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TOTAL SYNTHESIS OF (±)-SESQUICARENE[1]

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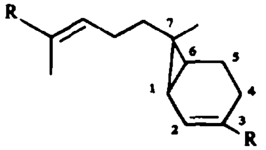
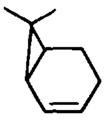
Abstract—Two synthetic routes from farnesol to (±)-sesquicarene (**1**) involving intramolecular carbenoid cyclization of acyclic precursors as the key step are described. The diazoketone (**4**) derived from 2,6,10-trimethylundeca-5,9-dienoic acid (**14**) undergoes efficient copper-catalyzed cyclization to sesquicarone (**5**). Sesquicarene is obtained by pyrolysis of the sodium salt of the *p*-toluenesulfonylhydrazone of **5**. A direct cyclization of farnesal *p*-toluenesulfonylhydrazone (**17**) also affords (±)-**1** in low yield.

A new sesquiterpene recently isolated from the essential oil of the fruit of *Schisandra chinensis* Baill. has been assigned structure **1**.[2] The name sesquicarene given to this hydrocarbon conveys its structural similarity to the related monoterpene Δ^2-carene **2**. The isopentenyl side was assigned the *exo* orientation with respect to the bicyclic nucleus on the basis of NMR and chemical evidence. Serenin, the sperm attractant of the female gametes of the water mold *Allomyces*, has been shown to be the sesquicarene diol **3**.[3] In this paper we describe two synthetic routes to (±)-sesquicarene originating from farnesol which confirm both the structure and stereochemistry of this new sesquiterpene hydrocarbon.[4-6]



1: R = Me
3: R = CH_2OH



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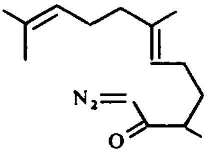
Our synthetic plan involved assembly of the bicyclo[4.1.0]-heptane nucleus by means of an intramolecular carbenoid addition. The copper catalyzed cyclization of unsaturated diazoketones[7,8] offers a facile and reliable experimental means for effecting this transformation and had in fact been used in a synthesis of 2-carone.[9] Thus diazoketone **4** with a *trans* geometry about the 6,7 double bond should give sesquicarone **5** with the correct *exo* configuration for the isopentyl side chain. Although the stereospecific nature of such keto-carbenoid additions to unsymmetrical double bonds was not in fact established until very recently, the stereospecific copper-catalysed addition of ethyl diazoacetate to *cis*- and *trans*-2-butene[10] presaged the outcome.[8]

Natural farnesol (**6**), known to have the internal (6,7) double bond in the required *trans* geometry,[11] was selected as the starting point for the preparation of diazoketone **4**. Oxidation of farnesol with chromium trioxide in pyridine gave farnesal (**7**) which when submitted to slightly modified retro-aldolization conditions[12] gave



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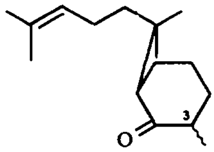
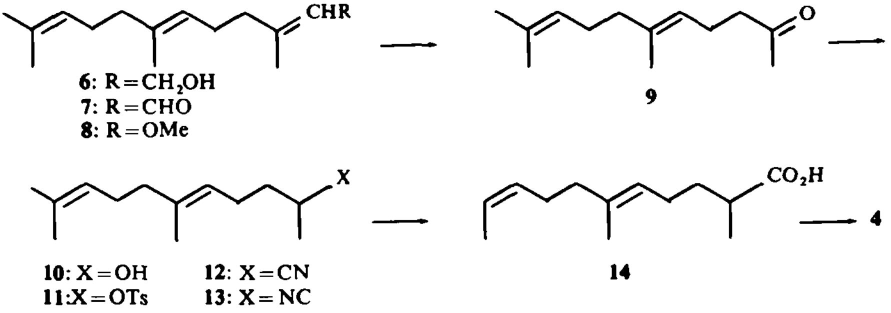


5a: 3-*endo*-Me
5b: 3-*exo*-Me

geranylacetone **9**. Sodium borhydride reduction of **9** furnished carbinol **10** which was next converted to the corresponding *p*-toluenesulfonate **11**.

Reaction of **11** with excess sodium cyanide in dimethylsulfoxide at 59° afforded mainly the desired nitrile **12** (46%) along with a small amount (11%) of the isonitrile **13**.

The latter was separated by column chromatography on silica gel. If dimethylformamide was used for the substitution reaction, higher temperature were required leading to increased elimination and lower yields of **12**. The conversion of **11** to **12** appears to be one of few reported cases of cyanide displacement of an unactivated secondary tosylate.[13]



6: R=CH_2OH
7: R=CHO
8: R=OMe

9

10: X=OH
11: X=OTs

12: X=CN
13: X=NC

14

The nitrile was hydrolyzed with potassium hydroxide in aqueous ethanol to the liquid carboxylic acid **14** in 93% yield.[*] The diazoketone **4** was obtained from the corresponding acid chloride by reaction with diazomethane in ether. The intramolecular cyclization of **4** was effected by treatment with copper powder in tetrahydrofuran producing sesquicarone (**5**) in 54% overall yield from **14**. The NMR spectrum of this material showed two sharp and approximately equally intense singlets ($\delta^{\mathrm{CDCl_3}}$ 1·09 and 1·20) for the quaternary Me group, thus indicating a 1 : 1 mixture of epimers at the secondary Me group.[†]

The higher field signal is assigned to the *endo* isomer **5a** (isosesquicarone) in view of the NMR data reported for the corresponding carone isomers (δ 1·07 and 1·18).[15] Equilibration with sodium ethoxide in ethanol increased the proportion of the more

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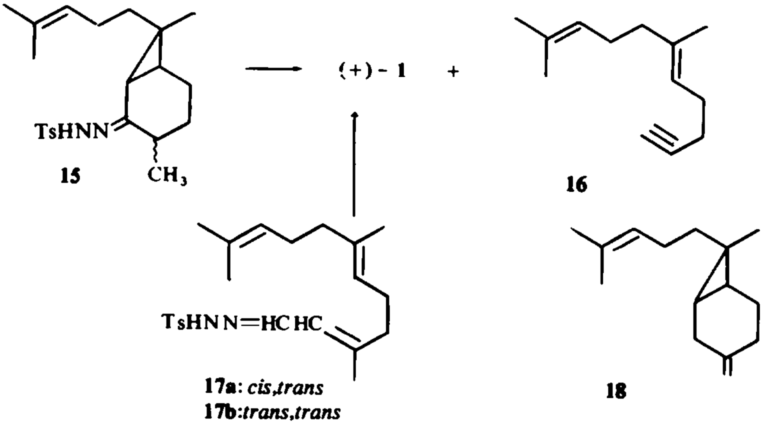
[*] An attempt to prepare **14** via the methyl enol ether **8** was unsuccessful owing to difficulties encountered in the acid-catalyzed hydrolysis of **8**.[14]

[†] In contrast Mori and Matsui report that cyclization of **4**[5b] and 1-diazo-3,7,11-trimethyldocen-6-en-2-one[9b] (as mixtures of *cis* and *trans* isomers about the 6,7 double bond) with copper powder and cupric sulfate in cyclohexane afford only the more stable 3-*exo* sesquicarones and dihydro-sesquicarones respectively (both as mixtures of C-7 epimers).

stable *exo* epimer **5b** (sesquicarone) to about 80%. The corresponding carone ⇌ isocarone equilibrium distribution is 87 : 13.[15]

The conversion of sesquicarone to sesquicarene was accomplished at best in poor yield. Although a variety of approaches were explored in a rather cursory way,[14] it appeared that side reactions involving cleavage of the cyclopropane occurred under quite mild conditions and could not be avoided.*

The equilibrated sesquicarone isomer mixture **5** was converted to the *p*-toluenesulfonylhydrazone by reaction with *p*-toluenesulfonylhydrazine. Pyrolysis of the sodium salt of the tosylhydrazone in diglyme at 140° produced (±)-sesquicarene (**1**) in 15% yield. The major product was the dienyne **16** (53%) resulting from scission of both cyclopropane ring bonds, i.e., the reverse of the original carbenoid cycloaddition reaction **4** → **5**. Similar results have recently been reported for the decomposition of carone *p*-toluenesulfonylhydrazone.[17]



A direct carbenoid cyclization of farnesol, to sesquicarene, a process which corresponds in the overall sense to the biogenesis of the bicyclic nucleus,† was also examined.[5c,d, 18] The mixture of *trans,trans* and *cis,trans*-farnesals **7** was converted to the corresponding *p*-toluenesulfonyl hydrazones (**17**). Pyrolysis of the mixed hydrazones in the presence of sodium hydride and copper powder afforded racemic sesquicarene in 5% yield after chromatography on silica gel impregnated with silver nitrate. In the absence of copper the yield decreased to about 1·5%.

Immediate thin layer chromatographic (TLC) analysis of the product mixture revealed the presence of two other components in the reaction mixture. One of these, possibly the cyclopropene resulting from cyclization with the 2,3-double bond,[18,19] disappeared rapidly and was not isolated. The other product (2%) although not fully characterized, was evidently obtained in a pure state. The NMR spectrum of this material is consistent with structure **18**, the exocyclic double bond isomer of sesquicarene.

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* For example, iodination of sesquicarone hydrazone at 12° evidently produced mainly a ring-opened monocyclic diiodide (rather than the expected 2-iodosesquicarene[16]) and the corresponding dehydroiodination products.

† The biosynthesis may in fact involve two discrete steps: initial formation of the 6-membered ring (bisabolene carbonium ion) followed by 1–3 proton elimination which leads to the cyclopropane ring.[3]

In order to test the geometric specificity of the cyclization, **17**→(±)-**1**, we separated *trans,trans*-farnesal tosylhydrazone **16b** from the isomer mixture and subjected it to the same reaction conditions. Although a small amount (~1%) of sesquicarene was detected in this reaction, it may have been due to the presence of 10–15% of the *cis,trans* isomer **16a**. The substantial reduction in yield indicates that the efficiency of the copper-catalyzed cyclization is dependent upon the double bond geometry. This result contrasts with the lack of specificity noted in the photochemically-induced cyclization of the diazo compounds derived from citral and neral hydrazones.[18] The sesquicarene formed from the mixture of tosylhydrazones **17** must be derived mainly from the *cis,trans* isomer **17a**. (The yield of ±-**1** based on **17a** would be about ~12–15%).

The NMR, IR and mass spectral data for the synthetic sesquicarene agree well with the values reported for the natural product.[2] In addition, the complete IR and NMR spectra of the synthetic and natural materials were found to be identical in a direct comparison.* These total syntheses, therefore, confirm both the structure and stereochemistry of natural sesquicarene.

EXPERIMENTAL

IR spectra were determined on a Perkin-Elmer Infracord instrument as thin films in all cases. The NMR spectral data were obtained with Varian A-60 instrument and refer to TMS as internal reference. M.p.s are uncorrected. Gas chromatographic analyses were performed with a Varian Aerograph Model 600D (HyFi, flame ionization detection) using a 5′ × $\frac{1}{8}$″ column of 5% SE-30 on chromosorb W.

Farnesal (3,7,11-*trimethyldodeca*-2,6,10-*trienal* (**7**). In a one liter 3-necked flask equipped with a mechanical stirrer, thermometer, and addition funnel, 490 ml (6·2 mol) pyridine was stirred with cooling by an ice-water bath. Chromium trioxide (43·4 g, 0·43 mol) was added over a period of 20 min. To the resulting suspension of pyridine and yellow complex was added dropwise 31·1 g (0·14 moles) farnesol (Givaudan Corp.) in 50 ml pyridine during 5 min. The black mixture was stirred for 30 min while warming to room temp, then allowed to stand for 16 hr. After this period, the reaction mixture was poured into 2 liters water, and the resulting mixture was extracted with 3 portions ether totaling 1750 ml. The combined ether extracts were washed successively with two 200 ml portions water, 3 portions 10% HCl totaling 800 ml, and two 100 ml portions water. The ethereal extract was dried over $NaSO_4$. Evaporation of solvent yielded 28·6 g (92%) of a yellow oil (**7**) which was used without further purification: δ^{CDCl_3} 10·00 and 9·90 (2d, $J = 8$Hz, 0·67 H and 0·33 H); 2,4-dinitrophenylhydrazone, m.p. 92–94°. (Found: C, 63·32; H, 7·11; N, 13·97; $C_{21}H_{28}N_4O_4$ requires; C, 62·98; H, 7·05; N, 13·99).

Geranyl acetone (6,10,-*dimethyl*-5,9-*undecadien*-2-*one*, (**9**).[12] A mixture of 27 g (0·12 mol) farnesal, 27 g (0·20 mol) K_2CO_3, 270 ml water, and 200 ml dioxan was heated at reflux under a stream of N_2 for 14 hr. The reaction was terminated when the gas chromatography peaks for the isomeric farnesals had disappeared. A dark red oily layer was separated from the mixture. The remaining water–dioxan soln was extracted with three 100 ml portions light petroleum (30–60°). The extracts were combines with the red oil and dried (Na_2SO_4). Evaporation of solvent yielded 31·3 g liquid which was distilled affording 13·4 g (57% of **9** as a clear oil, b.p. 94–95·5°/1 mm).

6,10-*Dimethylundeca*-5,9-*dien*-2-*ol* (**10**). To a stirred soln of 10·6 g (88·6 mmol) of (**9**) in 105 ml MeOH was added 2·58 g (68·2 mmol) $NaBH_4$. After 15 min at room temp the soln was extracted with three 100 ml portions light petroleum (30–60°), then diluted with 50 ml water and extracted with two additional 50 ml portions light petroleum. The combined extracts were washed twice with water and dried (Na_2SO_4). Removal of solvent yielded 11·5 g (100%) of a clear, colorless oil; ν_{max} 3340, 2910, 2880, 1430. 1360, and 1120 cm^{-1}; δ^{CDCl_3}1·19 (d, $J = 7$ Hz, —CHOHC$\underline{H}_3$), 1·61 and 1·69 (C=CCH$_3$), 1·9–2·2 (br,═C—CH$_2$—) 3·80 (sextet $J = 7$ Hz, —C$\underline{H}$OHCH$_3$), 5·15 (br t,═Ch—). (Found: C, 79·18; H, 12·41; $C_{13}H_{24}O$ requires: C, 79·53; H, 12·32).

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* We would like to thank Dr. Hirose for making this spectral comparison.

6,10-*Dimethylundeca-5,9-dien-2yl toluenesulfonate* (**11**). *p*-Toluenesulfonyl chloride (11·7 g, 61·4 mmol) in a small amount pyridine was added to a soln of 11 g (56·0 mmol) of **10** in 18 ml pyridine. The mixture was allowed to stand at room temp for 12·5 hr although precipitation of pyridine hydrochloride appeared complete within 1 hr. Water was added, and the mixture was extracted with three 100 ml portions light petroleum (30–60°). The extracts were washed with two 50 ml portions 1 NHCl, once with water, and dried (Na_2SO_4). Removal of solvent yielded 16·9 g (85%) of a clear, golden oil; ν_{max} 2900, 1500, 1435, 1350, 1180, 1168, 1092, 893, and 811 cm^{-1}; δ^{CDCl_3}1·29 (d, $J = 6$Hz, $-CHOTsC\underline{H}_3$), 1·53, 1·60, and 1·69 (s, $=C-CH_3$), 2·0 (br s, $=C-CH_2$), 2·43 (s, $ArCH_3$), 4·63 (sextet, $J = 6$ Hz, $-C\underline{H}OTsCH_3$), 4·97 (br t, $=CH-$), 7·34 and 7·78 (AB doublet, $J = 8$Hz, ArH).

2,6,10-*Trimethylundeca-5,9-diene nitrile* (**12**). To a stirred soln of 17·2 g (0·35 mol) NaCN in 350 ml DMSO under N_2 at 59° was added 14·9 g (42·6 mmol) of **11**. The soln was stirred for 2 hr, cooled, and poured into 1200 ml water. The aqueous mixture was extracted with three 300 ml portions light petroleum (30–60°). The light petroleum extracts were washed twice with 100 ml portions water and dried (Na_2SO_4). Removal of solvent yielded 8·7 g of a golden oil. This oil was dissolved in light petroleum (30–60°) and chromatographed on 366 g silica gel. The first 150 ml of 3% ether in light petroleum eluted mainly **13** (ν_{max} 2110 cm^{-1}). The next 150 ml of the same solvent eluted a mixture of **12**(70%) and **13** (30%). The next 650 ml eluted essentially pure **12** as a yellow liquid. The yield of nitrile was 46%, and of isonitrile 11%. The spectral data for **12** are as follows: ν_{max} 2890, 2210, 1439, 1368, 1100, and 830 cm^{-1}; δ^{CDCl_3} 1.30 (d, $J = 7$, $-CHCN\underline{CH}_3$), 1·62, 1·65, 1·68 (3 overlapping s, $=C-CH_3$), 2·56 (sexet, $J \sim 7$ Hz, $-C\underline{H}CNCH_3$), 5·08 (br t, $=CH$). (Found: C, 81·81; H, 11·12; N, 7·10; $C_{14}H_{23}N$ requires: C, 81·89; H, 11·29; N, 6·82).

2,6,10-*Trimethylundeca-5,9-dienoic acid* (**14**). The nitrile **12** (2·6 g, 12·7 mmol) was heated at reflux for 24 hr under a N_2 with 11·1 g (198 mmol) KOH in 36 ml (99 mmol water) 95% EtOH. The mixture was cooled and poured in 200 ml water. The resulting mixture was acidified with 10% H_2SO_4 and extracted with three 50 ml portions ether. The combined ether extracts were washed with two 15 ml portions water and dried (Na_2SO_4). Solvent removal yielded 2·5 g of a yellow oil. Purification was accomplished by extraction into 5% NaOH aq, acidification and extraction with ether. The acid was obtained in 93% yield: ν_{max} 2880, 1690, 1445, 1365, 1275, 1230, 1100, and 937 cm^{-1}; δ^{CDCl_3} 1·18 (d, $J = 7$ Hz, $-CHC\underline{H}_3$), 1·63 (s, 2 $=C-CH_3$), 1·63 (s, $=C-CH_3$), 1·9–2·1 ($=C-CH_2$), 2·46 (partially hidden sextet, $J = 7$ Hz, $-C\underline{H}CO_2H$), and 11·35 (br, $-COOH$). The corresponding amide was prepared from the acid chloride (see below): m.p. 76·5–77·5°, (Found: C, 75·59; H, 11·53; N, 6·37. $C_{14}H_{25}NO$ requires; C, 75·28; H, 11·28).

Diazoketone **4**. To a stirred soln of **14** (2·1 g, 9·9 mmol) in 48 ml benzene was added dropwise 5·8 ml (43·9 mmol) oxalyl chloride. The soln was allowed to stand at room temp for 2 hr. Solvent removal afforded 2·5 g of the acid chloride as a yellow oil: ν_{max} 2890, 1174, 1140, 1365, 930, and 702 cm^{-1}.

A soln of 2·5 g (10·8 mmol) of the acid chloride in 16 ml benzene was added dropwise to a stirred ethereal soln of diazomethane at 0° prepared from 4 g (38·8 mmol) N-methyl nitrosourea. The soln was allowed to stand at room temp for 3 hr. Removal of solvent yielded 2·6 g of a yellow oil: ν_{max} 2870, 2080, 1630, 1435, 1360, 1310, 1140, and 1040 cm^{-1}.

3,7-*Dimethyl-7-exo-(4-methyl-3-pentenyl)bicyclo*[4.1.0]*heptan-2-one* (*sesquicarone*, **5**). A soln of 2·6 g (10·8 mmol) of crude **4** in 16 ml THF was added dropwise to a stirred, refluxing suspension of 1·3 g Cu powder in 32 ml THF under N_2. After 17 hr, the mixture was cooled and filtered. Removal of solvent yielded 2·1 g of a golden brown oil. The oil was dissolved in 10% ether in light petroleum (30–60°) and chromatographed on silica gel. The first 270 ml solvent eluted 542 mg of less polar substances. An additional 230 ml of eluant contained 1·15 g (54% from **14**) of **5**: ν_{max} 2880, 1670, 1435, 1360, 1210, and 887 cm^{-1}; δ^{CDCl_3} 1·03 (partially hidden d, $J \sim 6$ Hz), 1·09 (s, C_7-CH_3 of **5a**), 1·20 (s, C_7-CH_3 of **5b**), 1·25–1·46 (m, cyclopropane H), 1·61 and 1·68 ($=C-CH_3$), 5·07 (br t, $=CH$). The mixture of sesquicarone isomers was equilibrated by treatment with 300 mg Na in 7 ml EtOH for 13 hr at room temp.[15] The NMR spectrum of the recovered material was unchanged except for the relative intensities of the signals at δ 1·09 and 1·20 (ca. 4 : 1 after correction for the overlapping half of the doublet at δ 1·03).

Sesquicarone p-*toluenesulfonylhydrazone* (**15**). To a stirred soln of 148 mg (0·7 mmol) of the equilibrated mixture of sesquicarones in 2 ml MeOH was added 131 mg (0·7 mmol) *p*-toluenesulfonylhydrazine in 2 ml THF. The soln was stirred for 47 hr under N_2 at room temp. Removal of solvent yielded 250 mg of viscous yellow oil. The oil was dissolved in 65/35 light petroleum/ether solvent and chromatographed on 10 g silica gel. After chromatography and crystallization from light petroleum there was obtained 177 mg (68%) of **15**: m.p. 99–100°, ν_{max} 3200, 2890, 1580, 1435, 1370, 1320, 1160, 1085, 1010, and 810 cm^{-1}; 0·53 and 0·64 (s, C$_7$—CH$_3$ for the two C-3 epimers, 1:4.4), 1·05 (d, $J=7$ Hz, —CHC$\underline{\mathrm{H}}_3$), 1·62 and 1·69 (s, =C—CH$_3$), 2·40 (s, Ar-CH$_3$), 5·05 (br t, =CH—), 7·25 and 7·78 (AB doublet, $J=8$Hz, Ar$\underline{\mathrm{H}}$); (Found: C, 68·26; H, 8·36; N, 7·24. $C_{22}H_{32}N_2SO_2$ requires: C, 68·01; H, 8·30; N, 7·21).

(+)-*Sesquicarene* (**1**). A. The *p*-toluenesulfonylhydrazone **15** (166 mg, 0·4 mmol) was added to a suspension of 18·5 mg (0·77 mmol) sodium hydride in 2 ml diglyme (distilled from sodium hydride). When H_2 evolution had subsided, the reaction vessel (equipped with a condenser and $CaSO_4$ drying tube) was immersed in an oil bath heated to 140°. When N_2 evolution had ceased, the mixture was cooled and poured into 5 ml water. This mixture was extracted 3 times with 5 ml portions light petroleum (30–60°). The combined extracts were washed 6 times with 5 ml portions water and dried (Na_2SO_4). Removal of solvent yielded 83 mg of a light yellow oil. After filtering this oil over silica gel, 62 mg material was recovered. A 48 mg portion of this oil was dissolved in light petroleum (30–60°) and chromatographed on 5 g of silica gel. The first 10 ml solvent eluted some nonpolar impurities. An additional 5 ml solvent eluted 10 mg (15%) (±)-sesquicarene with GLPC retention times and IR and NMR spectra identical to the material obtained in part B (see below). An additional 20 ml solvent eluted another 34 mg (55%) of **16**: $\nu_{\max}$ 3300, 2950, 2890, 2820, 2100 (weak), 1440, 1370, 1100, and 835 cm^{-1}; $\delta^{\mathrm{CCl_4}}$ (d, $J=7$ Hz, —CHCH$_3$), 1·62 (s, 2 =C—CH$_3$), 1·68 (s, =C—CH$_3$), 1·87 (d, $J = 2$ Hz, ≡C—H), 5·05 (br t, =CH); (Found: C, 88·02; H, 11·72. $C_{15}H_{24}$ requires: 88·16; H, 11·84).

B. To a stirred soln of 7 g (31·8 mmol) farnesal in 28 ml dry MeOH was added 8·4 g *p*-toluenesulfonylhydrazine in 42 ml THF. Removal of solvent yielded 15·4 g (100%) of **17** as a viscous yellow oil: $\nu_{\max}$ 3150, 2870, 1625, 1580, 1430, 1360, 1320, 1155, 1085, 1035, 910, 810, and 700 cm^{-1}.

To a suspension of 0·48 g (20 mmol) sodium hydride in 70 ml dry diglyme was added 3·83 g (10·4 mmol) crude *p*-toluenesulfonylhydrazone. When H_2 evolution had subsided, 3 g Cu powder was added and the reaction vessel was immersed in an oil bath heated to 140°. After 15 min when N_2 evolution was completed, the mixture was cooled, poured into 200 ml water, and extracted with three 100 ml portions light petroleum (30–60°). The combined extracts were washed with 6 portions water and dried (Na_2SO_4). Solvent removal yielded 1·76 g yellow oil. Filtering over silica gel resulted in recovery of 253 mg light yellow oil. This oil was dissolved on light petroleum (30–60°) and chromatographed on 25 g silica gel impregnated with 15% $AgNO_3$. The first 50 ml of 6% ether in light petroleum eluted 92 mg (5·3%) of **1** as a light yellow oil: $\nu_{\max}$ 2920, 1670, 1450, 1375, and 828 cm^{-1}; $\delta^{\mathrm{CCl_4}}$ 0·82 (s, C$_7$—CH$_3$), 1·10–1·33 (m, cyclopropane H), 1·59 (s, =C—CH$_3$), 1·65 (s, 2 =C—CH$_3$), 5·03 (br t, side chain =CH), 5·54 (br s, ring =CH). The mass spectrum had an M$^+$ peak of 204 and base peak of 119. These spectral data are in excellent agreement with the values reported for natural sesquicarene.[2] Further elution with 50 ml of 6% ether and 100 ml of 10% ether afforded fractions containing 39 mg (2·2%) of another light yellow oil **18**. $\delta^{\mathrm{CCl_4}}$ 0·05–0·50 (m, cyclopropane H), 1·20 (s, C$_7$—CH$_3$), 1·60 and 1·65 (s, =C—CH$_3$), 4·51 (br s) and 4·83 (t, $J=2$Hz, =CH$_2$), 5·06 (br, t, =CH); $\nu_{\max}$ 887 cm^{-1} (=CH$_2$). Later fractions (20% and 50% ether) yielded 78 mg of a third unidentified component.

A 750 mg portion of crude **17** was dissolved in 60:40 light petroleum (30–60°)/ether and chromatographed on 40 g of silica gel. The initial 140 ml of solvent removed less polar impurities.

The next 50 ml solvent eluted 203 mg of mixed *p*-toluenesulfonylhydrazones somewhat enriched in the *cis, trans*-isomer **17a**. The final 150 ml of solvent eluted 418 mg of fairly pure *trans,trans* hydrazone **17b**: $\delta^{\mathrm{CDCl_3}}$ 1·59 (s, 2 =C—CH$_3$) 1·68 (s, =C—CH$_3$) 1·78 (d, $J=1$ Hz, =C—CH$_3$), 2·41 (s, ArCH$_3$), 5·09 (br s, 2=CH), 5·90 (br d, $J=10$ Hz, =C$\underline{\mathrm{H}}$—CH=N—), 7·24 and 7·80 (AB doublet, $J=8$ Hz, ArH), 7·76 (d, $J=10$ Hz, overlaps 7·80 d, —CH=N—), 8·58 (br s, —NH—). The original mixture and the earlier fractions gave very similar NMR spectra except that two doublets were observed at δ 1·78 and 1·82 (2 d, $J=1$ Hz, =C—CH$_3$), presumably due to the presence of the *cis,trans* isomer **17a**. The more polar component may be assigned the *trans,trans* geometry in view of the relatively high yield.

A portion of the purified *trans,trans-p*-toluenesulfonylhydrazone **17b** (133 mg, 0·34 mmol) was subjected to the reaction with sodium hydride and Cu powder exactly as described above. GLPC analysis (farnesol as internal standard) on the crude product (43 mg) indicated with presence of about 1 mg (~ 1%) of sesquicarene.

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