mp >300 °C; UV (0.1 N HCl) λ_{max} 271 nm (ϵ 18 400); UV (H_2O) λ_{max} 280 nm (ϵ 14 500); UV (0.1 N NaOH) λ_{max} 279 nm (ϵ 14 400); ^{31}P NMR (DMSO-d_6 + D_2O) δ 1.66 (P-8); CD $[\theta]^{25}$ (nm) −5460 (280) (negative shoulder), −13 400 (263) (negative maximum), −17 080 (221) (negative maximum); for ^{1}H NMR parameters, see Tables I and II. Anal. Calcd for $C_{12}H_{16}N_5O_6P{\cdot}CF_3CO_2H$: C, 35.68; H, 3.64; N, 14.86. Found: C, 35.78; H, 3.87; N, 14.72.

Ethyl Hydrogen *P*(*R*),5′-Anhydroadenosine-8-phosphonate Trifluoroacetic Salt (4b). A solution of **3b** (160 mg, 0.40 mmol) in 80% CF_3CO_2H (2 mL) was kept at room temperature for 30 min. After evaporation of the solvent, the residue was triturated with a small amount of water to afford white needles (120 mg, 62%): mp >300 °C; UV (0.1 N HCl) λ_{max} 272 nm (ϵ 17 600); UV (H_2O) λ_{max} 281.5 nm (ϵ 13 600); UV (0.1 N NaOH) λ_{max} 279 nm (ϵ 13 500); ^{31}P NMR (DMSO-d_6 + D_2O) δ −1.50 (P-8); CD $[\theta]^{25}$ (nm) +11 370 (280) (positive maximum), −6520 (257) (negative maximum), −34 800 (220) (negative maximum); for ^{1}H NMR parameters, see Tables I and II. Anal. Calcd for $C_{12}H_{16}N_5O_6P{\cdot}{}^{4}/_{5}CF_3COOH{\cdot}2H_2O$: C, 33.71; H, 4.33; N, 14.45. Found: C, 33.68; H, 4.48; N, 14.74.

***P*,5′-Anhydroadenosine-8-phosphonic Acid (5). i.** Compound **4a** (100 mg, 0.21 mmol) was dissolved in concentrated NH_4OH (5 mL), and the mixture was warmed in a steel bomb at 50 °C overnight. After cooling, the solution was concentrated to 1 mL to give white crystals (47.3 mg, 62%): mp >300 °C; FAB-MS (positive), *m/z* 330 (M^+ + H); FAB-MS (negative), *m/z* 328 (M^+ − H); UV (0.1 N HCl) λ_{max} 269.5 nm (ϵ 19 100), 278 (sh, ϵ 13 400); UV (H_2O) λ_{max} 269.5 nm (ϵ 15 400), 275 (sh, ϵ 15 100), 285 (sh, ϵ 9700); UV (0.1 N NaOH) λ_{max} 269.5 nm (ϵ 15 400), 275 (sh, ϵ 15 000), 285 (sh, ϵ 9800); for ^{1}H NMR parameters, see Tables I and II. Anal. Calcd for $C_{10}H_{12}N_5O_6P{\cdot}NH_3{\cdot}H_2O$: C, 32.97; H, 4.70; N, 23.07. Found: C, 33.02; H, 4.47; N, 23.32.

ii. Compound **4b** (50 mg, 0.103 mmol) was treated in a similar manner to that described in section i to give white crystals (19.6 mg, 52%). The product had the same UV and ^{1}H NMR spectra as those of an authentic sample described above.

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Registry No. **1**, 13089-45-7; **2**, 103022-70-4; **3a**, 115794-10-0; **3b**, 115794-11-1; **4a**, 115705-88-9; **4b**, 115794-13-3; **5**, 115705-89-0; $ClP(OEt)_2$, 589-57-1.

Synthesis of Ethylenes with Acyclic Quaternary Carbons by Dehydration of Neopentyl Alcohols. Application of the 2-D INAPT Technique

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Di- and triquaternary ethylenes (**5**, **12** and **7**, **19**, Scheme I) have been synthesized by dehydration of *sec*- and *tert*-neopentyl alcohols (**4**, **11** and **6**, **18**) without rearrangement. It is thought that steric factors determine the structures of the products. The intermediate imines **2** and **14**, from the reaction of nitriles **1** and **13** with $t\text{-}C_4H_9Li$, may be hydrolyzed only in the first case to ketones (**3**). More highly substituted ketones (**10** and **16**) were obtained by the reaction of *t*-RMgX (**9**) or $(CH_3)_3CMgCl$ with 3,3-dialkyl and 2,3,3-trialkyl acid chlorides (**8** and **15**). Ketones **3** and **10** were reduced by $LiAlH_4$ to secondary carbinols **4** and **11**. The tertiary carbinols **6** were prepared from **3** by treatment with $t\text{-}C_4H_9Li$. The more hindered ketones **16** failed to add $t\text{-}C_4H_9Li$, but were reduced to secondary alcohols **18**, instead of the desired tertiary alcohols **17**. The carbinols **4**, **6**, **11**, and **18** were dehydrated by heating with $KHSO_4$. The 2-D INAPT NMR technique was used to establish the stereostructure of **19** by measuring the long-range heteronuclear coupling constants about the ene.

Methods of synthesis of highly hindered olefins have been investigated during the last many years with the goal of obtaining the apparently unknown tetra-*tert*-butylethylene.[1] Bulky 1,2-di- and tri-*tert*-alkylethylenes are known, and several approaches have been developed to obtain them. Among these are the extrusion method of Barton,[2] the McMurry coupling reaction of carbonyls,[3] and others of more limited applicability.[4]

Perhaps the closest approach to tetra-*tert*-butylethylene has afforded the highly strained ethyltri-*tert*-butylethylene.[5] Other crowded molecules such as tetrakis(2-formyl-2-propyl)ethylene,[6] tetrasubstituted ethylenes with "tied-back" structures,[5] tetraisopropylethylene[7] and its cyclic analogues,[8] and tri-*tert*-butylethylene are known.[9] The *tert*-butyl group has been employed most frequently to produce crowding in compounds because of its size, symmetry, and availability. Also, a number of studies of the physical and, to some extent, chemical properties of such strained substances have been carried out.[10] In the present investigation, the availability of procedures and materials for changing the structure of quaternary carbon groups[11] suggested a way of obtaining a series of trialkylethylenes with more structural variability than from the usual three- and four-carbon reagents. 3,3-Dialkyl

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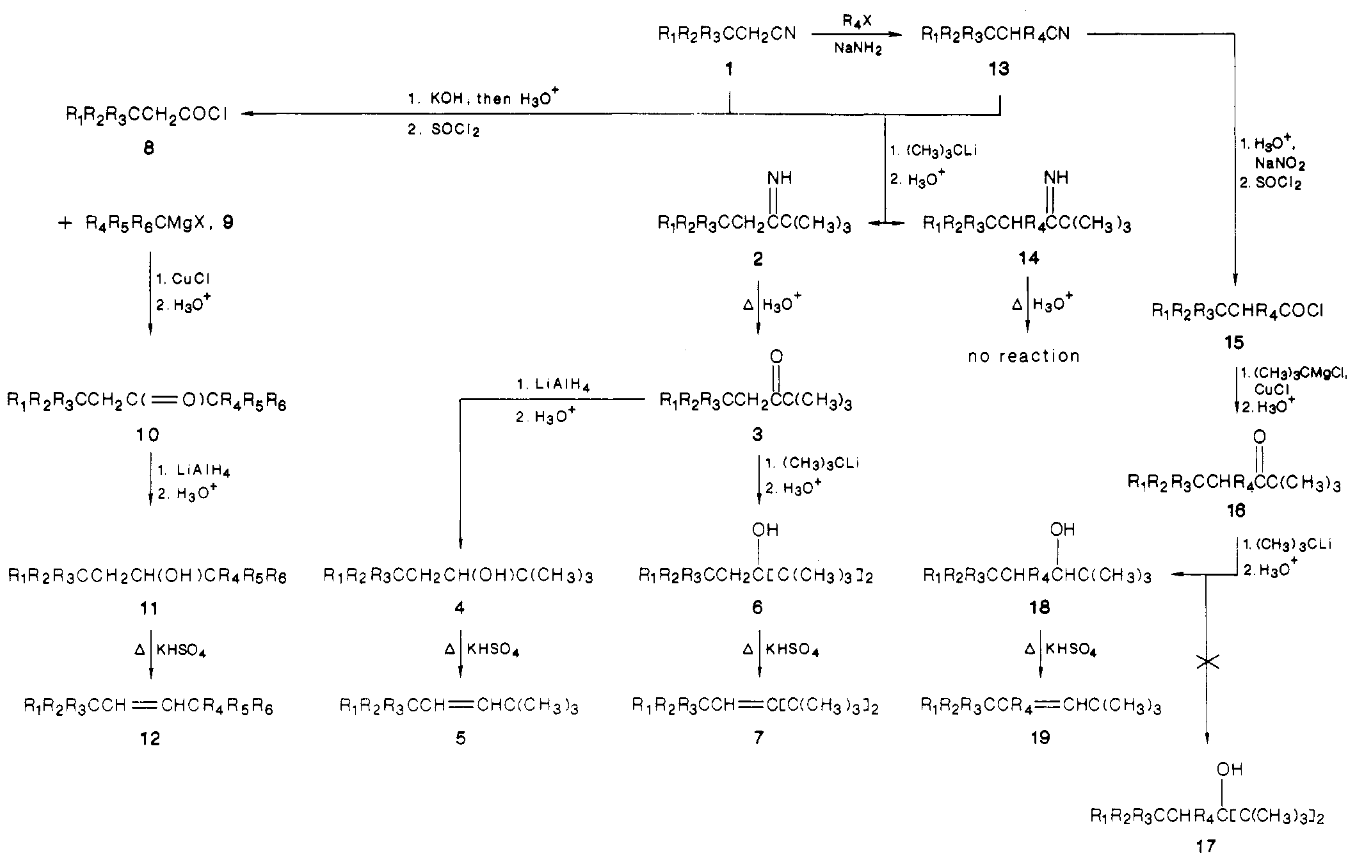
0022-3263/88/1953-4555$01.50/0

Scheme I



nitriles (1) (Scheme I) were selected as materials for building the desired molecules.

Results and Discussion

The 3,3-dialkyl nitriles (1) were available from previous studies[11] and appeared to offer an approach to 1,2-diquaternary-substituted alkenes like **5**, **7**, and **12**. Such nitriles react with *n*-alkylmagnesium halides nearly quantitatively to give 3,3-dialkyl-substituted ketones, but the reaction failed with *t*-C_4H_9MgCl.[12] In the present study, however, it was found that *t*-C_4H_9Li reacts rapidly with these nitriles and, after acidification, affords high yields of ketimines (**2**) instead of the expected ketones (**3**).[13] These ketimines are relatively stable in aqueous acid and give only a faint odor of ammonia after several months in air. Attempts to reduce them with Adams's catalyst or $LiAlH_4$ were unsuccessful. Hydrolysis of **2** to ketones **3** was accomplished only after refluxing with 50 wt % H_2SO_4 for several hours.

Addition of $(CH_3)_3CLi$ to **3** gave the tertiary carbinols **6** in yields of 65–90%. After addition of the lithium reagent at room temperature, the reaction mixtures were heated at reflux for several hours. In contrast, Bartlett and co-workers reported that 2,2,4,4-tetramethyl-3-pentanone is reduced to 66% of the carbinol plus 15% of a bimolecular product, when reacted with $(CH_3)_3CLi$ in ether at 35 °C.[14] Later Bartlett and Lefferts found that the same conditions at −60 to −70 °C produced 81% of tri-*tert*-butylcarbinol.[15] Molecular models of the two types of ketones suggest that crowding is comparable and the related carbinols are still more closely packed. The differences in results might be ascribed to the solvent systems and the $(CH_3)_3CLi$ reagents employed.

The secondary alcohols **4** were obtained by reduction of **3** and were distilled without decomposition. Prior studies indicated that *sec*-neopentyl alcohols such as **4** may undergo rearrangement on dehydration. Howard and co-workers observed that the dehydration of 2,2,5,5-tetramethyl-3-hexanol over Al_2O_3 gave, with 2,2,5,5-tetramethyl-3-hexene, a mixture of 2,3,5,5-tetramethyl-1- and -2-hexenes.[16] It might be expected that **4** would undergo similar Whitmore or Wagner–Meerwein-type rearrangements;[17] however, as reported earlier,[18] only 5,5-diethyl-2,2-dimethyl-3-nonene (**5b**) was formed when the alcohol

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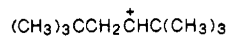
4b was heated with $KHSO_4$. The proposed structure of the product is supported by spectral data and by preparation of 3-(deuteriooxy)-5,5-diethyl-2,2-dimethylnonane-*3,4,4-d*$_3$ (**4h**), which on heating with $KHSO_4$ gave an olefin whose ^1H NMR spectrum was devoid of vinyl proton absorption. Also, its ^1H NMR spectrum is superimposable on that of 3,3-diethylheptanenitrile (**1b**), with the expected exceptions, which further supports the view that rearrangement of the carbon skeleton did not occur.

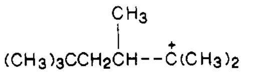
The other carbinols (**4**) were dehydrated similarly by $KHSO_4$ to afford unrearranged olefins **5a,c–f**. Since, as started earlier, 2,2,5,5-tetramethyl-3-hexanol is dehydrated over alumina to rearranged olefins, we considered the possibility that $KHSO_4$ in unique. However, heating of this carbinol with $KHSO_4$ produced essentially the same mixture of olefins as reported.[16] On the other hand, dehydration of **4b** with alumina gave over 85% of unrearranged **5b**.

These data indicate structural differences between **4b** and 2,2,5,5-tetramethyl-3-hexanol. Molecular models of the carbonium ions expected from each alcohol, as well as those that might arise from Wagner–Meerwein shifts, were constructed. The initial planar ion **20**, from the 3-hexanol, shows little steric strain, as does the cation **21** which is responsible for the two rearranged hexenes. The ion **22** from **4b** is not strained excessively; however, **23**, resulting from a methyl shift, has an extreme amount of crowding. Accordingly, it appears that the dehydration of carbinols **4** produces unrearranged alkenes **5** due to the instability of intermediate carbocations which could lead to rearranged products.



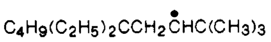
$(CH_3)_3CCH_2\overset{+}{C}HC(CH_3)_3$

20



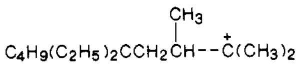
$(CH_3)_3CCH_2\overset{\overset{CH_3}{|}}{C}H{-}{-}\overset{+}{C}(CH_3)_2$

21



$C_4H_9(C_2H_5)_2CCH_2\overset{\bullet}{C}HC(CH_3)_3$

22



$C_4H_9(C_2H_5)_2CCH_2\overset{\overset{CH_3}{|}}{C}H{-}{-}\overset{+}{C}(CH_3)_2$

23

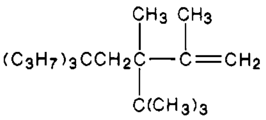
The carbinols **6** were heated with $KHSO_4$ at 180 °C for 20 h, and mixtures resulted which consisted of unchanged alcohols, ketones (**3**), and olefinic materials. The latter were separated by preparative GC to the olefins **7**. Five carbinols were dehydrated, and only in two instances were olefins obtained other than the unrearranged **7**; however, the presence of other unsaturated compounds was indicated.

Rearrangements of tertiary carbocations from highly crowded molecules such as **6** are well-known.[17] The solvolysis of tri-*tert*-butylcarbinyl *p*-nitrobenzoate gave only 2-*tert*-butyl-3,3,4,4-tetramethyl-1-pentene, which apparently arose by methyl and *tert*-butyl shifts. Similarly, the triisopropylcarbinyl ester afforded the unrearranged olefin by the loss of a proton, and an olefin formed by a methyl shift or one involving the latter followed by the rearrangement of an isopropyl group.[19] Carbinol **6c** gave a mixture of olefins, which was separated by preparative GC into three components. Their probable structures are supported by IR, NMR, and mass spectra and are represented by **7b** (38%), **24** (14%), and **25** (3%).

The method described here for synthesizing 1,2-di- or 1,1,2-tri-*tert*-alkylethylenes (**5**, **7**) is limited to the availability of tertiary organolithium reagents. At present, methods for preparing them in the laboratory do not seem to be at hand. Another approach to a more general synthesis of alkenes such as **12** appeared to be by the addition of more easily obtainable tertiary organopotassium reagents to nitriles **1**. An attempt to cause ethylmethylphenylcarbinylpotassium to react with **1c** gave only starting materials.

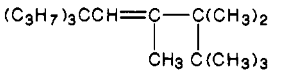
$(C_3H_7)_3CCH{=}C[C(CH_3)_3]_2$

7b



$(C_3H_7)_3CCH_2\underset{\underset{C(CH_3)_3}{|}}{\overset{\overset{CH_3}{|}}{C}}{-}\overset{\overset{CH_3}{|}}{C}{=}CH_2$

24



$(C_3H_7)_3CCH{=}\underset{\underset{CH_3}{|}}{C}{-}\underset{\underset{C(CH_3)_3}{|}}{C}(CH_3)_2$

25

The condensation of Grignard reagents with acid chlorides in the presence of inorganic salts has been shown to produce ketones in satisfactory yields in a number of cases.[20] The acids required for obtaining **12** were available from the hydrolysis of **1** and were converted to acid chlorides **8** by using $SOCl_2$. Condensation of the acid chlorides with dimethylethyl-, triethyl-, and butyldimethylcarbinylmagnesium chlorides, using CuCl, gave ketones **10** in 65–89% yield. Reduction to carbinols **11** followed by dehydration with $KHSO_4$ led to **12** in 75–91% yields. Their ene IR absorptions near 980 cm^{-1} and ^1H NMR coupling constants of 16.4 and 16.5 Hz for **12a,c** indicate trans arrangements.

Although this method offers more possibility for the synthesis of 1,2-di-*tert*-alkylethylenes, it is limited also by the accessibility of *tert*-alkylmagnesium halides. Whitmore reported that he was unable to prepare such compounds larger than butylethylmethylcarbinyl chloride.[21] Birch and Robinson found that 11-chloro-11-methylheneicosane failed to react with Mg.[22] Present attempts to make Grignard reagents larger than triethylcarbinylmagnesium chloride were difficult, and the latter was obtained only with high-speed stirring. Even this method failed with dipropylhexylcarbinyl chloride.

The alkylation of **1** has been investigated[13] and seemed to offer a way to increase the bulk in the highly substituted olefins. The 2-substituted nitriles **13** reacted readily with *tert*-butyllithium to give imines **14**. Attempts to hydrolyze them to ketones by using 10–95% H_2SO_4 were unsuccessful. An alternative approach to the substituted ketones, i.e., alkylation of **3** by alkyl halides and $NaNH_2$, failed.

The nitriles **13** were hydrolyzed to acids by the method of Sarel and Newman[23] and then converted to acid chlorides (**15**), which were reacted with $(CH_3)_3CMgCl$ in the presence of CuCl[20] to give ketones **16**. Further reaction of the ketones with $(CH_3)_3CLi$ with the intent of obtaining the highly hindered tertiary carbinols **17** gave alcohols which, on dehydration by heating with $KHSO_4$, furnished olefins whose ^1H NMR spectra displayed one vinyl proton signal. This suggested that the olefins resulted from a series of rearrangements or that the ketones **16** had been reduced to **18**. ^{13}C NMR studies of **19a–c** using the DEPT method[24] gave carbon multiplicities, and 2-D ^{13}C–^{13}C au-

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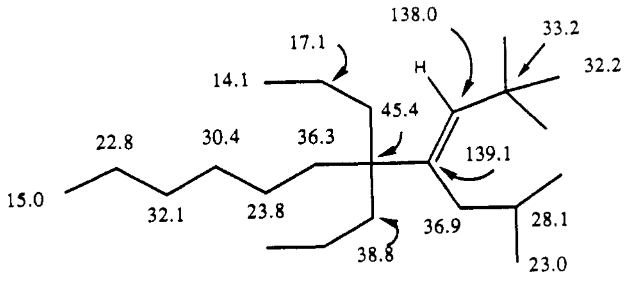

Figure 1. ^{13}C NMR assignments (75.45 MHz, ppm in $CDCl_3$) on **19c** from the 2-D autocorrelated experiment.

tocorrelated double quantum coherence spectroscopy[25] on **19c** allowed peak assignments to be made and indicated that olefins **19** have the trisubstituted ethylene structure (Figure 1). A 2-D INAPT (two-dimensional insensitive nuclei assigned by polarization transfer) spectrum[26] (see Figure 2) of **19c** afforded $^2J_{CH}$, $^3J_{CH}$, $^4J_{CH}$ values for the coupling of the olefinic proton with the adjacent olefinic C and one *tert*-butyl group, as well as the isobutyl and quaternary carbon group $R_1R_2R_3C$ (Figure 3A,B). This allowed assignment of the ene stereochemistry as depicted (*E*). Values of $^3J_{CH}$ for enes depend on geometry and generally are larger for trans- than for cis-coupled nuclei.[27] For **19c**, the $^3J_{CH}$ values found between the vinyl proton and the quaternary (δ 45.4) and the methylene (δ 36.9) carbons are 5.8 and 10.1 Hz, respectively, and are in accord with the structure depicted in Figure 1. Mass spectra of **19** are those expected of the trisubstituted ethylenes, and the UV absorptions of **19b**, λ_{max} 200.5 nm, ϵ 8930, are comparable to those of several highly branched trialkylethylenes.[28]

Obviously, **16** were reduced by $(CH_3)_3CLi$ to secondary alcohols. The reduction of carbonyls by Grignard reagents is well-known.[29] In general, it is felt that this type of reaction is less important when alkyllithium reagents are used,[30] particularly at lower temperatures; as mentioned earlier, di-*tert*-butyl ketone and $(CH_3)_3CLi$ give 81% of tri-*tert*-butylcarbinol at −60 to −70 °C,[14] but at 30–35 °C, 66% reduction occurred.[15]

Experimental Section

Boiling points are uncorrected, and IR spectra were taken on a Perkin-Elmer Model 237-B grating or 576 ST spectrophotometer. The ^1H NMR spectra were run on a Varian A-60 or a Nicolet NT-300 WB spectrometer. The latter was used also for ^{13}C NMR, operating at 300.06 and 75.45 MHz, respectively, with TMS as an internal standard for ^1H spectra and $CDCl_3$ (77.0 ppm) as an internal standard for ^{13}C spectra. Mass spectra were obtained with a Kratos MS-25 instrument with a DS-55 data system, and GC was performed on a Wilkens Aerograph or a Nester/Faust Prepko apparatus. Elemental analyses for all new compounds were supplied by Galbraith Laboratories, Inc., Knoxville, TN, and Weiler and Strauss Laboratories, Oxford, England, and were within accepted limits (0.3% or better).

Materials. The needed ethyl 2-cyano-3-alkyl-2-alkenoates were prepared by a published method.[31] They were converted to 2-cyano-3,3-dialkylalkanoates in 41–89% yields by the previously described procedure.[11] The reactants (R_3CMgBr and $R_1R_2C{=}CHCH(CN)CO_2C_2H_5$) and properties (bp, °C; $n^{25}{}_D$) for the 2-cyano-3,3-dialkylalkanoates follow: (a) R_1–R_3 = C_2H_5; 142–144 (15 mm);[11] (b) $R_1 = R_2 = C_2H_5$, $R_3 = C_4H_9$; 112–115 (0.5 mm); 1.4500;[32] (c) $R_1 = R_2 = C_2H_5$, $R_3 = C_5H_{11}$; 130–132 (2 mm); 1.4513;[33] (d) $R_1 = R_2 = C_3H_7$, $R_3 = C_5H_{11}$; 144–145 (2 mm); 1.4512; (e) $R_1 = C_2H_5$, $R_2 = C_6H_5$, $R_3 = C_4H_9$; 143–144 (0.6 mm); 1.5029; (f) $R_1 = R_2 = C_3H_7$, $R_3 = C_6H_{13}$; 150–152 (2 mm); 1.4520; (g) $R_1 = C_2H_5$, $R_2 = C_4H_9$, $R_3 = C_8H_{17}$; 153–155 (0.7 mm); 1.4539; (h) $R_1 = C_{10}H_{21}$, $R_2 = C_{11}H_{23}$, $R_3 = C_{12}H_{25}$ (see ref 11).

3,3-Dialkyl Nitriles 1. The **1** were obtained from the 2-cyano-3,3-dialkylalkanoates by hydrolysis and decarboxylation; yields 72–95%. See Table I for physical properties.

5,5-Dialkyl-2,2-dimethyl-3-alkanimines 2. The procedure used for preparing **2a** is representative. To 300 mL of *t*-C_4H_9Li (0.5 mol) in pentane was added dropwise with stirring 28 g (0.2 mol) of **1a** in 50 mL of pentane. After the addition, the solution was heated at reflux for 4 h, cooled, and treated with 10% HCl. The aqueous layer was extracted with pentane, and the combined organic layers were washed with H_2O, $NaHCO_3$, and H_2O and dried ($MgSO_4$). After removal of the pentane by distillation, the residue was distilled through a spinning-band column to give 25.7 g (65%) of **2a**.

5,5-Dialkyl-2,2-dimethyl-3-alkanones 3. These were prepared by hydrolysis of the imines **2**, as illustrated for obtaining **3a**. A mixture of 15 g (0.08 mol) of **2a** and 75 mL of 50 wt % H_2SO_4 was heated at reflux for 4 h. It was worked up, and the residue was distilled through a spinning-band column to give 11.1 g (74%) of **3a**.

5,5-Diethyl-2,2-dimethyl-3-nonanone-*4,4*-d_2 (3h). A mixture of 17.5 g (0.08 mol) of 5,5-diethyl-2,2-dimethyl-3-nonanone (**3b**), 20 g (1 mol) of D_2O, and 16.2 g (0.3 mol) of $NaOCH_3$ was heated at reflux for 50 h. The layers were separated, the D_2O–H_2O layer was extracted twice with $(C_2H_5)_2O$, and the extract was combined with the organic layer. After drying ($MgSO_4$) and removal of the $(C_2H_5)_2O$, the ^1H NMR spectrum of the crude product indicated about 80% exchange of the CH_2—C=O protons. The material was heated first with 20 g (1 mol) of D_2O and 16.2 g (0.3 mol) of $NaOCH_3$ for 90 h (ca. 90% exchange) and, finally, with 18 g (0.9 mol) of D_2O and 10 g (0.2 mol) of $NaOCH_3$ for 90 h. After workup, there resulted 16.5 g (94%) of **3h**: bp 133–135 °C (12 mm); $n^{25}{}_D$ 1.4423; IR 1715 (s), 2190 (br) cm^{-1}; ^1H NMR δ 1.09 (s, 9 H), 0.55–1.68 (m, 19 H); ca. δ 2.5 missing.

5,5-Dialkyl-2,2-dimethyl-3-alkanols 4. The alcohols were prepared from **3** by the usual $LiAlH_4$ reduction procedure. They were obtained in 76–97% yields.

5,5-Diethyl-2,2-dimethyl-3-heptanol (4a) from 3,3-Diethylpentanal. The 3,3-diethylpentanal, 13 g (58%), was obtained from the reduction of 35 g (0.2 mol) of 3,3-diethylpentanoyl chloride, bp 99–100 °C (2.5 mm), *p*-nitroanilide, mp 117–118 °C, from the corresponding acid[34] and $SOCl_2$, using 4.5 g of Pd–$BaSO_4$ catalyst, 0.5 g of quinoline-S poison, and 200 mL of xylene; bp 75–76 °C (9 mm), $n^{25}{}_D$ 1.4346. A solution of 10 g (0.07 mol) of the aldehyde in 50 mL of pentane was added dropwise to a solution of 120 mL (0.22 mol) of *t*-C_4H_9Li in pentane. The mixture was heated at reflux for 3 h, cooled, and treated with 10% HCl. The layers were separated, washed (H_2O, then $NaHCO_3$), dried ($MgSO_4$), and concentrated. On distillation, there was obtained 5.95 g (43%) of **4a**.

5,5-Diethyl-2,2-dimethyl-3-nonanol-*4,4*-d_2 (4g) and 3-(Deuteriooxy)-5,5-diethyl-2,2-dimethylnonane-*3,4,4*-d_3 (4h). A mixture of 1.15 g (0.03 mol) of $LiAlH_4$, 9 g of **3h**, and 200 mL of $(C_2H_5)_2O$ afforded 7.4 g (82%) of **4g**, bp 122–123 °C (9 mm), $n^{25}{}_D$ 1.4528.

A solution of 13.1 g (0.057 mol) of **3h** in 30 mL of $(C_2H_5)_2O$ was added to 1.45 g (0.034 mol) of $LiAlD_4$ and 100 mL of $(C_2H_5)_2O$.

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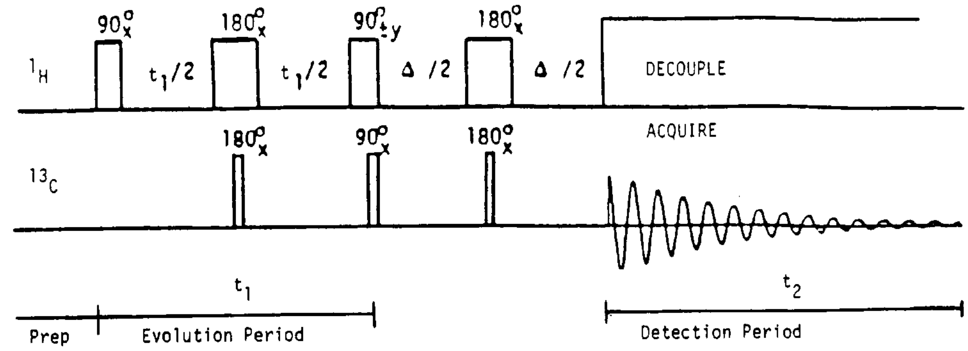

Figure 2. Basic pulse sequence of 2-D INAPT. This sequence was like Bax's 1-D INAPT pulse sequence[26] with the modification that the evolution period t_1 was incremented regularly. All proton pulses were soft and applied to a single proton resonance. This afforded a selective long range heteronuclear 2-D J-resolved spectrum (Figure 3A) that contained only resonances from carbon atoms two, three, or four bonds removed from the proton, with coupling constants ranging from ~1 to 10 Hz.

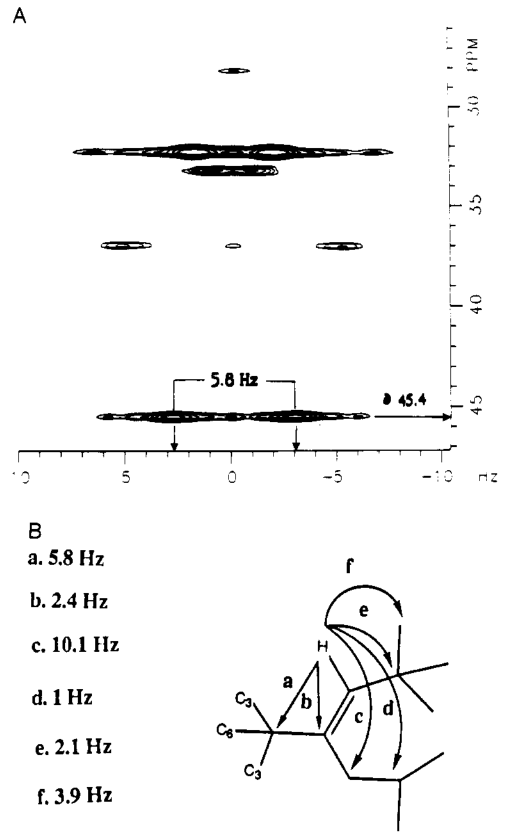

Figure 3. (A) The 2-D INAPT spectrum showing long-range heteronuclear couplings of the vinyl proton to the adjacent carbons in **19c**. The $^3J_{CH}$ coupling of 5.8 Hz from the vinyl proton to the quaternary carbon at δ 45.4 is detailed. (B) A summary of the couplings obtained by the 2-D INAPT technique on **19c**.

The mixture was heated at reflux for 4 h and worked up and the residue distilled through a spinning-band column. There was obtained 10.2 g (77%) of **4h**.

Dehydration of 2,2,5,5-Tetramethyl-3-hexanol with $KHSO_4$ and Alumina. A mixture of 5 g (0.05 mol) of the carbinol[16] and 1 g of freshly fused $KHSO_4$ was heated at 180 °C for 24 h. After cooling, it was washed with H_2O and extracted twice with $(C_2H_5)_2O$, and the latter was washed (H_2O, $NaHCO_3$) and dried ($MgSO_4$). The solvent was removed, and the residue was analyzed by GC (SE-30, 15%, on Chromosorb W, 130 °C). There resulted unchanged carbinol, plus a mixture of olefins, which by GC analysis consisted of 60% of 2,2,5,5-tetramethyl-3-hexene, 10% of 2,3,5,5-tetramethyl-1-hexene, and 30% of 2,3,5,5-tetramethyl-2-hexene.

When the carbinol was passed through a column of alumina (400 °C), the resulting olefins were 2,2,5,5-tetramethyl-3-hexene (60%), 2,3,5,5-tetramethyl-1-hexene (30%), and 2,3,5,5-tetramethyl-2-hexene (10%). No starting material was observed.

Dehydration of 4 with $KHSO_4$. The preparation of 5,5-diethyl-2,2-dimethyl-3-heptene (**5a**) is typical. A mixture of 4.7 g (0.024 mol) of **4a** and 1 g of $KHSO_4$ was heated (180 °C, 24 h). After workup, the residue was examined by GC (10-ft Carbowax 20M, 15%, on Chromosorb W, 150 °C). Only starting material (60%) and **5a** were present. Analysis by other columns on different instruments gave the same results. The residue was distilled through a spinning-band column to give 3 g of **4a** and 1.1 g (72%) of **5a**.

3-*tert*-Butyl-5,5-dialkyl-2,2-dimethyl-3-alkanols 6. The preparation of 3-*tert*-butyl-5,5-diethyl-2,2-dimethyl-3-heptanol (**6a**) is typical. A solution of 6.5 g (0.033 mol) of 5,5-diethyl-2,2-dimethyl-3-heptanone in 20 mL of pentane was added to 50 mL (0.1 mol) of t-C_4H_9Li in pentane which had been flushed with N_2. After the addition, the mixture was refluxed for 10 h and worked up in the usual way. The residue was distilled through a spinning-band column to give 3.6 g (43%) of product.

3-*tert*-Butyl-5,5-dialkyl-2,2-dimethyl-3-alkenes 7. The procedure from the previous dehydration experiment was used with 3-*tert*-butyl-5,5-diethyl-2,2-dimethyl-3-nonanol (**6b**). The product showed (GC) the presence of five components: unchanged carbinol, the ketone from which the carbinol had been prepared, and three other compounds. The reaction mixture was distilled through a spinning-band column at ca. 0.2 mm to give 1.6 g of 5,5-diethyl-2,2-dimethyl-3-nonanone, 3.8 g of 3-*tert*-butyl-5,5-diethyl-2,2-dimethyl-3-nonanol, and residue. This was separated by preparative GC using a 6-ft, $^3/_4$-in. biwall SE-30 on a Chromosorb W column at 200 °C and a He flow rate of 200 mL/min. There was collected 2.1 g of 3-*tert*-butyl-5,5-diethyl-2,2-dimethyl-3-nonene (**7a**): $n^{25}{}_D$ 1.4685; IR (no characteristic absorptions); MS, m/e 266; ^1H NMR δ 5.18 (s, 1, C=CH), 1.21 and 1.29 (s, 9 each, 2 $(CH_3)_3C$), 0.55–1.90 (m, 19, CH_3 and CH_2); ^{13}C NMR ($CDCl_3$) δ 153.1, 132.8, 42.4, 41.4, 38.2, 36.5, 33.8, 33.6, 26.6, 23.6, 14.3, 9.0. There also was obtained 0.4 g of 3-*tert*-butyl-5,5-diethyl-2,3-dimethyl-1-nonene: $n^{25}{}_D$ 1.4681; IR (neat) 3120 (m), 1630 (m), 895 (s) cm^{-1}; ^1H NMR δ 0.55–2.10 (m, 27, CH_3, CH_2), 0.88 (s, 9, $(CH_3)_3C$), 5.00 (m, 2, $C=CH_2$). A third component was present, but could not be isolated. The spectra are representative of the other 7 that were synthesized: 3-*tert*-butyl-2,2-dimethyl-5,5-dipropyl-3-octene (**7b**) ($n^{25}{}_D$ 1.4674) and also 3-*tert*-butyl-2,3-dimethyl-5,5-dipropyl-1-octene (**24**) [$n^{25}{}_D$ 1.4680; IR (neat) 3090 (m), 1620 (m), 890 (s) cm^{-1}; ^1H NMR δ 4.65–5.05 (m, 2, $C=CH_2$), 0.86 [s, 9, $(CH_3)_3C$], 0.65–1.90 (m, 32, CH_3CH_2)] and 6,6-dipropyl-2,2,3,3,4-pentamethyl-4-nonene (**25**) [$n^{25}{}_D$ 1.4575; IR (neat) (no alkene absorptions); ^1H NMR δ 5.10 (s, 1, C=CH), 1.08 [s, 9, $(CH_3)_3C$], 0.65–1.55 (m, 39, CH_3, CH_2); MS, m/e 280]; 3-*tert*-butyl-2,2-dimethyl-5,5-dipropyl-3-decene (**7c**) ($n^{25}{}_D$ 1.4660); 3-*tert*-butyl-2,2-dimethyl-5-ethyl-5-phenyl-3-nonene (**7d**) ($n^{25}{}_D$ 1.5607); 5-butyl-3-*tert*-butyl-2,2-dimethyl-5-ethyl-3-tridecene (**7e**) ($n^{25}{}_D$ 1.4670).

3,3-Dialkylalkanoic Acid Chlorides 8. Nitriles **1** were converted to the corresponding acids by heating with KOH in ethylene glycol for 30 h;[34] yields 88–92%. The acid chlorides were prepared from the acids by treatment with $SOCl_2$. In some cases they were not distilled, due to a tendency to decompose; however, they gave satisfactory elemental analyses.

Table I. Yields and Physical Properties of Compounds 1–19

compd	R_1	R_2	R_3	R_4	R_5	R_6	yield, %	bp (°C)/mm	n_D	spectral, other data
							$R_1R_2R_3CCH_2CN$, 1			
1a	C_2H_5	C_2H_5	C_2H_5				86	95–97/15	1.4351	ref 34
1b	C_2H_5	C_2H_5	C_4H_9				82	110–111/10	1.4405	ref 32
1c	C_3H_7	C_3H_7	C_3H_7				75	119–123/15	1.4410	
1d	C_2H_5	C_2H_5	C_5H_{11}				92	110–111/5	1.4420	
1e	C_3H_7	C_3H_7	C_5H_{11}				95	90–92/0.8	1.4445	
1f	C_2H_5	C_4H_9	C_6H_5				76	95–97/0.25	1.5081	
1g	C_3H_7	C_3H_7	C_6H_{13}				93	118–120/2	1.4462	
1h	C_2H_5	C_4H_9	C_8H_{17}				72	110–111/0.2	1.4492	
1i	C_7H_{15}	$C_{10}H_{21}$	$C_{12}H_{25}$				78	not purified		ref 11
							$R_1R_2R_3CCH_2C({=}NH)C(CH_3)_3$, 2			
2a	C_2H_5	C_2H_5	C_2H_5				65	107–109/11	1.4623	IR (neat) 1640 (s), no 3200 cm^{-1}; ^1H NMR (neat) δ 9.24 (s, 1 H), 2.12 (s, 2 H), 1.08 (s, 9 H), 0.50–1.75 (m, 15 H)
2b	C_2H_5	C_2H_5	C_4H_9				82	136–137/10	1.4531	
2c	C_3H_7	C_3H_7	C_3H_7				81	121–122/5	1.4524	
2d	C_3H_7	C_3H_7	C_5H_{11}				88	134–135/5	1.4521	
2e	C_2H_5	C_4H_9	C_6H_5				73	140–142/12	1.5056	
2f	C_2H_5	C_4H_9	C_8H_{17}				86	146–147/2	1.4562	
2g	C_7H_{15}	$C_{10}H_{21}$	$C_{12}H_{25}$				not purified			
							$R_1R_2R_3CCH_2C({=}O)C(CH_3)_3$, 3			
3a	C_2H_5	C_2H_5	C_2H_5				74	94–95/4	1.4392	IR (neat) 1710 (s) cm^{-1}; ^1H NMR (neat) δ 2.35 (s, 2 H), 1.09 (s, 9 H), 0.55–1.75 (m, 15 H)
3b	C_2H_5	C_2H_5	C_4H_9				70	74–75/2	1.4419	
3c	C_3H_7	C_3H_7	C_3H_7				94	112–113/5	1.4428	
3d	C_3H_7	C_3H_7	C_5H_{11}				82	101–102/0.75	1.4454	
3e	C_2H_5	C_4H_9	C_6H_5				80	91–93/0.5	1.4948	
3f	C_2H_5	C_4H_9	C_8H_{17}				95	137–139/0.75	1.4492	
3g	C_7H_{15}	$C_{10}H_{21}$	$C_{12}H_{25}$				82	220–221/0.15	1.4648	
3h	C_2H_5	C_2H_5	C_4H_9				94	133–135/12	1.4423	$C_{15}H_{28}D_2O$ (deuteriated **2b**)
							$R_1R_2R_3CCH_2CH(OH)C(CH_3)_3$, 4			
4a	C_2H_5	C_2H_5	C_2H_5				76	52–53/0.2	1.4499	IR (neat) 3600 (s), 3480 (m), 1000 cm^{-1}; ^1H NMR (CCl_4) δ 0.55–1.55 (m, 16 H), 0.86 (s, 9 H), 3.23 (br, 1 H, no D_2O exchange)
4b	C_2H_5	C_2H_5	C_4H_9				89	93–94/1.4	1.4528^a	
4c	C_3H_7	C_3H_7	C_5H_{11}				76	77–78/0.3	1.4520	
4d	C_2H_5	C_4H_9	C_6H_5				79	101–102/0.25	1.4980	
4e	C_2H_5	C_4H_9	C_8H_{17}				94	119–120/0.2	1.4553	
4f	C_7H_{15}	$C_{10}H_{21}$	$C_{12}H_{25}$				not purified			
4g	C_2H_5	C_2H_5	C_4H_9				82	122–123/9	1.4528	$C_{15}H_{30}D_2O$
4h	C_2H_5	C_2H_5	C_4H_9				77	125–126/9	1.4512^a	$C_{15}H_{28}D_4O$; IR (neat) 2150 (br, m), 2630, 2700 (m), 1100 (s) cm^{-1}; ^1H NMR (CCl_4) δ 0.55–1.55 (m, 19 H), 0.86 (s, 9 H), no OH
							$R_1R_2R_3CCH{=}CHC(CH_3)_3$, 5			
5a	C_2H_5	C_2H_5	C_2H_5				72	101–102/30	1.4310	IR (neat 2980 (m), 995 (s, trans) cm^{-1}; ^1H NMR (neat) δ 0.55–1.55 (m, 15 H), 1.01 (s, 9 H), 5.17 (q, 2 H, trans, J_{AB} = 16.5 Hz)
5b	C_2H_5	C_2H_5	C_4H_9				75	121–122/40	1.4394	
5c	C_3H_7	C_3H_7	C_5H_{11}				80	157–158/43	1.4413	
5d	C_2H_5	C_4H_9	C_6H_5				68	150–152/20	1.4912	
5e	C_2H_5	C_4H_9	C_8H_{17}				89	146–148/10	1.4460	
5f	C_7H_{15}	$C_{10}H_{21}$	$C_{12}H_{25}$				75	200–204/0.1	1.4580	
5g	C_2H_5	C_2H_5	C_4H_9				67	122–123/40	1.4370	$C_{15}H_{29}D$, IR 2230 (m), 900 (m), cm^{-1}; ^1H NMR δ 0.55 (m, 19 H)8 1.00 (s, 9 H)8 5.29(t, 1 H, J = 2.4 Hz)
5h	C_2H_5	C_2H_5	C_4H_9				74	133–134/80	1.4365^a	$C_{15}H_{28}D_2$, IR 2240 (m), 730 (s) cm^{-1}; ^1H NMR δ 0.55–1.55 (m, 19 H), 0.98 (s, 9 H), no absorption near δ 5
							$R_1R_2R_3CCH_2C(OH)[C(CH_3)_3]_2$, 6			
6a	C_2H_5	C_2H_5	C_2H_5				43	81–82/0.1; mp 35–37 °C		IR (Nujol) 3580 (s), 1080 (s) cm^{-1}; ^1H NMR (CCl_4) δ 0.65–1.68 (m, 17 H), 1.09 (s, 9 H)
6b	C_2H_5	C_2H_5	C_4H_9				64	114–116/0.2; mp 78–79 °C	1.4771	
6c	C_3H_7	C_3H_7	C_3H_7				91			
6d	C_3H_7	C_3H_7	C_5H_{11}				72	128–129/0.2; mp 58–61 °C	1.4740	
6e	C_2H_5	C_4H_9	C_6H_5				66			
6f	C_2H_5	C_4H_9	C_8H_{17}				68	160–161/0.3	1.4729	
							$R_1R_2R_3CCH{=}C[C(CH_3)_3]_2$, 7			
7a	C_2H_5	C_2H_5	C_4H_9					GC separation		*b*
7b	C_3H_7	C_3H_7	C_3H_7					GC separation		
7c	C_3H_7	C_3H_7	C_5H_{11}					GC separation		
7d	C_2H_5	C_4H_9	C_6H_5					GC separation		
7e	C_2H_5	C_4H_9	C_8H_{17}					GC separation		

Table I (Continued)

compd	R_1	R_2	R_3	R_4	R_5	R_6	yield, %	bp (°C)/mm	n_D	spectral, other data
							$R_1R_2R_3CCH_2CO_2H$ and $-COCl$, **8**			
8a	C_2H_5	C_2H_5	C_2H_5				94	99–100/25		*p*-nitroanilide, mp 117–118 °C; acid, mp[c] 42–44 °C, bp[c] 155–158 °C/1 mm
8b	C_3H_7	C_4H_9	C_5H_{11}				not purified			
							$R_1R_2R_3CCH_2C(=O)CR_4R_5R_6$, **10**			
10a	C_2H_5	C_2H_5	C_2H_5	CH_3	CH_3	C_2H_5	89	132–133/15	1.4448	
10b	C_2H_5	C_2H_5	C_2H_5	C_2H_5	C_2H_5	C_2H_5	80	148–149/7	1.4561	
10c	C_3H_7	C_4H_9	C_5H_{11}	C_2H_5	C_2H_5	C_4H_9	65	135–136/0.7	1.4580	
							$R_1R_2R_3CCH_2CH(OH)CR_4R_5R_6$, **11**			
11a	C_2H_5	C_2H_5	C_2H_5	CH_3	CH_3	C_2H_5	95	107–108/6	1.4567	
11b	C_2H_5	C_2H_5	C_2H_5	C_2H_5	C_2H_5	C_2H_5	97	153–154/14	1.4648	
11c	C_3H_7	C_4H_9	C_5H_{11}	C_2H_5	C_2H_5	C_4H_9	87	160–162/0.5	1.4636	
							$R_1R_2R_3CCH{=}CHCR_4R_5R_6$, **12**			
12a	C_2H_5	C_2H_5	C_2H_5	CH_3	CH_3	C_2H_5	75	112–113/40	1.441	IR (neat) 3040 (m), 970 (s) cm^{-1}; ^1H NMR δ 0.55–1.62 (m, 30 H), 4.98 (s, 2 H, trans)
12b	C_2H_5	C_2H_5	C_2H_5	C_2H_5	C_2H_5	C_2H_5	80	120–122/17	1.4452	
12c	C_3H_7	C_4H_9	C_5H_{11}	C_2H_5	C_2H_5	C_4H_9	91	117–118/1	1.4580	
							$R_1R_2R_3CCHR_4CN$, **13**			
13a	C_2H_5	C_2H_5	C_5H_{11}	C_4H_9			93	162–164/13	1.4531	
13b	C_3H_7	C_3H_7	C_6H_{13}	C_3H_7			83	146–147/2	1.4532	
13c	C_3H_7	C_3H_7	C_6H_{13}	*i*-C_4H_9			73	148–150/2	1.4538	
							$R_1R_2R_3CCHR_4C(=NH)C(CH_3)_3$, **14**			
14a	C_2H_5	C_2H_5	C_5H_{11}	C_4H_9			77	128–129/0.2	1.4653	
							$R_1R_2R_3CCHR_4CO_2H$ and $-COCl$, **15**			
15a	C_2H_5	C_2H_5	C_5H_{11}	C_4H_9			91	142–145/0.5	1.4571	acid chloride not purified
15b	C_3H_7	C_3H_7	C_6H_{13}	C_3H_7			95	160–162/0.5	1.4577	acid chloride not purified
15c	C_3H_7	C_3H_7	C_6H_{13}	*i*-C_4H_9			71	165–168/0.5	1.4568	acid chloride not purified
							$R_1R_2R_3CCHR_4C(=O)C(CH_3)_3$, **16**			
16a	C_2H_5	C_2H_5	C_5H_{11}	C_4H_9			20	126–127/3	1.4585	
16b	C_3H_7	C_3H_7	C_6H_{13}	C_3H_7			20	134–135/2	1.4582	
16c	C_3H_7	C_3H_7	C_6H_{13}	*i*-C_4H_9			23	128–129/2	1.4575	
							$R_1R_2R_3CCHR_4CH(OH)C(CH_3)_3$, **18**			
18a	C_2H_5	C_2H_5	C_5H_{11}	C_4H_9			49	118–120/0.5	1.4652	
18b	C_3H_7	C_3H_7	C_6H_{13}	C_3H_7			62	153–155/1	1.4642	
18c	C_3H_7	C_3H_7	C_6H_{13}	*i*-C_4H_9			47	158–160/1	1.4640	
							$R_1R_2R_3CCR_4{=}CHC(CH_3)_3$, **19**			
19a	C_2H_5	C_2H_5	C_5H_{11}	C_4H_9			48	122–124/8	1.4542	*d*
19b	C_3H_7	C_3H_7	C_6H_{13}	C_3H_7			46	105–108/2	1.4584	
19c	C_3H_7	C_3H_7	C_6H_{13}	*i*-C_4H_9			40	112–114/2	1.4562	

[a] Reference 18. [b] See Experimental Section for details. Also isolated were 3-*tert*-butyl-5,5-diethyl-2,3-dimethyl-1-nonene, **24**, and **25**. [c] Reference 34. [d] See Experimental Section for spectral properties.

Tetraalkylalkanones 10. These ketones were prepared by a modification of the method of Percival, Wagner, and Cook.[20] 6,6-Diethyl-3,3-dimethyl-4-octanone (**10a**) was obtained when 260 mL (0.27 mol) of a Grignard reagent, prepared from 8 g (0.33 mol) of Mg, 30 g (0.29 mol) of 2-chloro-2-methylbutane, and 300 mL of $(C_2H_5)_2O$, was added (1 h) to a mixture of 46 g (0.27 mol) of 3,3-diethylpentanoyl chloride (**8a**), 2 g of CuCl, and 200 mL of $(C_2H_5)_2O$ at reflux. The solvent was distilled, and the residue was heated at 100 °C for 2 h. It was decomposed (ice–HCl) and worked up. The residue gave 48.5 g (89%) of product. Ketones **10b,c** were prepared similarly from 3-chloro-3-ethylpentane and 3,3-diethylpentanoyl chloride and from 3-chloro-3-ethylheptane and 3-butyl-3-propyloctanoyl chloride, respectively.

Preparation of Tetraalkylalkanols 11 and Dehydration to Olefins 12. Ketones 10 were reduced with $LiAlH_4$ as in the preparation 4. They were dehydrated by the method described previously for obtaining 5.

2,3,3-Trialkyl Nitriles 13 and 4-Butyl-5,5-diethyl-2,2-dimethyl-3-decanimine (14). The nitriles 1 were alkylated in the 2-positions by the method of Rabjohn and Stapp.[13] The 2-butyl nitrile **13a** was caused to react with *t*-C_4H_9Li as described for the preparation of imines **2**. There was obtained 77% of 14: bp 128–129 °C (0.2 mm); $n^{25}{}_D$ 1.4656. A mixture of 20 g (0.07 mol) of the imine 14 and 100 mL of 50% H_2SO_4 was heated at reflux for 12 h and worked up as usual. IR analysis of the reaction mixture showed the presence of only starting imine and no ketone. The above procedure was repeated with 25%, 75%, and 95% H_2SO_4, but only unchanged imine resulted.

2,3,3-Trialkyl Carboxylic Acids and Acid Chlorides 15. 2-Butyl-3,3-diethyloctanoic acid was made by a modification of the procedure of Sarel and Newman.[23] A mixture of 117 g (0.47 mol) of 2-butyl-3,3-diethyloctanenitrile (**13a**) and 500 g of 75% H_2SO_4 was stirred and heated at 100 °C for 8 h. To the flask was added 205 g (3 mol) of $NaNO_2$ at a rate to maintain the contents of the flask at 80–85 °C. After separation of the layers and extraction with ether, followed by the usual cleanup, the residue was distilled to give 116 g (91%) of the desired acid **15a**. Two other acids (**15b,c**) were prepared similarly.

The acids were treated with $SOCl_2$ in the usual way to afford acid chlorides. These were not distilled due to a tendency to decompose at the high temperatures required.

2,2-Dimethyl-4,5,5-trialkyl-3-alkanones 16. 4-Butyl-5,5-diethyl-2,2-dimethyl-3-decanone (**16a**) was obtained by adding a $(C_2H_5)_2O$ solution of 660 mL, containing 0.61 mol of *t*-C_4H_9MgCl, to 111 g (0.4 mol) of 2-butyl-3,3-diethyloctanoyl chloride (**15a**), 5 g of CuCl, and 500 mL of $(C_2H_5)_2O$. The reaction mixture produced 22.5 g (20%) of the ketone.

2,2-Dimethyl-4,5,5-trialkyl-3-alkanols 18. These compounds resulted when the ketones **16** were treated with *t*-C_4H_9Li. From a mixture of 250 mL (0.25 mol) of *t*-C_4H_9Li in pentane and 22.5 g (0.076 mol) of 4-butyl-5,5-diethyl-2,2-dimethyl-3-decanone (**16a**) in 50 mL of pentane there were obtained 7 g (49%) of stereoisomeric 4-butyl-5,5-diethyl-2,2-dimethyl-3-decanols (**18a**) and 8.4 g of unchanged ketone: bp 118 °C (0.5 mm); n^{25}_{D} 1.4652; IR (neat) 3645 (s), 3583 (s), 3535 (br) cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 0.75–0.87 (m), 0.90–0.93 (s), 0.96–0.98 (s), 1.20–1.23 (s), 1.24–1.64 (m), 3.93–3.41 (d), 3.42–3.44 (s); ^{13}C NMR (CDCl$_3$) δ 84.7, 44.8, 43.6, 36.0, 35.1, 33.3, 33.2, 33.1, 28.2, 27.2, 27.0, 26.9, 24.7, 24.5, 23.8, 23.8, 23.7, 22.8, 14.2, 14.0, 9.4, 9.3, 8.7, 8.6. Two other secondary alcohols (**18b**,**c**) were prepared in the same manner.

2,2-Dimethyl-4,5,5-trialkyl-3-alkenes 19. The dehydration of the carbinols **18** was accomplished by heating them with KHSO$_4$ in essentially the same way as used for preparing alkenes **5**. Those obtained and their spectral properties are as follows: 4-butyl-5,5-diethyl-2,2-dimethyl-3-decene (**19a**) [IR (neat) 1625 (w) cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 5.04 (s, 1, C=CH), 2.00–2.5 (t, 3, allylic H's), 1.12 [s, 9, C(CH$_3$)$_3$], 0.64–0.95 (m, 30, CH$_2$CH$_3$); ^{13}C NMR (CDCl$_3$) δ 140.7, 136.4, 45.4, 36.5, 34.0, 32.8, 31.8, 30.8, 28.8, 27.5, 27.0, 23.9, 23.3, 22.8, 14.2, 14.1, 8.3]; 3-*tert*-butyl-2,2-dimethyl-4,5,5-tripropyl-3-undecene (**19b**) [IR (neat) 1635 (w) cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 5.01 (s, 1, =CH), 1.95–2.00 (t, 2, allylic H's), 1.16–1.40 (m, 12, CH$_2$), 1.11 [s, 9, C(CH$_3$)$_3$], 0.82–1.17 (m, 20, CH$_2$, CH$_3$); ^{13}C NMR (CDCl$_3$) δ 141.6, 136.0, 45.5, 38.3, 35.8, 33.5, 32.2, 31.9, 30.5, 30.2, 25.3, 23.9, 23.0, 17.2, 15.2, 15.1, 14.3]; 3-*tert*-butyl-2,2-dimethyl-5,5-dipropyl-4-isopropyl-3-undecene (**19c**) [IR (neat) 1620 (w) cm^{-1}; UV (hexane) $\lambda_{\max}$ 200.5 nm (ϵ 8923); ^{1}H NMR (CDCl$_3$) δ 5.17 (s, 1, =CH), 2.04–2.07 (d, 2, allylic), 1.96–2.00 (m, 1, CH), 1.23–1.36 (m, CH$_2$), 1.12 [s, 9, C(CH$_3$)$_3$], 0.83–0.97 (m, CH$_2$, CH$_3$); ^{13}C NMR (CDCl$_3$) δ 139.1, 138.0, 45.5, 38.8, 36.9, 36.3, 32.2, 32.1, 30.4, 28.1, 23.8, 23.0, 22.8, 17.1, 15.0, 14.2; H–C long-range correlations (C=CH) irradiated; δ 139.06 (q, J_{CH} = 2.4 Hz), 45.43 (q, J_{CH} = 5.8 Hz), 36.93 (CH$_2$, J = 10.1 Hz), 33.16 (q, J = 2.1 Hz), 32.23 (CH$_3$, J = 3.9 Hz), 28.11 (CH, $J \cong 1$ Hz).

NMR Procedures. The 2-D INAPT sequence shown in Figure 2 is similar to Nagayama's modification[35] of the 1-D selective refocused INEPT experiment,[36] except that all of the proton pulses were soft, $\gamma(\mathrm{H}_2)$ = 25 Hz giving a 90° proton pulse width of 10 ms. This modification was necessary on the Nicolet NT series of spectrometers which only allow rapid switching of the decoupler power between two levels. The F$_1$ spectral window was equal to $^{1}/_{2}t$ and was set to 40 Hz in this case. The delay Δ was optimized for J_{CH} = 7 Hz, and a 32 × 2K data set was acquired in approximately 2 h. This was processed with standard Nicolet software to yield a 64 × 1K frequency domain spectrum with DM = 4 and DM = 3 in the t_2 and t_1 dimensions, respectively.

The 2-D autocorrelated double quantum coherence spectroscopy experiment was performed ca. 500 mg of **19c** in a 5-mm carbon probe. A 64 × 4K data set was acquired in 47 h and processed to yield a 256 × 2K frequency domain spectrum. This experiment was optimized for J_{CC} = 42 Hz, and 12 correlations were observed.

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Revised Structures of Robustadials A and B from *Eucalyptus robusta*[1]

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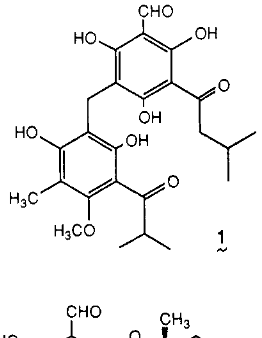
Robustadials A and B have been isolated from the leaves of *Eucalyptus robusta* Smith (Myrtaceae), separated as their dimethyl ethers, and their structures reinvestigated by spectroscopic techniques. The structures are shown to include the pinane skeleton by using various one- and two-dimensional NMR methods. Particularly useful were the 2D relayed coherence transfer and XCORFE pulse sequences.

Introduction

The Chinese traditional medicine "Da Ye An", prepared from the leaves of *Eucalyptus robusta* Smith (Myrtaceae), has a long, successful history for treating malaria and other ailments.[2] Activity against the malaria-inducing protozoan *Plasmodium berghei* has been traced to the phenolic components of the 95% ethanol extract, from which an active compound, robustaol A (1), was subsequently isolated.[3] A mixture of four chromans with even greater activity yielded two new compounds, robustadials A and B, which were assigned structures **2** and **3**.[4] The separation of **2** and **3** was accomplished after conversion to their dimethyl ethers. The remaining two chromans were identical with euglobals Ia$_1$ (**4**) and Ia$_2$ (**5**), previously reported from *Eucalyptus globulus*.[5]

Recently, the synthesis of **6**, the dimethyl ether of **2**, revealed that the structures of the robustadials were misassigned.[6] A new structure (**7**) was then suggested for robustadial A, robustadial B being the 7-epimer.[7] We now report the reisolation of robustadials A and B as their



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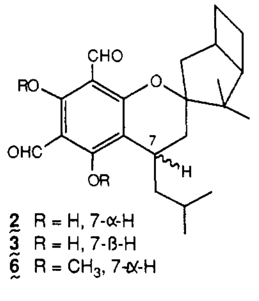
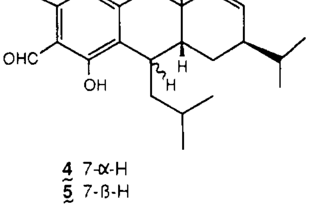
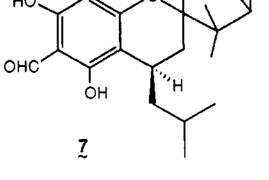


2 R = H, 7-α-H
3 R = H, 7-β-H
6 R = CH$_3$, 7-α-H



4 7-α-H
5 7-β-H



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(1) This paper is dedicated to Professor Herman Kalckar on the occasion of his 80th birthday (March 26, 1988).

(2) In *Zhong Cao Yao Xue* (Nanjing Yao Xue Yuan); 'Zhong Cao Yao Xue' Bian Xie Zu, Jiang Su Ren Min Chu Ban She: Nanjing; Part 3, p 705.

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