(m), 1.66(1H,m), 2.02(1H,m), 2.61(1H, dd, $J \simeq 5$ and 5Hz), 2.69(1H,m), 2.97 (1H, dd, $J \simeq 2$ and 5Hz); δ(ppm).
14. C_{23} sulfone: GCMS (70 eV): m/z = 380 (M^+, 25%), 365(70), 267(60), 229(19), 201(18), 191(45), 163(22), 137(29), 123(100), 109(61), 95(65), 81(62), 69(70), 55(64); GCMS (70 eV), (Deuterated): m/z = 383 (M^+, 25%), 368(75), 270(58), 232(18), 204(18), 191(47), 166(21), 137(35), 123(100), 109(62), 95(64), 81(61), 69(68), 55(55). In reference 1 the highest molecular weight C_{31} member of this series was erroneously described as having a 3,7-dimethyl nonyl side chain: the correct structure is 6-methyl non-2-yl. We have found members with side chains extending up to 6,10-dimethyl-dodec-2-yl.

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