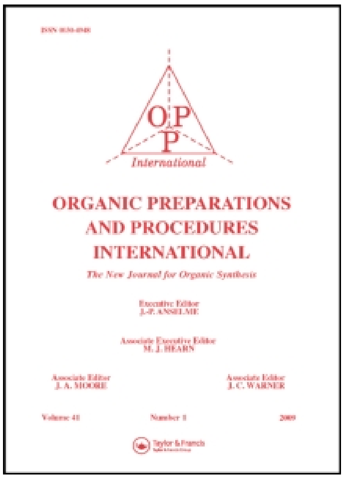

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INTERNALLY BRANCHED 1,5,9-TRIMETHYLALKANES

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INTERNALLY BRANCHED 1,5,9-TRIMETHYLALKANES

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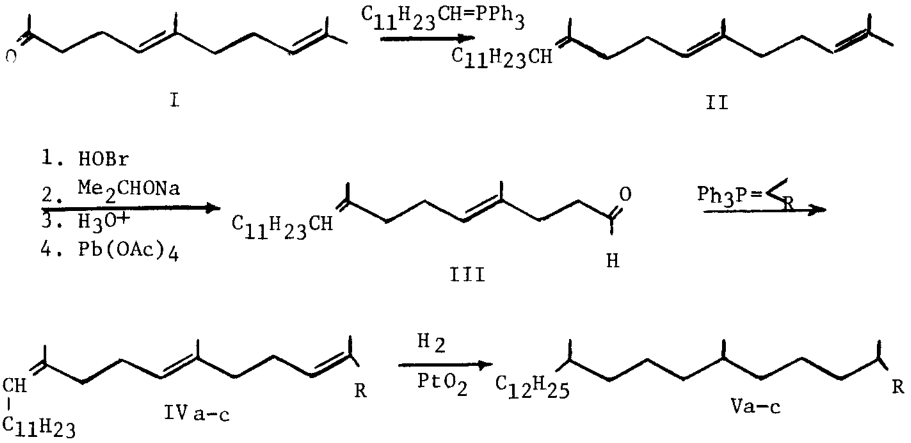
Examination of insect cuticular hydrocarbons has revealed the presence of both normal, methyl-,1,5-dimethyl- and 1,5,9-trimethylalkanes.[1] The dimethyl- and trimethylalkanes are internally branched, the methyl branches being so located as to suggest a hybridization of fatty acid and isoprene biosynthesis. These compounds have heretofore not been readily accessible although an elegant but lengthy synthesis of a 1,5,9-trimethylalkane has been described.[2] Insect-borne hydrocarbons have been occasion-



a, R = $C_{12}H_{25}$; b, R = $C_{14}H_{29}$; c, R = $C_{16}H_{33}$

ally implicated as sex attractants,[3] as stimulants to mating [4] or as parasite oviposition stimulants.[5] Because of their potential utility in insect pest control and because the natural mixtures are sufficiently complex so as to hinder identification, a general route to the more highly substituted hydrocarbons was sought. This would permit the routine preparation of compounds in sufficient quantity for corroboration of structure and for biological evaluation. We recently reported two routes to the 1,5-dimethylalkanes [6] and now describe a synthesis of the 1,5,9-trimethylalkanes.

The compounds prepared were 13,17,21-trimethyltri- 13,17,21-trimethylpenta- and 13,17,21-trimethylheptatriacontane, Va-c. Compounds Vb and Vc have been identified from the tobacco hornworm, *Manduca sexta* (L.).[7] The preparations of Va-c indicate how a common intermediate (in this case dienal III) can be employed when several structurally related hydrocarbons are sought. Geranylacetone (I) [8] was allowed to react with *n*-dodecylidene-triphenylphosphorane [9] to produce the triene II. The double bond at the 2-position of II was expected to react preferentially in polar media with electrophiles since it has been demonstrated that internal unsaturation is less exposed to attack.[10] The sequence (HOBr addition, cyclization to epoxide with isopropoxide-isopropanol, hydrolysis to the diol with acid in aqueous THF and cleavage with lead tetraacetate) was accomplished with purification only at the epoxide and final stages to provide the dienal III. The reaction of II with the appropriate (α-methylalkylidene)triphenylphosphorane gave trienes IIIa-c as mixtures of the geometrical isomers. Hydrogenation with either 5% Pd/C or PtO_2 yielded the internally branched trimethylalkanes Va-c as mixtures of the diastereomers.

Although this route involves several steps the effort was considerably minimized by limiting the number of intermediate purifications. These purifications were done using column chromatography and were easily performed because of the low polarity of the compounds. Overall yields from geranylacetone were about 10%. Thus sufficient material was provided for evaluation from readily available chemicals.

EXPERIMENTAL [11]

Infrared spectra were obtained as films using a Perkin Elmer 137 infrared spectrophotometer. Nmr spectra were obtained from CCl_4 solutions using a Varian T-60 spectrometer with TMS as an internal standard and shifts are reported in ppm relative to TMS. Gas chromatographic analyses were performed on a Hewlett Packard 7620A instrument employing an OV-1 column (3% on Gas Chrom Q, 93 cm x 6.3 mm) at 270°. Thin layer chromatograms were obtained by using Brinkmann Sil G-25 UV_{254} plates (0.25 mm) with 15% ether/85% petroleum (pet.) ether as the developing solvent. Such chromatograms were convenient for monitoring column chromatographic purifications.

Synthesis of 2,6,10-trimethyl-2,6,10-docosatriene (II).- Dodecyltriphenylphosphonium bromide (26.6 g, 52 mmoles) and THF (80 ml) were slurried in an inert atmosphere and cooled in an ice bath. Butyllithium (21.6 ml of 2.4 M in hexane) was injected to form the ylid. Geranylacetone (9.7 g, 50 mmoles) was added (syringe) by using a few ml of pet ether as a rinse. The ice bath was removed and after 1 hr, the mixture was diluted with water and extracted with pet ether (this eliminated most of the triphenylphosphine oxide). The extract was washed with water, dried ($MgSO_4$) and concentrated. The crude product was placed on a column of silica gel (50 g) and the triene was eluted with pet ether (200 ml). The product was contaminated with a small amount of geranylacetone. Passage through another 50 g column of a silica gel provided pure triene 3 (6.7 g, 39%): n_D^{25} 1.4703; nmr δ 5.07 (broad triplet, $C\underline{H}=$).

Anal. Calcd for $C_{25}H_{46}$: C, 86.62; H, 13.38. Found: C, 86.59; H, 13.28.

Synthesis of 4,8-dimethyl-4,8-eicosadienal (III).- A solution of the triene 3 (6.2 g, 17.9 mmoles) and N-bromosuccinimide (3.4 g, 19 mmoles) in 1,2-dimethoxyethane was prepared. Water was added until slight cloudiness persisted in the mixture, and this mixture was allowed to stand overnight. The reaction mixture was diluted with water and extracted with pet ether. The extract was dried ($MgSO_4$), concentrated and then added to a solution of sodium isopropoxide (from 45 mmoles of hexane-washed NaH) in isopropanol (100 ml). This mixture was stirred at ambient temperature overnight. The mixture was diluted with water and extracted with pet ether. The extract was dried ($MgSO_4$), concentrated and chromatographed on silica gel (100 g) with pet ether (300 ml) and 15% ether/85% pet. ether (400 ml). The epoxide was present in the latter eluate and was sufficiently pure (tlc) to use for the next step.

The epoxide was dissolved in THF (15 ml) and water (15 ml) added; THF was added until homogeneity was achieved. Perchloric acid (5 drops of 70%) was added and the mixture was allowed to stand overnight. The solution was diluted with water and extracted with ether. The extract was dried ($MgSO_4$) and concentrated. The crude diol was added to a slurry of lead tetraacetate (4.45 g 9.4 mmoles) in benzene (50 ml). The resulting mixture was stirred at 40° for 0.75 hr. The mixture was diluted with 20% HOAc/80% H_2O (200 ml) and extracted with pet ether. The extract was washed until neutral with aqueous $NaHCO_3$, dried ($MgSO_4$) and concentrated. The crude dienal was purified by elution through silica gel (50 g), with pet. ether (150 ml) and then with 15% ether/85% pet. ether (150 ml). The latter solvent mixture eluted the aldehyde 4 (2.2 g, 38% from 3). The aldehyde was sufficiently pure for the next step: ir 3.7, 5.8 μ; nmr δ 0.35 ($C\underline{H}_2$ CHO), 5.08 ($C\underline{H}C=$), 9.70 ($C\underline{H}=O$).

Synthesis of the 1,5,9-Trimethylalkanes (Va-c).- Ethyltriphenylphosphonium bromide [9] (1.85 g, 5.0 mmoles) was converted to a phosphorane in THF (10 ml) in the usual manner.[9] The 1-bromoalkane (C_{12},C_{14}, or C_{16}) (6 mmoles) was injected and, after 5 minutes, HMPA (5 ml) was injected. The mixture was stirred overnight at room temperature. It was then diluted with 1,2-dichloroethane and washed with water several times. The organic phase was dried ($MgSO_4$) and concentrated. The residue was washed with pet ether several times to remove unreacted bromide. The crude (α-methylalkyl)triphenylphosphonium salt was dissolved in THF (10 ml) and converted to the ylid (deep red) with butyllithium (2.1 ml of 2.4 M). Aldehyde III (0.6 g, 1.9 mmoles) was added to the solution and after 0.5 hr, the mixture was diluted with water and extracted with pet ether. The extract was dried ($MgSO_4$), concentrated and filtered through silica gel (15 g) by using pet ether (50 ml). Concentration of the eluent provided the trienes which were then hydrogenated over 0.1-0.2 g of either 5% Pd/C or PtO_2in hexane (25 ml). Filtration and concentration provided the alkanes Va-c (40-50% from III). These compounds could be further purified by recrystallization from acetone at -20°.

Compound Va: n_D^{25} 1.4536

Anal. Calcd for $C_{36}H_{74}$: C, 85.29; H, 14.71. Found: C, 85.49; H, 14.52.

Compound Vb n_D^{25} 1.4548.

Anal. Calcd for $C_{38}H_{78}$: C, 85.30; H, 14.70. Found: C, 85.24; H, 14.76.

Compound Vc n_D^{25} 1.4557.

Anal. Calcd for $C_{40}H_{82}$: C, 85.31; H, 14.69. Found: C, 85.42; H, 14.58.

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11. Mention of a proprietary product does not constitute an endorsement by the U.S. Department of Agriculture.

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