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BIOMIMETIC METHYL TRANSFER TO OLEFINS

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Abstract - Conditions have been found under which trisubstituted olefins can be methylated with diaryl methyl sulfonium salts in 2,6-di-t-butylpyridine. The pattern of methylated compounds formed is similar to that of the enzymatic methylation of Δ^{24} steroids side chains with S-adenosylmethionine as a methyl donor.

The transfer of methyl groups to a variety of nucleophilic acceptors (O, N, S, C) is an important step in a number of fundamental metabolic pathways[1]. The enzymes responsible for these methylation processes very often use the same cofactor : S-Adenosylmethionine (SAM), a sulfonium salt.

These facts led us to carry out a comparison of the alkylating power of sulfonium salts (which have recently become readily available) with those of the more commonly used alkylating agents. The sulfonium salts indeed proved to be extremely efficient alkylating agents towards, O, N, S and C (enolate) nucleophiles[2].

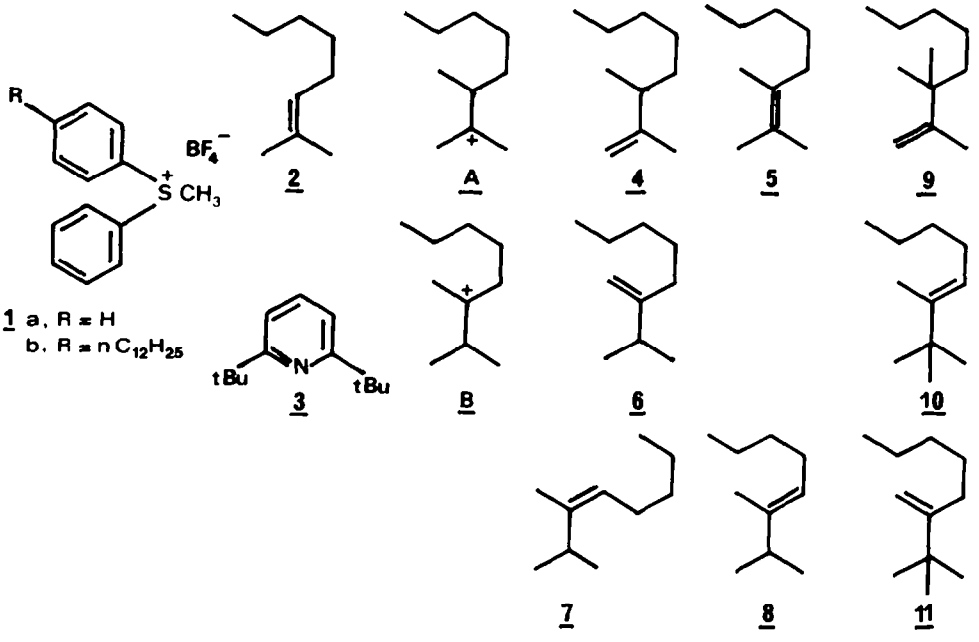
A particularly intriguing group of methylases transfer a methyl group from SAM to olefins[3]. This C-methylation takes place in many plants, bacteria and marine organisms[4]. Commonly methylated substrates include Δ^{24} steroids, unsaturated fatty acids... The details of the enzymatic reaction have been worked out. The pattern of isomers formed, particularly the hydride shift, points to an ionic process[3]. The intact methyl group is transferred from SAM with inversion of configuration[5].

Attempts have been made to carry out a similar alkylation of olefins in the laboratory. Particularly noteworthy is the solvolysis of cycloheptenylmethyl dimethyl sulfonium p-bromobenzenesulfonate, in which intramolecular C-alkylation of an olefin was observed by CHUIT and FELKIN[6]. Very recently the methylation of C-C double bonds by electrochemically generated "methyl cations" has been reported[7].

Following up on previous studies on the biomimetic synthesis of isoprenoids by acid promoted prenylation of various olefinic substrates, we investigated the prenylation of isopentenol derivatives with dialkyl prenyl sulfonium salts[8]. Of particular interest was the fact that prenylation did occur in an apolar medium. On the other hand methylation of aromatic compounds under Friedel Crafts conditions is thought to proceed by a "direct displacement mechanism" rather than through a methyl carbocation[9]. This gave us the incentive to attempt the long sought after methylation of olefins with SAM like compounds. We selected diaryl methyl sulfonium salts 1 (Scheme 1) as diphenyl sulfide had been shown to be a better leaving group than dimethylsulfide[2,10].

As counter anion methanesulfonate could not be used since it was methylated by the methyl sulfonium anion (half life : 2 h at 75°C) leading to methyl methane sulfonate and diphenylsulfide, we therefore chose the tetrafluoroborate anion which would be much less easily methylated[11] . The base which is necessarily present to take care of the proton lost by the intermediary carbocation, proved to be of crucial importance. It does not need to be a strong base, but it must be of very low nucleophilicity in order not to be itself alkylated under the reaction conditions. Thus diisopropyl ethylamine (Hünig's base) was easily methylated when heated with diphenyl methyl sulfonium tetrafluoroborate. 1,8-Bis-dimethylamino naphtalene (proton sponge) was methylated in the ring. We eventually selected 2,6-di-t-butyl pyridine 3 which was completely inert under the methylation conditions used.

2-Methyl-2-octene 2[12] was chosen as a substrate to be methylated because of its structural analogy with the Δ^{24} steroid side chain.



SCHEME 1

Authentic samples of the methylation products expected in analogy with the biosynthetic process were prepared by classical reactions (see experimental part). Methylation would be expected to proceed in a Markovnikov direction leading to a carbonium ion A which would lose a proton and lead to 2,3-dimethyl-1-octene 4 and 2,3-dimethyl-2-octene 5. Carbocation A might be converted by 1,2-hydride shift into B which, by loss of a proton, would give 2-methyl-3-methylene octane 6 or the isomeric 2,3-dimethyl-3-octenes Z : 7 and E : 8.

In the first experiments (Table 1, entry 1) olefin 2 was heated with di-t-butyl pyridine 3 and diphenyl methyl sulfonium tetrafluoroborate 1a at 160°C in a sealed tube. G.L.C. analysis of the reaction products showed that indeed the five methylated olefins had been formed although in a very small yield (about 4%). Noticing that salt 1a was very sparingly soluble in the reaction mixture even at a higher temperature we tried to increase its solubility by grafting a long alkyl chain (1b) in the para position of one of the rings. This could be done by classical reactions (see experimental part). Using now salt 1b instead of 1a, we were gratified to observe a substantial increase in the yield of methylated products, up to

53%, particularly at higher temperatures (Table 1, entry 6). It has been pointed out by J.K. COWARD that "an active site of very low dielectric constant might facilitate nucleophilic attack on SAM"[3a]. In a control experiment the half life of salt 1b, in the presence of 2,6-di-t-butyl pyridine 3 was found to be approximately 35 h at 175°C with formation of p-dodecylphenyl phenyl sulfide and, presumably, methyl fluoride an boron trifluoride[13]. The distribution of products is very much as expected. The tetrasubstituted olefin 5 is the main product with a small amount of the terminal olefin 4. Interestingly, all three olefins expected after hydride shift were present including the methylene compound 6. However olefins 6, 7, 8 could have been formed by subsequent isomerisation of 5. Control experiments (17 h at 175°C as in entry 5) showed that olefin 5 was stable when heated with 3 (0% isomerization) or 3, HBF_4 (2-3% isomerisation), but was isomerised (11%) when BF_3, Et_2O was added to 3. Since the proportion of olefins 4, 6, 7, 8 in the mixture of monomethylated olefins formed in the methylation experiments was much higher (40%, entry 6) we can reasonably presume that significant hydride shift (A → B) has taken place.

TABLE 1 : Methylation of 2-methyl-2-octene 2

ENTRY	Methyl transfer reagent (eq)	2 eq	3 eq	T°C	Time (h)	4	5	6	7	8	9	10	11	Yield[a] %
1	1a 1	1	1.2	160	72	9	51	6		14	20			5
2	1b 1	1	1.2	130	100	7	68	5		14	6			19[b]
3	1b 1	1.5	1.5	150	120	10	53	8		18	11			27
4	1b 1	1.5	2	160	288	8	47	2	4	15	6	16	2	46[c]
5	1b 1	1	1.2	175	17	7	44	6		15	28			42
6	1b 1	1	1.2	175	48	6	39	3	7	20	5	18	2	53[c]
7	$(CH_3O)_2SO_2$ 1	1	1.5	130	24	-	-	-	-	-	-	-	-	0
8	$(CH_3)_3O^+BF_4^-$ 1	1	1.5	130	24	6	47	5		13	29			24
9	" 1.35	1	1.5	160	72	5	36	6		14	39			23
10	$CF_3SO_3CH_3$ 1	1	1.5	80	19	27	45	4		10	5	7	2	7
11	" 1	1	1.5	130	24	46	22	3		6	8	11	4	39

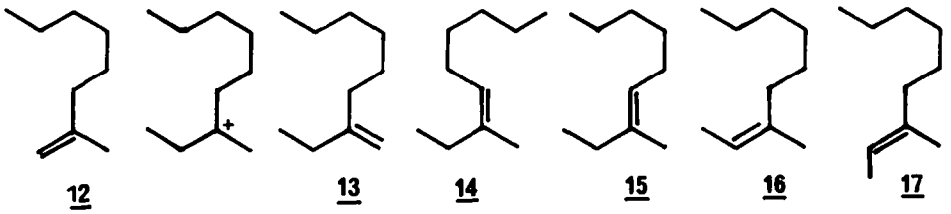
a) based on % sulfonium salt methyls transferred to olefins 2 and 5
b) 45% of sulfonium salt recovered
c) all sulfonium salt was consumed

GLC-MS analysis of the reaction mixtures had shown a peak with a molecular weight corresponding to double methylation. The higher conversions achieved made it possible to investigate this interesting fact. The main compound of the methylation reaction 5 would be expected to be more nucleophilic than the starting olefin and therefore to compete with it for the methylating agent. Methylation at C_3 would lead to 2,3,3-trimethyl-1-octene 9 whereas methylation at C_2 could lead to E 2,2,3-trimethyl-3-octene 10 (the Z isomer would suffer considerable strain) and to 2,2-dimethyl-3-methylene octane 11. Authentic samples of these olefins were

prepared and found identical with the reaction products. The reaction mixtures contained about 70% mono and 30% dimethylated products. When olefin 5 itself was treated with 1b and 3 for 24 h at 175°C, it was converted into the olefins 9, 10 and 11 (20:70:10, respectively) in up to 50% yield. The starting olefin was partially (10%) isomerized into olefins 4, 6, 7, 8. A longer reaction time (48 h) led to a 64% yield of methylated products with higher (30%) isomerization of the starting material. It is of interest that similar double methylations have been observed in Nature[3a]. Under similar reaction conditions (48 h, 160°C), didodecyl methyl sulfonium perchlorate did not react with olefin 2 in the presence of 3.

Preliminary experiments have been carried out in order to compare diaryl methyl sulfonium salts with other strong methylating agents. It was found that, with 2,6-di-t-butyl pyridine as base, dimethyl sulfate at 130°C, 24 h, did not methylate olefin 2. Trimethyl oxonium tetrafluoroborate (Meerwein salt), however, gave a 24% yield of olefins 4 - 11. Methyl trifluoromethane sulfonate gave a 39% yield. Remarkably enough a much larger proportion of olefin 4 was found. It is tempting to speculate that in that case the departing mesylate anion might be responsible for the proton removal[14].

The isomeric 2-methyl-1-octene 12[12], which might be considered as a model for the side chain "ethylation" of steroids, was submitted to the same methylation conditions (Scheme 2 and Table 2). Five monomethylated compounds 13, 14, 15, 16 and 17 were identified by comparison with authentic samples. The conversion was however lower (about 20%) than with olefin 4.



SCHEME 2

TABLE 2 : Methylation of 2-methyl-1-octene 12

Methyl transfer reagent 1 eq	 12 eq	3 eq	T°C	Time (h)	 13	 14	 15	 16	 17	Yield[a] (%)
1b	2	1.5	135	65	7	10	26	24	33	7
1b	2	1.5	150	24	7	11	24	26	32	7
1b	1.2	1.5	150	130	9	13	29	18	31	17[b]
1b	1.2	1.5	160	144	8	12	28	18	34	20[b]
1b	1.2	1.5	175	17	9	13	30	13	35	11[c]

a) based on sulfonium salt methyls transferred to olefin 12
b) not including 6% methyl groups transferred to olefin 2 formed by isomerisation of 12 in situ
c) 15% transferred to 2.

A small amount of monomethylated 4 - 8 and doubly methylated 9 - 11 products was also formed. They appeared to be the result of methylation of 2-methyl-2-octene 2, itself formed by isomerisation of the starting olefin.

It thus appears that some methyl sulfonium salts, under appropriate reaction conditions, can indeed methylate intermolecularly as "weak" nucleophiles as carbon - carbon double bonds. They compare favorably with Meerwein salt or methyl trifluoromethane sulfonate as strong methylating agents.

EXPERIMENTAL

Melting points were determined on a Reichert apparatus and were not corrected. PMR spectra were recorded on a Cameca 250 (250 MHz) spectrometer ($CDCl_3$; δ, ppm from TMS). Mass spectra were obtained by GC-MS coupling on a Nermag R10-10 apparatus using electron impact mode. High resolution mass spectra were recorded on a KRATOS MS-50 instrument in the mass spectrometry laboratory of the Université de Paris VI (FRANCE). Microanalyses were determined by the Service Central d'Analyses du CNRS, 69390 VERNAISON (FRANCE).

GLC analyses of C_{10} olefins were performed on a Girdel serie 30 chromatograph using a 50 m SE-52 GC glass capillary column. Preparative GLC was performed on a Carlo Erba 4200 instrument using a 2.5 m x 6 mm column of 15% ov 101 on Chromosorb AW-DMCS 60-80. TLC was carried out using Merck silica gel 60 F_{254} plastic sheets (Art. 5735). Silica gel 60-H (Art. 7736) or 60 (Art. 7734) Merck was used for flash or short column chromatographies.

All solvents were dried and purified in the usual manner.

Synthesis of p-dodecylphenyl methyl phenyl sulfonium salts 1b : p(1-oxododecyl) phenyl phenyl sulfide

To a freshly distilled solution of lauroyl chloride (54.75 g, 0.25 mol.) and diphenyl sulfide (45.89 g, 0.25 mol.) in dichloromethane (400 ml) was slowly added aluminium chloride (80 g, 0.6 mol.) with ice cooling and stirring. After stirring for 15 h at 20°C, the mixture was poured into ice cold aqueous hydrochloric acid (6N, 300 ml). The organic layer was decanted and washed with water. The usual work-up gave a solid which was recrystallized from ether-methanol. After filtration through silica gel the mother liquors gave a second crop. Combined yield 57.49 g (63%) : mp 46°C ; Anal. : calc. for $C_{24}H_{32}OS$, M=368.22 : C 78.21, H 8.76, O 4.34, S 8.68, found : C 77.95, H 8.62, O 4.64, S 8.75 ; PMR : δ 0.87 (3H, t, J=7 Hz), 1.17-1.45 (16H, m), 1.61-1.78 (2H, m), 2.90 (2H, t, J=7.5 Hz), 7.22 (2H, d, J=8.5 Hz), 7.35-7.42 (3H, m), 7.46-7.56 (2H, m), 7.86 (2H, d, J=8.5 Hz).

p-Dodecylphenyl phenyl sulfide[15]

Lithium aluminium hydride (17.2 g, 0.453 mol.) in anhydrous ether (300 ml) was carefully added at 0°C to a solution of aluminium chloride (120.9 g, 0.906 mol.) in ether (300 ml). p(1-Oxodecyl)phenyl phenyl sulfide (41.7 g, 0.113 mol.) was added portionwise at 0°C and the mixture was stirred overnight at r.t. After careful hydrolysis the organic layer was washed with water and worked up as usual. A pale yellow oil (38.59 g, 0.109 mol.), 96%) was isolated. PMR : δ 0.89 (3H, t, J=7 Hz), 1.20-1.40 (18H, m), 1.6 (2H, m), 2.60 (2H, t, J=8 Hz), 7.12-7.42 (9H, m).

p-Dodecylphenyl methyl phenyl sulfonium methanesulfonate

A mixture of the above sulfide (19 g, 54 mmol.), methane sulfonic acid (70 ml, 1.075 mol.) and methanol (26 ml, 644 mmol.) was heated four days at 80°C with stirring. The brown solution was poured into ice - water and the mixture extracted with CH_2Cl_2. The solvent was evaporated under vacuum, leaving a mixture of sulfonium salt and sulfide (90:10), containing some methyl methanesulfonate (PMR : two singlets at δ 3.03 and 3.94). Washing with ether - pentane (30:70) gave the salt (15.44 g) which should be used rapidly (half life at 75°C = 2 h ; formation of methyl methanesulfonate). PMR : δ 0.87 (3H, t, J=7 Hz), 1.17-1.36 (18H, m),1.50-1.66 (2H, m), 2.65 (2H, t, J=8 Hz), 2.71 (3H, s), 3.81 (3H, s), 7.42 (2H, d, J=8.5 Hz), 7.58-7.64 (3H, m), 7.84 (2H, d, J=8.5 Hz), 7.90-7.96 (2H, m).

Tetrafluoroborate 1b

To a solution of the crude methanesulfonate (13.12 g) in methanol (80 ml) an aqueous solution of tetrafluoroboric acid (34%, 12 ml) was added at 0°C. The mixture was stirred for 2 h and extracted with CH_2Cl_2. The organic phase was washed with water (twice) and with aqueous sodium bicarbonate. Drying and evaporation of the solvent gave a viscous oil which slowly crystallized (11.06 g, 90%) : m.p. 52°C (ethyl acetate - pentane) ; Anal. : calc. for $C_{26}H_{37}BF_4S$, M=456.26 : C 65.75, H 8.17, S 7.01, found : C 65.97, H 8.23, S 7.06. PMR : δ 0.87 (3H, t, J=7 Hz), 1.15-1.39 (18H, m), 1.51-1.67 (2H, m), 2.66 (2H, t, J=8 Hz), 3.61 (3H, s), 7.45 (2H, d, J=8.5 Hz), 7.59-7.71 (3H, m), 7.80 (2H, d, J=8.5 Hz), 7.83-7.92 (2H, m).

Synthesis of reference olefinic compounds

2,3-Dimethyl-3-octene Z 7 and E 8, 2,2,3-trimethyl-3-octene E 10 were synthesized according to the literature[16].

2,3-Dimethyl-2-octanol

To a Grignard reagent prepared from 2-bromoheptane (7.16 g, 40 mmol.) in ether, acetone (5.87 ml, 4.65 g, 80 mmol.) in ether was added at 0°C. The mixture was allowed to stay one night at room temperature with stirring. After the usual work-up, the desired alcohol was isolated by chromatography on silica gel (3.8 g, 60%).

2,3-Dimethyl-1-octene 4 and 2,3-dimethyl-2-octene 5

Phosphorus oxychloride (3 ml) was added at 0°C with stirring to a solution of the above alcohol (3.8 g) in pyridine (10 ml). After heating at 60°C for 2 h the mixture was worked up as usual to give a mixture of olefins 4 + 5 (49:51, 65% yield). The compounds were isolated by preparative glc.

4 : PMR : δ 0.89 (3H, t, J=7 Hz), 1.02 (3H, t, J=8 Hz), 1.17-1.39 (8H, m), 1.93-2.09 (4H, m), 4.69 (2H, m) ; MS, m/z (relative intensity) : 140.1565, calc. for $C_{10}H_{20}$=140.1564 (2) $M^{+\cdot}$, 97 (4), 84 (10), 83 (9), 70 (100), 69 (42), 55 (54).

5 : PMR : δ 0.89 (3H, t, J=7 Hz), 1.17-1.41 (6H, m), 1.63 (9H, s), 2.01 (2H, t, J=7 Hz) ; MS, m/z (relative intensity) : 140.1566, calc. for $C_{10}H_{20}$=140.1564 (21) $M^{+\cdot}$, 97 (13), 84 (22), 83 (68), 70 (15), 69 (31), 55 (100).

2-Methyl-3-methylene-octane 6

A solution of trisylhydrazine[17] (3.39 g, 11.2 mmol.) in 3-methyl-2-butanone (10 ml) was stirred 2 h at room temperature and evaporated in vacuo. Toluene (20 ml) was added and evaporated in vacuo. The residue was recrystallized from aqueous methanol (3.4 g, 93% ; PMR : 92% anti +8% syn)[18]. PMR (anti isomer) : δ 0.96 (6H, d, J=7 Hz), 1.24 (6H, d, J=7 Hz), 1.26 (12H, d, J=7 Hz), 1.73 (3H, s), 2.40 (1H, hept, J=7 Hz), 2.90 (1H, hept, J=7 Hz), 4.22 (2H, hept, J=7 Hz), 7.15 (2H, s). A solution of n-butyllithium in hexane (1.4 M, 15 ml) was added[19] at -78°C to a solution of the trisylhydrazone (3.4 g, 9.3 mmol.) in THF (10 ml). After 5 mn the mixture was allowed to warm up to 0°C. When the evolution of nitrogen had ceased (~10 mn) n-pentyl bromide (3.75 g, 25 mmol.) was added and the mixture was stirred 2 h at 20°C. The olefin 6 (45%, glc) was extracted with pentane and purified by preparative glc. PMR : δ 0.89 (3H, t, J=7 Hz), 1.03 (6H, d, J=7 Hz), 1.22-1.51 (6H, m), 2.03 (2H, t, J=7.5 Hz), 2.25 (1H, hep, J=7 Hz), 4.71 (1H, m), 4.76 (1H, m). MS, m/Z (relative intensity) : 140.1564, calc. for $C_{10}H_{20}$=140.1564 (4), $M^{+\cdot}$, 97 (8), 84 (25), 83 (19), 69 (100), 55 (48).

2,2-Dimethyl-3-methylene-octane 11

2,2-Dimethyl-3-butanone trisylhydrazone was prepared as above and crystallized from methanol : 85% yield, m.p.=163-166°C. Anal. : calc. for $C_{21}H_{36}N_2O_2S$, M=380.25 : C 66.27, H 9.54, N 7.36, O 8.41, S 8.41, found : C 66.32, H 9.47, N 7.42, O 8.59, S 8.60. PMR : δ 0.97 (9H, s), 1.25 (18H, d, J=7 Hz), 1.73 (3H, s), 2.91 (1H, hept, J=7 Hz), 4.20 (2H, hept, J=7 Hz), 7.15 (2H, s). Treatment of the trisylhydrazone (1.65 g, 4.34 mmol.) with n-butyllithium (2.2 eq.) followed by n-pentyl bromide as above gave olefin 11 (47%, glc) which was purified by preparative glc. PMR : 0.92 (3H, t, J=7 Hz), 1.05 (9H, s), 1.19-1.63 (6H, m), 2.02 (2H, t, J=7.5 Hz), 4.68 (1H, m), 4.84 (1H, m). MS, m/Z (relative intensity) : 154.1718, calc. for $C_{11}H_{22}$=154.1721 (1) $M^{+\cdot}$, 98 (12), 97 (7), 84 (23), 83 (100), 69 (21), 67 (10), 57 (19), 55 (44).

Methyl 2,2-dimethyl heptanoate

A solution of n-butyllithium in hexane (1.4 M, 27 ml, 37.8 mmol.) was added at -78°C with stirring to 5.4 ml (3.84 g, 38 mmol.) of diisopropylamine. After 0.5 h at room temperature, THF (30 ml) was added, the mixture was cooled to -78°C and methyl heptanoate (5 g, 35 mmol.) in THF (10 ml) was added. After standing for 0.5 at 20°C the mixture was cooled to 0°C and methyl iodide (3 ml in 5 ml HMPA) added. After 2 h at 20°C the reaction was complete (glc). Excess methyl iodide was evaporated in vacuo and the mixture transferred, under argon, into a solution of LDA prepared as above from diisopropylamine (6.5 ml) and n-butyllithium (1.4 M in hexane, 32 mmol.). After 0.5 h at 20°C, methyl iodide (3 ml) was added at 0°C After another 2 h at 20°C the reaction mixture was poured into dilute N.HCl and extracted with pentane. After the usual work-up the dimethylated ester was purified by flash chromatography : 3.76 g (63%). PMR : δ 0.88 (3H, t, J=7 Hz), 1.16 (6H, s), 1.13-1.37 (6H, m), 1.45-1.55 (2H, m), 3.66 (3H, s).

2,3,3-Trimethyl-2-octanol

To a solution of the preceding ester (1 g, 5.8 mmol.) in anhydrous ether (20 ml) methyllithium (1.19 M in ether, 20 ml, 23.8 mmol.) was added slowly at 0°C. After stirring overnight at room temperature, the reaction mixture was carefully neutralized with ethyl acetate and worked up as usual. Flash chromatography afforded the pure alcohol (0.48 g, 48%). PMR : δ 0.89 (6H, s), 0.91 (3H, t, J=7 Hz), 1.18

(6H, s), 1.23-1.35 (8H, m). MS, m/z (relative intensity) : no molecular ion peak, 157 (3), 155 (0.3), 85 (5), 84 (4), 83 (8), 71 (16), 69 (9), 59 (100).

2,3,3-Trimethyl-1-octene 9

Phosphorus oxychloride (1 ml) was slowly added at 0°C to the above alcohol (0.48 g) in pyridine (5 ml) and the solution was heated at 60°C. After cooling the mixture was poured into ice - water and extracted with pentane. After the usual work-up the olefin 9 (65%, glc) was purified by preparative glc. PMR : δ 0.87 (3H, t, J=7 Hz), 1.02 (6H, s), 1.05-1.37 (8H, m), 1.69 (3H, m), 4.67 (1H, m), 4.72 (1H, m), 4.72 (1H, m). MS, m/z (relative intensity) : 154.1717, calc. for $C_{11}H_{22}$= 154.1721 (2) $M^{+\cdot}$, 139 (1), 98 (12), 97 (7), 84 (23), 83 (100), 69 (46), 67 (22), 55 (75).

3-Methyl-3-nonanol

To a Grignard reagent prepared from bromoethane (7.4 ml, 10.9 g, 0.1 mol.) in ether, 2-octanone (10 ml, 8.19 g, 64 mmol.) was added slowly at 0°C. The mixture was allowed to stay overnight at room temperature with stirring. After the usual work-up the desired alcohol was obtained (8.66 g, 85%).

Olefins 13 - 17 from 3-methyl-3-nonanol

Phosphorus oxychloride (3 ml) was added at 0°C with stirring to the above alcohol (3.16 g) in pyridine (10 ml). After heating at 60°C for 2 h the usual work-up gave a mixture of olefins 13 - 17 (62%) after filtration on silica gel. This mixture was analyzed by GC-MS. Preparative glc afforded a mixture of olefins 13 and 14, then a mixture of olefins 15 and 16, and finally pure 17. Their structures were established by PMR spectroscopy and comparison with literature data.

13[20] (12%) : PMR : δ 0.89 (3H, t, J=7 Hz), 1.02 (3H, t, J=8 Hz), 1.17-1.39 (8H, m), 1.93-2.09 (4H, m); 4.69 (2H, m). MS, m/z (relative intensity) : 140 (23), $M^{+\cdot}$, 111 (17), 83 (38), 70 (73), 69 (56), 67 (17), 55 (100).

14 (13%) : PMR : δ 0.89 (3H, t, J=7 Hz), 0.96 (3H, t, J=8 Hz), 1.27-1.39 (6H, m), 1.69 (3H, m), 1.93-2.09 (4H, m), 5.08 (1H, t, J=7 Hz). MS, m/z (relative intensity) : 140 (11), $M^{+\cdot}$, 111 (10), 83 (27), 70 (63) 69 (52), 67 (14), 55 (100).

15[19a] (24%) : PMR δ 0.89 (3H, t, J=7 Hz), 0.99 (3H, t, J=8 Hz), 1.21-1.45 (6H, m), 1.60 (3H, d, J=1.5), 2.00 (4H, m), 5.11 (1H, tq, J=7 Hz, J=1.5 Hz). MS, m/z (relative intensity): 140 (54) $M^{+\cdot}$, 111 (35), 97 (4), 84 (6), 83 (73), 70 (36), 69 (48), 55 (100).

16[21] (20%) : PMR : δ 0.89 (3H, t, J=7 Hz), 1.21-1.45 (8H, m), 1.56 (3H, d, J=6.5 Hz), 1.66 (3H, m), 2.03 (2H, t, J=7.5 Hz), 5.19 (1H, q, J=6.5 Hz). MS, m/z (relative intensity) : 140 (7) $M^{+\cdot}$, 111 (4), 84 (8), 83 (15), 70 (100), 69 (40), 68 (15), 55 (70).

17[21] (31%) : PMR : δ 0.88 (3H, t, J=7 Hz), 1.19-1.45 (8H, m), 1.57 (3H, d, J=6.5 Hz), 1.59 (3H, s), 1.97 (2H, t, J=7.5 Hz), 5.2 (1H, qm, J=6.5 Hz). MS, m/z (relative intensity) : 140 (8) $M^{+\cdot}$, 111 (5), 84 (8), 83 (7), 70 (100), 69 (33), 68 (13), 55 (54).

Methylation procedures

Methylation of 2-methyl-2-octene 2
(general procedure according to Table 1)

The methyl transfer reagent was mixed with the olefin 2 (1-1.5 eq) and base 3 1.2-1.5 eq), with undecane as an internal standard, in a pyrex glass tube which was sealed and heated during various lengths of time at different temperatures. In each experiment crystallization of the salt of 3 was observed. The olefinic content of the resulting mixture was analyzed by GLC on a capillary column and by GC-MS (olefins 6 and 7 as well as olefins 9, 10, 11 could not be resolved). After distillation mono and dimethylated olefins could be partially separated by preparative GLC. A mixture of monomethylated compound 4, 6, 7, 8 was isolated first, then pure 5 and finally dimethylated compounds 9, 10, 11. The proportions of olefins 6 and 7 and olefins 9, 10, 11 were deduced by PMR spectroscopy. The structures of all mono and dimethylated olefins were finally established after comparison (PMR, GC-MS, retention time) with authentic samples.

Methylation of 2-methyl-1-octene 12
(general procedure according to Table 2)

The olefin 12 (1.2 - 2 eq) was heated in a sealed pyrex glass tube with sulfonium salt 1b (1 eq) in the presence of base 3 (1.5 eq) with undecane as internal standard. Crystallization of the salt of 3 was observed in each experiment. The yields of monomethylated olefins 13 - 17 were determined by GLC and their structures established, after preparative GLC by comparison (GC, GC-MS, PMR) with the mixture of the corresponding olefins obtained after dehydratation of 3-methyl-3-nonanol (see above).

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