A New Tetracyclic Sesquiterpene Hydrocarbon from *trans*-Farnesic Acid; *X*-Ray Crystal Structure of 8-Bromomethyl-1,4-dimethyl-9-methylenetetracyclo[5.2.1.1^{5,8}.0^{4,10}]undecane

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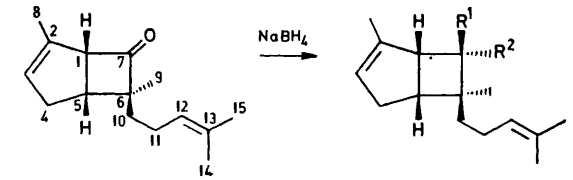
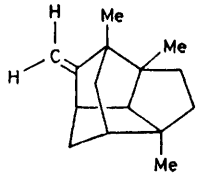
Sesquifilifolone (1), a cyclisation product of farnesic acid, has been reduced to the corresponding epimeric alcohols. These epimers (2) and (3) cyclise with rearrangement when treated with 50% sulphuric acid to give a new sesquiterpene hydrocarbon $C_{15}H_{22}$, the structure of which has been determined by analysis of its spectroscopic properties, its reactivity, and by *X*-ray analysis of the rearranged monobromo-derivative 8-bromomethyl-1,4-dimethyl-9-methylenetetracyclo[5.2.1.1^{5,8}.0^{4,10}]undecane (8).

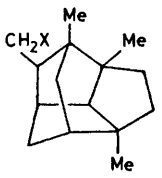
WE have reported previously [1] that the cyclisation of a mixture of 2*E*,6*E*- and 2*Z*,6*E*-farnesic acids gives four products: three monocyclic compounds, and a new bicyclic sesquiterpene ketone (1) which we have named sesquifilifolone. We now report the results of further investigations of sesquifilifolone (1).



(1) (2) R^1 = H; R^2 = OH (3) R^1 = OH; R^2 = H



(4)



(5) X = OH (6) X = $OCOC_6H_3(NO_2)_2$-3,5

Sodium borohydride reduction of a methanolic solution of (1) afforded a mixture of the two epimeric alcohols (2) and (3) in a ratio of 9 : 1 which was separated by silica gel chromatography. The stereochemistry of the hydroxy-group could be assigned on the basis of simple considerations; in fact it was to be expected that the less sterically hindered *exo*-side of the molecule (1) would have been preferentially attacked by the hydride ion leading to (2). This conclusion was confirmed by the ^{1}H n.m.r. spectrum of compound (2): 7-H gave a triplet signal which, after exchange with deuterium oxide, became a doublet with $J_{1,7}$(*cis*) 8 Hz, while 7-H in (3) was a doublet with $J_{1,7}$(*trans*) 2 Hz.

Compound (2) stimulated our interest as a possible synthetic precursor of bourbonene [2] derivatives; in fact it contains the appropriate structural features to lead to an interaction between the double bond of the side chain and an electrophilic centre generated in position 7.

In our first attempt to induce cyclisation under mild conditions, we tried to synthesise the toluene-*p*-sulphonate or the methanesulphonate of the alcohol (2). Even under drastic conditions (refluxing pyridine) sulphonic ester formation was not observed and therefore we examined the products of treatment of (2) with acids. The reaction of (2) with tin tetrachloride in carbon disulphide afforded a very complex mixture, while boron trifluoride in diethyl ether or mild exposure to protic acids such as toluene-*p*-sulphonic acid in diethyl ether or Dowex W 50-X4 ion exchange resin in diethyl ether left the alcohol (2) unchanged.

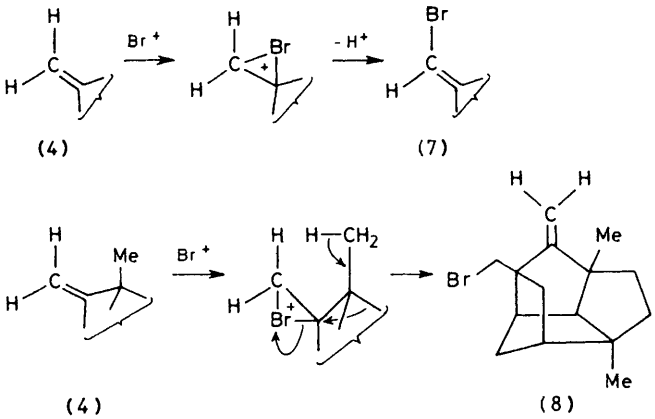
Stirring of an ethereal solution of (2) with an equal volume of 50% aqueous sulphuric acid at room temperature led to a gradual transformation into a less polar substance, and compound (4) was obtained as an oily liquid after silica gel chromatography. Treatment of the epimeric sesquifilifolol (3) under analogous conditions afforded the same hydrocarbon (4).

Elemental analysis of (4) together with its mass spectrum ($M^{\cdot+}$, *m*/*z* 202; 1%) were in agreement with a molecular formula $C_{15}H_{22}$. The ^{1}H n.m.r. spectrum of (4) showed $=CH_2$ signals at δ 4.52br (1 H, s) and 4.36br (1 H, s) and three singlets at δ 1.03, 0.76, and 0.74 due to methyl groups bound to fully substituted sp^3-carbon atoms; in contrast, the starting material had three methyl groups on sp^2-carbon atoms and only one methyl group on an sp^3-carbon atom. The ^{13}C n.m.r. spectrum of (4) showed four quaternary carbon signals together with three methine, five methylene, and three methyl signals. Its i.r. spectrum showed absorptions at 3 070, 1 660, and 870 cm^{-1} confirming the presence of the methylene. These data indicated a tetracyclic structure for compound (4) with an exocyclic double bond and hence we studied its reactivity in order to obtain further information on its structure.

Treatment of (4) with ozone in ethyl acetate at −30 °C afforded one compound which showed major mass spectral fragmentations at *m*/*z* 218 ($M^{\cdot+}$, 11%), 122

(53%), and 95 (100%). A single product with the same g.l.c. retention time (Carbowax 20M 10%, 2 m; temperature programmed 100—180 °C, 10 °C min^{-1}) and the same mass spectral fragmentations was obtained from the reaction of (4) with *m*-chloroperoxybenzoic acid in methylene chloride at room temperature for 30 min. These results showed that epoxidation of the double bond of (4) took place with ozone before cleavage to the ozonide; this is a well known process for sterically hindered alkenes.[3] The bulkiness of the groups around the double bond in (4) was also shown by hindrance to the reaction with 9-borabicyclo[3.3.1]nonane, whereas hydroboration of (4) took place readily with diborane affording the primary alcohol (5) [$\nu_{max.}$ 3 500—3 150 cm^{-1}; $M^{\cdot+}$, *m/z* 220; δ 3.72 (2 H, m)] which on treatment with 3,5-dinitrobenzoyl chloride in pyridine gave the crystalline 3,5-dinitrobenzoyl derivative (6) [$\nu_{max.}$ 1 720 cm^{-1}; $M^{\cdot+}$, *m/z* 414; δ 9.20 (3 H, m) and 4.50 (2 H, m)].

Addition of bromine to a carbon tetrachloride solution of the hydrocarbon (4) until the bromine colour persisted gave a mixture of the two monobromo-derivatives (7) and (8) ($M^{\cdot+}$, *m/z* 282 and 280 for both), in a ratio of 6 : 4, which was separated by silica gel chromatography. The ^{1}H n.m.r. spectrum of the oily compound (7) showed one vinyl proton signal at δ 5.50 and three methyl singlets at δ 1.05, 0.79, and 0.75 indicating that during the bromination leading to (7) only a formal substitution of a vinyl proton by a bromine atom took place according to the mechanism in Scheme 1.

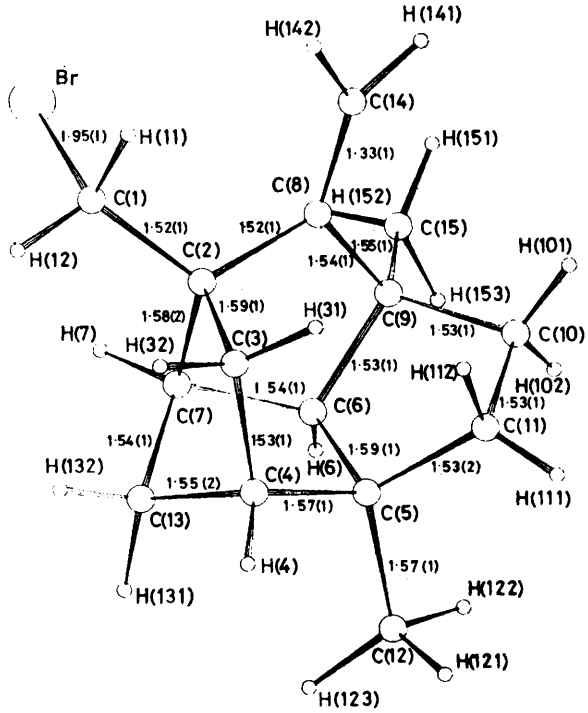


SCHEME 1

The ^{1}H n.m.r. spectrum of the crystalline monobromo-derivative (8) showed two $=CH_2$ singlets (δ 4.95 and 4.88), two AB doublets (δ 3.53, *J* 11 Hz) for the CH_2Br protons, and only two methyl singlets (δ 1.15 and 1.10), suggesting that a skeletal rearrangement had taken place (Scheme 1).

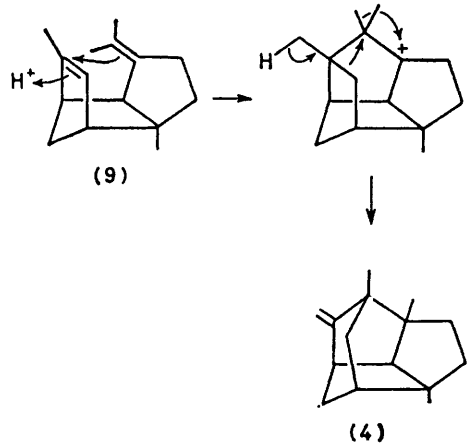
As these data did not allow us to assign the structure of the hydrocarbon (4) unequivocally, and in order to substantiate a plausible mechanism for the cyclisation from (2) to (4) on the basis of a reliably determined configuration, we determined the structure of the monobromo-derivative (8) by single-crystal *X*-ray analysis (see Experimental section). The molecular geometry and bond distances are shown in the Figure.

We suggest that the cyclisation pathway from (2) to the new sesquiterpene hydrocarbon (4) probably proceeds *via* the intermediate hydrocarbon (9) or its equivalent (Scheme 2).



Molecular structure of compound (8)

The rearrangement of the epimeric sesquifilifolols (2) and (3) to (9) is interpreted as a conversion of the bicyclo-[3.2.0]-system present in structure (2) into the thermodynamically more stable bicyclo[2.2.1]-system and a reaction of the side-chain double bond with the norbornene cation represented by (12).

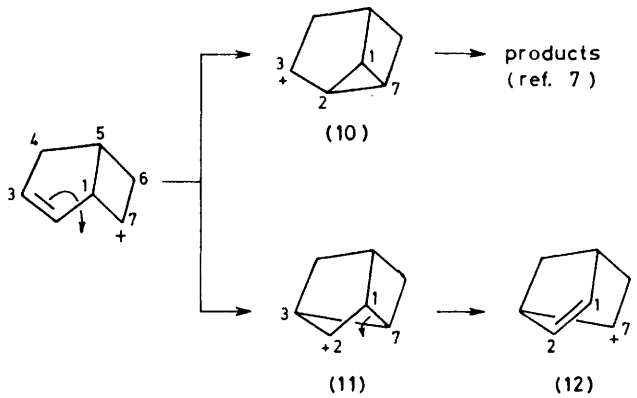


SCHEME 2

The [1,3] sigmatropic rearrangement of the bicyclo-[3.2.0]heptene system to the norbornene system is well

documented[4] and the reverse rearrangement is also known in photochemical reactions of suitable bornenones.[5]

Although [1,3] sigmatropic rearrangements of bicyclo-[3.2.0]hept-2-en-7-olates can occur under mild conditions,[6] the initial formation of a cation at C-7 of the epimeric sesquifilifolols (2) and (3) seems more likely under our very acidic conditions. This cation appears well suited for interacting with the double bond in the five-membered ring, as shown in Scheme 3 and as is well documented for the bicyclo[3.2.0]hept-2-ene-7-diazonium ion[7] and its rearrangement to the tricyclo[3.2.0.0^{2,7}]-heptan-3-yl system (10). In our case the attack of the



SCHEME 3

double bond on the C-7 electrophilic centre could lead to bond formation between C-3 and C-7 rather than C-2 and C-7, and thus to the new cation (11) stabilised by the presence of a methyl group on C-2; cleavage of the C-1–C-7 bond of the very strained system (11) containing two four-membered rings could induce the rearrangement of (11) to the norbornene cation (12) and its subsequent reaction with (or its formation assisted by) the side-chain double bond affording the hydrocarbon (9).

It is noteworthy that all the proposed steps of the conversion of sesquifilifolols into the hydrocarbon (4) are consistent with the stereochemical demands of the mechanism, and that the attack of the trisubstituted side-chain double bond on the norbornene system affords the expected five-membered ring with an *exo*-tetrasubstituted double bond.

EXPERIMENTAL

All m.p.s were measured on a Kofler hot stage apparatus. N.m.r. spectra were recorded on a Varian XL 100A spectrometer for $CDCl_3$ solutions using $SiMe_4$ as internal standard; mass spectra were measured with a Varian MAT 112 mass spectrometer; i.r. spectra were run on a Perkin-Elmer 257 Infracord spectrophotometer. Gas-chromatographic analyses were run on an F30 Perkin-Elmer gas chromatograph equipped with a 0.6 × 200 cm glass column; Carbowax 20M 10% on Chromosorb was used for compounds (5), (7), and (8), and OV 1 3% on Chromosorb for compounds (2), (3), and (4).

Sesquifilifolol (2) *and* (3).—Sesquifilifolone (1) (1.2 g) in methanol (30 ml) was stirred at 0 °C with an excess of sodium borohydride for 2 h. After removal of the solvent and partition between water and diethyl ether, the organic layer was dried over sodium sulphate and evaporated *in vacuo*. The crude mixture of (2) and (3) was chromatographed on silica gel with light petroleum–ethyl acetate (95 : 5) as eluant to give (2) (840 mg, 65% yield) and (3) (90 mg, 7% yield): (2): oil (decomp. during vacuum distillation); $\nu_{max.}$ (liquid film) 3 550—3 350 and 1 650 cm^{-1}; δ 5.55 (1 H, m, 3-H), 5.12 (1 H, m, 12-H), 4.00 (1 H, t, *J* 8 Hz, 7-H), 3.35 (1 H, m, 1-H), 1.81 (3 H, d, *J* 1.2 Hz, 8-H_3), 1.70br (3 H, s, 14- or 15-H_3), 1.62br (3 H, s, 15- or 14-H_3), and 0.93 (3 H, s, 9-H_3); *m/z* 220 (2%), 140 (10), 121 (22), 81 (100), 70 (74), and 69 (46); (3): oil (decomp. during vacuum distillation); $\nu_{max.}$ (liquid film) 3 500—3 250 and 1 650 cm^{-1}; δ 5.30 (1 H, m, 3-H), 5.14 (1 H, m, 12-H), 3.55 (1 H, d, *J* 2 Hz, 7-H), 1.73 (3 H, d, *J* 1.5 Hz, 8-H_3), 1.71br (3 H, s, 14- or 15-H_3), 1.62br (3 H, s, 14- or 15-H_3), and 0.97 (3 H, s, 9-H_3); *m/z* 220 (1%), 140 (10), 81 (78), 70 (100), and 69 (52).

Cyclisation of Sesquifilifolol (2).—A solution of (2) (748 mg) in diethyl ether (40 ml) was stirred with an equal volume of 50% aqueous sulphuric acid at 0 °C for 30 min and then at room temperature. After 3 h the mixture was diluted with ice–water, neutralized with sodium hydrogencarbonate, and extracted with n-pentane. After removal of solvent the residue was chromatographed on silica gel with n-pentane as eluant and distilled *in vacuo* to give the pure *hydrocarbon* (4) (180 mg, 30% yield); b.p. 140—145 °C (15 Torr) (Found: C, 88.9; H, 10.7. $C_{15}H_{22}$ requires C, 89.1; H, 10.9%); $\nu_{max.}$ (liquid film) 3 070, 1 660, and 870 cm^{-1}; δ 4.52br (1 H, s), 4.36br (1 H, s), 2.72 (1 H, m), 2.27 (1 H, m), 1.03 (3 H, s), 0.76 (3 H, s), and 0.74 (3 H, s); ^{13}C n.m.r. δ (p.p.m. from $SiMe_4$) 146.03(s), 96.28(t), 61.47(d), 55.95(s), 54.66(s), 48.84(s), 45.90(d), 43.73(d + t), 42.06(t), 36.45(t), 33.28(t), 25.51(q), 22.37(q), and 15.48(q); *m/z* 202 (1%), 107 (4), and 95 (100).

Cyclisation of Sesquifilifolol (3).—Treatment of the isomer (3) (85 mg) with sulphuric acid as just described for compound (2) gave the same hydrocarbon (4) (21 mg, 30% yield).

Hydroboration–Oxidation of (4).—To a stirred solution of (4) (40 mg) in anhydrous tetrahydrofuran (10 ml) a solution of diborane (9 μl) (*ca.* 2M in borane) was added at room temperature under argon. After 2 h, water (5 μl) was added followed by 3M-sodium hydroxide (8 μl) and 30% hydrogen peroxide (8 μl). After 30 min at room temperature and 30 min at 50 °C, sodium chloride was added and the mixture was extracted three times with diethyl ether. The organic layer was dried over sodium sulphate and evaporated *in vacuo* affording a crude product which was purified by silica gel chromatography. Elution with light petroleum–ethyl acetate (8 : 2) gave the pure *alcohol* (5) (40 mg, 90% yield), m.p. 65—66 °C (from light petroleum) (Found: C, 81.9; H, 11.0. $C_{15}H_{24}O$ requires C, 81.8; H, 10.9%); $\nu_{max.}$ (Nujol) 3 500—3 150 and 1 020 cm^{-1}; δ 3.72 (2 H, m), 1.00 (3 H, s), 0.85 (3 H, s), and 0.83 (3 H, s); *m/z* 220 (4%), 202 (5), 189 (11), 122 (100), 107 (37), and 95 (100).

3,5-*Dinitrobenzoate of* (5).—Compound (5) (30 mg) in dry pyridine (1 ml) was treated with 3,5-dinitrobenzoyl chloride (32 mg) for 10 min at 50 °C and for 30 min at room temperture. After evaporation, the mixture was partitioned between iced 2% hydrochloric acid and diethyl ether. The aqueous phase was extracted three times with diethyl ether. The combined organic layers were washed with 10% sodium hydrogencarbonate solution and water, dried over sodium sulphate, and evaporated *in vacuo*. The residue

was chromatographed on silica gel. Elution with light petroleum–ethyl acetate (90 : 10) led to the pure *dinitrobenzoate* (6) (45 mg, 71% yield), m.p. 107 °C (from Pr^i_2O) (Found: C, 63.8; H, 6.3; N, 6.75. $C_{22}H_{26}N_2O_7$ requires C, 63.7; H, 6.3; N, 6.8%); $\nu_{max.}$ (Nujol) 1 720, 1 550, and 1 350 cm^{-1}; δ 9.20 (3 H, m, ArH), 4.50 (2 H, m, $-CH_2OCO-$), 1.02 (3 H, s), 0.98 (3 H, s), and 0.92 (3 H, s); *m/z* 414 (2%), 202 (8), 195 (3), 122 (100), 107 (20), and 95 (45).

Treatment of (4) *with Bromine.*—To a solution of (4) (40 mg) in carbon tetrachloride (1 ml) a solution of bromine (0.2 ml) in carbon tetrachloride (10 ml) was added until the bromine colour persisted. After 1 h at room temperature, evaporation afforded a crude mixture which was chromatographed on silica gel. Elution with n-pentane led to pure (7) (33 mg, 60% yield) and pure 8-*bromomethyl*-1,4-*dimethyl*-9-*methylenetetracyclo*[5.2.1.$1^{5,8}$.$0^{4,10}$]*undecane* (8) (22 mg, 40% yield); (7): oil; $\nu_{max.}$ (liquid film) 2 960, 2 870, 1 650, and 800 cm^{-1}; δ 5.50 (1 H, m), 3.12 (1 H, t, *J* 6.5 Hz), 2.25 (1 H, m), 1.05 (3 H, s), 0.79 (3 H, s), and 0.75 (3 H, s); *m/z* 282 and 280 (1%), 202 (9), 201 (38), 107 (22), and 95 (100); (8): m.p. 43 °C (from very concentrated light petroleum solution) (Found: C, 64.1; H, 7.4 Br, 28.4. $C_{15}H_{21}Br$ requires C, 64.1; H, 7.5; Br, 28.5%); $\nu_{max.}$ (Nujol) 3 080, 1 650, and 885 cm^{-1}; δ 4.95 (1 H, s), 4.88 (1 H, s), 3.53 (2 H, dd, AB system, *J* 11 Hz), 2.55 (1 H, m), 1.15 (3 H, s), and 1.10 (3 H, s); *m/z* 282 and 280 (1%), 202 (5), 201 (33), 107 (22), and 95 (100).

Fractional atomic co-ordinates (× 10^4) with estimated standard deviations in parentheses

Atom	*x/a*	*y/b*	*z/c*
Br	7 488(1)	5 528(1)	3 123(1)
C(1)	9 026(10)	4 536(7)	3 164(8)
C(2)	8 342(9)	3 429(6)	2 687(7)
C(3)	9 740(9)	2 685(6)	2 859(7)
C(4)	9 541(9)	1 655(6)	3 399(7)
C(5)	7 862(9)	1 136(6)	2 460(8)
C(6)	6 671(9)	1 975(6)	2 471(8)
C(7)	7 800(9)	2 800(6)	3 453(7)
C(8)	6 912(9)	3 394(6)	1 351(7)
C(9)	5 770(8)	2 490(6)	1 189(7)
C(10)	5 709(10)	1 611(7)	347(8)
C(11)	7 351(10)	1 064(7)	1 110(8)
C(12)	7 757(12)	28(7)	2 978(10)
C(13)	9 277(10)	2 129(7)	4 381(7)
C(14)	6 653(10)	4 053(7)	453(8)
C(15)	4 085(10)	2 936(8)	744(9)
H(11)	9 325(83)	4 850(59)	2 503(67)
H(12)	9 940(93)	4 510(65)	4 060(71)
H(31)	9 495(82)	2 576(57)	1 988(63)
H(32)	10 808(75)	3 006(50)	3 496(57)
H(4)	10 637(76)	1 162(54)	3 842(60)
H(6)	5 944(96)	1 682(69)	2 656(75)
H(7)	7 419(85)	3 399(61)	3 910(69)
H(101)	5 456(88)	1 865(62)	−470(68)
H(102)	4 821(99)	1 172(67)	221(77)
H(111)	7 256(103)	389(73)	773(80)
H(112)	8 153(89)	1 595(64)	975(70)
H(121)	8 462(128)	−548(88)	2 793(96)
H(122)	6 584(120)	−144(81)	2 270(91)
H(123)	8 295(112)	−19(79)	4 004(87)
H(131)	9 101(118)	1 542(86)	5 013(93)
H(132)	10 132(74)	2 566(49)	5 008(56)
H(141)	5 726(100)	4 044(70)	−448(77)
H(142)	7 533(102)	4 604(70)	600(77)
H(151)	3 405(120)	3 380(120)	12(120)
H(152)	4 264(70)	3 444(48)	1 353(54)
H(153)	3 410(89)	2 213(63)	818(68)

Crystal Data for Compound (8).—$C_{15}H_{21}Br$, M = 280.9. Monoclinic, a = 9.948(1), b = 12.537(1), c = 12.944(1) Å, β = 123.37(1)°, V = 1 348.1 $Å^3$, D_c = 1.38 g cm^{-3}, Z = 4, μ = (Cu-K_α) 4.33 mm^{-1}. Space group $P2_1/c$. Small crystals were exposed in a Lindemann glass capillary to Ni-filtered Cu-K_α radiation on an automated Siemens AED single-crystal diffractometer at room temperature. Cell parameters and intensity measurements were made with the ω–2θ scanning technique. 1 822 Reflections were collected in the 2θ range 5—120° of which 1 465 [$I > 2\sigma(I)$] were considered to be observed and were used in the subsequent analysis. The structure was solved by application of the heavy-atom method followed by Fourier synthesis. Full matrix least-squares refinement gave a final *R*-factor of 0.059. Final positional parameters are in the Table, and C–Br and C–C distances are shown in the Figure.*

[0/016 *Received*, 21*st January*, 1980]

* Tables of observed and calculated structure factors, and thermal parameters are available as Supplementary Publication No. SUP 22922 (6 pp.). For details, see Notice to Authors No. 7 in *J. Chem. Soc., Perkin Trans. 1*, 1980, Index issue.

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