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STRUCTURE - ODOR CORRELATION - IX[1]

FROM 1,8-CINEOL TO SESQUICINEOL - CHANGE OF ODOR WITH STRUCTURE

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Abstract: Cu(I)catalyzed 1,4-Grignard reaction of the key compound 6 led to the bicyclic keto ethers 7-15 together with small amounts of the alcohols 16-25. Wolff-Kishner reduction of 8-15 gave the 1,8-cineol homologues 26-32 and sesquicineol (2). - The fresh and camphoraceous odor of 1 changes stepwise with increasing side chain to herbaceous and spicy notes, compounds with branched side chains show lavender undertones. 2 has a pleasant fruity, floral and sweet fragrance.

Introduction

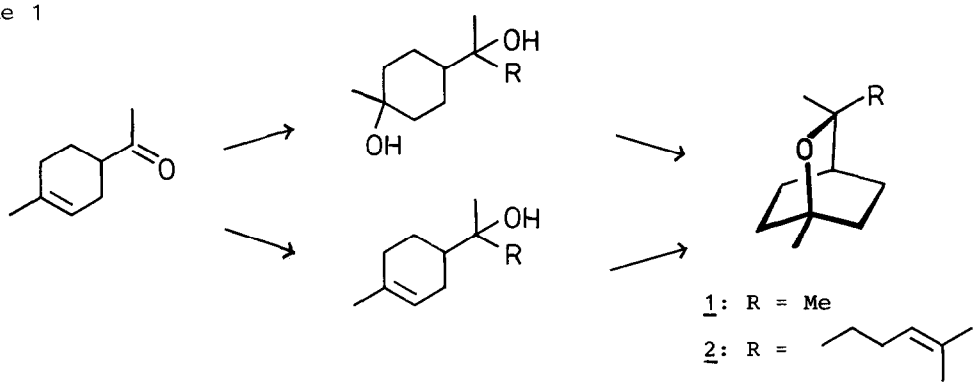
The absolute obtained from the flowers of Boronia megastigma Nees. is finding increased usage in both the perfume and flavor industry. Its very pleasant odor can be described as sweet, floral and fruity. A detailed investigation[2] of the constituents of Boronia oil resulted in the statement that for the overall aroma impression the most important compounds would seem to be the ionones, some esters, dihydroactinidiolide, methyl jasmonate isomers, and a new compound, called sesquicineol (2). The synthesis of 2 should give the evidence whether this compound contributes in fact to the pleasant flavor and fragrance of Boronia absolute. Simultaneously, the structurally related compounds described below should be prepared. The idea was that 1,8-cineol (1) possesses a partial structure of 2, and that it has a well known eucalyptus-like odor. Elongation of the chain at C-7 should lead stepwise from cineol (1) to sesquicineol (2). It should be interesting to investigate whether the odor would change also stepwise, proceeding from fresh, camphoraceous, cool to sweet, floral, or whether there would be any particular molecular requirement.

2 has been isolated first from Senecio subrubriflorus,[3] from Anthemis alpestris,[4] and was found later in Brazilian Ayou oil (Aydendron barbeyana).[5] A synthesis leading to 2 together with its double bond isomer has been published,[6] but no olfactive evaluation was given. We looked for a sequence not only convenient for the synthesis of 2 itself, but also for the related ethers 26-32, including identical steps. Such a procedure is necessary to avoid different types of contamination from different types of reagents which can alter the odor.

Results and Discussion

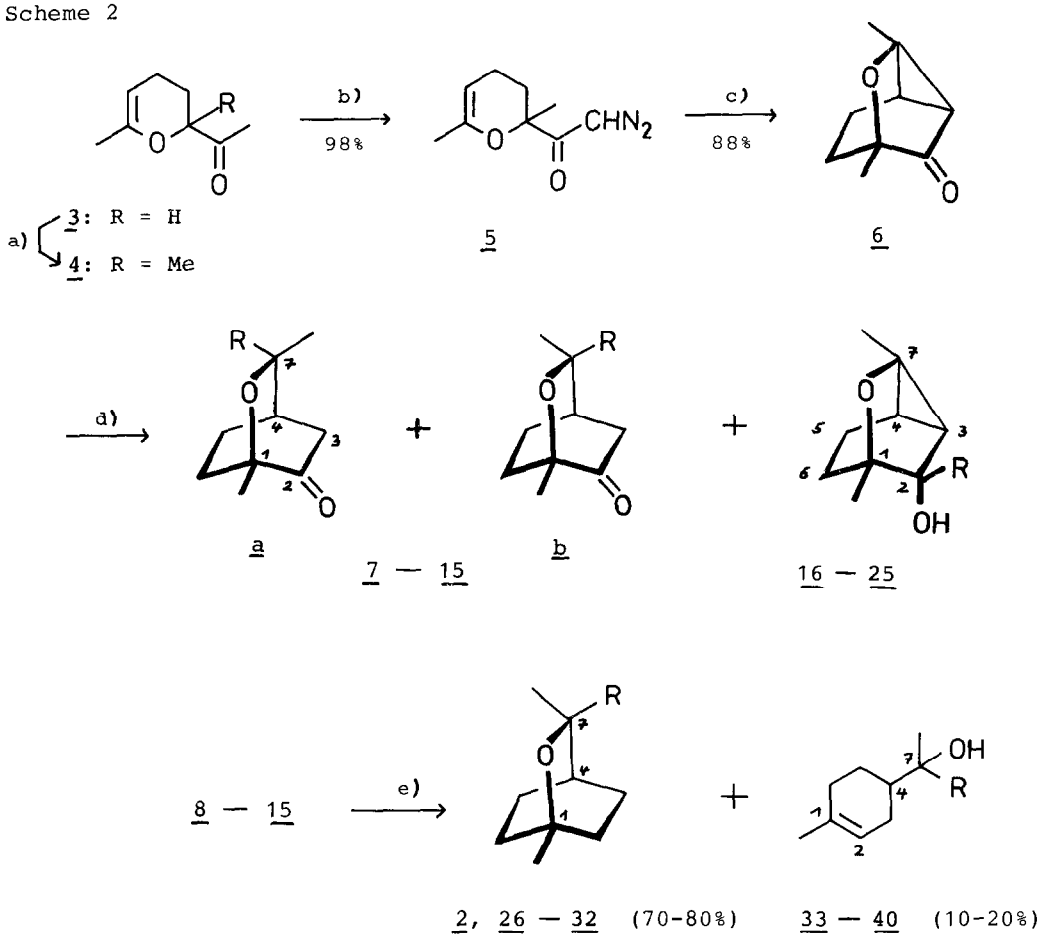
Obvious ideas to synthesize 2 and 26-32 according to Scheme 1 have been ruled out since preliminary experiments showed some disadvantages. From the diol the cyclization could not be achieved at all, the terpineol derivatives on the other hand needed hazardous and unpleasant smelling reagents,[7] and the cyclization gave mixtures (see also ref.[6]).

Scheme 1



Most attractive seemed to be to use the tricyclic ketone 6 as key compound. Its synthesis and homoconjugate addition of $Me_2CuLi/BF_3.Et_2O$ to give the 2-oxocineol 7 was described recently.[8] Transfer of this reaction step to various substituents should lead to the desired compounds.
Slightly modified dimerization[9] of methylvinyl ketone gave 3 in 60% yield. Methylation of 3 to furnish 4 must be carried out with freshly prepared $NaNH_2$ to obtain very good yields. In contrast to ref.[8] we were not very successful with the reaction sequence using ethyl oxalate/tosyl azide to obtain the diazoketone 5. Much cheaper and easier was the reaction with ethyl formate/mesyl azide[10] forming 5 in almost quantitative yield including purification by flash chromatography (FC). Intramolecular cyclization of 5, mediated by $[Rh(OAc)_2]_2$ in CH_2Cl_2 in presence of K_2CO_3, led readily to the tricyclic ketone 6.[8]
To find the most convenient method for the homoconjugate addition to 6 we performed some preliminary experiments. Neither lithium dialkyl cuprates[11] nor mixed organo cuprates[12] gave satisfactory results. The old fashioned Grignard method in presence of Cu_2I_2 at -75°C furnished the bicyclic ketones 8-15 in 70-85% yield together with mostly small amounts of the tricyclic alcohols 17-20 and 22-24 formed by 1,2-addition of the Grignard reagent to 6. With vinyl bromide only the alcohol 25 but no trace of the resp. ketone could be isolated. The alcohol 21 was not formed, probably due to steric hindrance.

Scheme 2



a) $NaNH_2$, MeI, ether, 24 h, rfl.; b) NaH, ether, HCOOEt, 18 h, r.t.; then MsN_3, ether, 3.5 d. r.t.; c) 1.5 mol% $[Rh(OAc)_2]_2$, K_2CO_3, CH_2Cl_2, 2 h, r.t.; d) RX, Mg, Cu_2I_2, ether/THF, 5 h, 75°C → 0°C; e) H_2NNH_2, K_2CO_3, triethylene glycol, 5 h, 160-250°C.

Comp. No.				R
7	16	1		Me
8	17	26	33	Et
9	18	27	34	Pr
10	19	28	35	$CHMe_2$
11	20	29	36	Bu
12	21	30	37	CH_2CHMe_2
13	22	31	38	$(CH_2)_3CHMe_2$
14	23	32	39	CH_2CHEt_2
15	24	2	40	$CH_2CH_2CH{=}CMe_2$
	25			$CH{=}CH_2$

Since these alcohols could be separated easily from the ketones 8-15 we did not investigate the Grignard reaction in presence of TMS/TMEDA,[13] TMS/HMPA,[14] or $Cu_2Br_2.Me_2S$.[15] Such S- or N-containing reagents are always prone to alter the odor.

The ketones 8-15 are mixtures of diastereoisomers a and b (4:1 to 30:1). As expected, the isomers a are main products. Evidence was given by NOED spectra. The ^1H NMR signal of the methyl group syn standing to the keto function is upfield shifted (about 0.15 ppm) in comparison to the anti standing group due to the shielding effect of the carbonyl group.

The Dreiding model of 6 shows that the attack to the carbonyl group can occur only from the exo side. The configuration of the alcohols 16-24 with endo OH group could be proven by the NOED spectrum of 17.

The ketones 8-15 were subjected to Wolff-Kishner reduction with hydrazine hydrate and K_2CO_3 in triethylene glycol at 200°C.[16] The ethers 2 and 26-32 were formed in good yields together with small amounts of the diastereoisomeric alcohols 33-39 and 40 (α-bisabolol). Separation was easy by FC, but the ethers 2 and 26-32 must be purified from subtraces of musty smelling contaminants (obviously N-heterocycles, not detectable by GC) by chromatography on Florisil® with pentane.

Reduction of tosylhydrazones with $[(Ph_3P)_2Cu]BH_4$[17] is milder than the Wolff-Kishner method. However, in our hands the yield of 2 from 15 was much lower and in addition the odor of 2 was affected by non separable traces of volatile phosphines.

Olfactive Properties

The typical eucalyptus odor (fresh, camphoraceous, cool) of 1,8-cineol (1) decreases slowly with elongation of the side chain (1 → 26 → 27 → 29). Simultaneously herbaceous (rosemary/sage) and spicy notes increase. In addition, the butyl derivative 29 possesses sweet and floral undertones. The branched compounds 28, 30 and 32 show a typical odor of lavender besides the herbaceous and spicy character. Sesquicineol (2), however, has the expected pleasant complex fragrance described as fruity, floral (narcissus, tuberose, mimosa), sweet and green, of medium strength. A similar way from eucalyptus to spicy, floral sweet and woody notes is observed with the ketones 7-12, 14 and 15. In addition, 8, 11, 14 and 15 show typical ginger odor. Even the weak odor of oxosesquicineol 15 still possesses eucalyptus undertones besides its spicy, fruity, floral and sweet tonality.

All these results show that the eucalyptus odor will be replaced continuously by spicy and herbaceous notes with increasing size of a saturated substituent at C-7. The unsaturated prenyl structure obviously is responsible for the big step to the beautiful odor of 2. This minor structural change such as introducing a double bond obviously has a major effect on the odor perceived.

This corresponds well with recent investigations in the amber field.[18] In addition, these findings fit well with the three-point binding model[19] where functional groups will meet the receptor surface sites which usually are 3 Å distant from each other. Although 2 possesses a flexible side chain, conformations matching this requirement are favorable. It is to realize, that sesquicineol (2) contributes well to the sensory properties of the Boronia absolute as described above.

EXPERIMENTAL

^{1}H NMR: Bruker WH 400 (internal TMS). - ^{13}C NMR: Bruker WH 270 with DEPT program. - IR: in CCl_4, Perkin-Elmer 257. - MS: Varian-MAT 711, 70 eV. - Purity control by GC: Packard 437a, 25 m glass capillary column CP Sil 5 CB. - Melting points: Büchi SMP-20. - Kugelrohr distillation (KRD): b.p. means temp. of the air bath. - Flash chromatography (FC): ICN Biomedicals silica gel 32-63. - Benzene, hexane, pentane, THF were purchased from Merck. - Ether was distilled from NaH; acetone from $KMnO_4$; pyridine from KOH; CH_2Cl_2 was filtered through molecular sieve. - Petroleum ether (PE) had b.p. 40-60°C. - All reactions were run in flamed vessels under an atmosphere of nitrogen except those in which water was present. - Usual work-up: Reaction products were isolated by the addition of water and extracted with the specified solvent. The combined extracts were washed to neutrality and then with saturated brine and dried over $MgSO_4$. The solvent was removed (after filtration) in vacuo on a rotary evaporator.

1-(6-Methyl-3,4-dihydro-2H-pyran-2-yl)-1-ethanone (3)

According to ref.[9] 126 g (1.80 mol) of methyl vinyl ketone and 2.8 g of hydroquinone were heated to 145°C in a stainless steel autoclave for 24 h. The viscous oil was distilled through a 20 cm Vigreux column to give 75 g (60%) of pure (GC: 99%) 3, b.p. 52-55°C/7Torr (ref.[9] b.p. 68°C/13 Torr). - ^{1}H NMR (C_6D_6): δ = 1.6-1.8 (m; 3-, 4-H_2), 1.70 (d, J = 1 Hz, 6-Me), 1.99 (s; MeCO), 4.01 (ddd, J = 6; 2; 2 Hz; 2-H), 4.36 (mc; 5-H). - ^{13}C NMR ($CDCl_3$): δ = 19.2 (t; C-4), 20.0 (q; 6-Me), 23.6 (t; C-3), 25.9 (q; MeCO), 80.3 (d; C-2), 96.4 (d; C-5), 149.9 (s; C-6), 209.5 (s; CO).

1-(2,6-Dimethyl-3,4-dihydro-2H-pyran-2-yl)-1-ethanone (4)[20]

To a suspension of freshly prepared $NaNH_2$ [from 4.9 g (0.21 mol) of Na, liq. NH_3, and 0.5 g of $FeCl_3$] in 150 ml of ether 30 g (0.21 mol) of 3 was added. After 45 mim a solution of 57 g (0.40 mol) of MeI in 150 ml of ether was added dropwise and the mixture refluxed for 24 h. After work-up the crude product (33 g) was distilled through a 20 cm Vigreux column to give 29.1 g of 4 (GC: 75%), b.p. 66-70°C/10 Torr (ref.[20] 66°C/19 Torr). - ^{1}H NMR ($CDCl_3$): δ = 1.19 (s; 2-Me), 1.37 (ddd, J = 13; 10.5; 6 Hz; 3-H), 1.69 (d, J = 1 Hz; 6-Me), 1.7 (mc; 4-H_2), 2.02 (s; MeCO), 4.37 (mc; 5-H). - ^{13}C NMR ($CDCl_3$): δ = 18.1 (t; C-4), 20.2 (q; 6-Me), 24.0, 24.4 (2 q; 2-Me, MeCO), 28.5 (t; C-3), 82.6 (s; C-2), 96.3 (d; C-5), 149.5 (s; C-6), 213.2 (s; CO).

1-(2,6-Dimethyl-3,4-dihydro-2H-pyran-2-yl)-2-diazo-1-ethanone (5)

According to ref.[10] a stirred mixture of 6.7 g (0.22 mol) of 80% NaH, 1.5 ml of ethanol and 100 ml of ether was treated dropwise at -5°C with a solution of 15.1 g (73 mmol) of 4 (GC: 75%) and 16.3 g (0.22 mol) of ethyl formate in 100 ml of ether. Stirring was continued for 3.5 h at -5°C and 18 h at 20°C. 26.4 g (0.22 mol) of mesyl azide[21] in 200 ml of ether were slowly added dropwise, and stirring was continued for 3.5 d. The mixture was quenched with 130 ml of water. The organic layer was washed with three 200 ml portions of 10% NaOH, and the aqueous layer was back extracted with four 50 ml portions of ether. The combined organic layers were treated as usual to give 20 g of dark red oil. FC (PE/ether 20:1) afforded 12.9 g (98%) of 5. - IR: 2120,

1685 (N_2CHCO), 1640 (C=C) cm^{-1}. - ^1H NMR ($CDCl_3$): δ = 1.38 (s; 2-Me), 1.56 (ddd, J = 13; 9.5; 6.5 Hz; 3-H), 1.78 (d, J = 1 Hz; 6-Me), 1.85-2.0 (m; 4-H_2), 2.22 (dddd, J = 13; 6; 4; 1 Hz; 3-H), 4.55 (mc; 5-H), 5.69 (s; CHN_2). - ^{13}C NMR (C_6D_6): δ = 18.4 (t; C-4), 20.4 (q; 6-Me), 24.9 (q; 2-Me), 29.0 (t; C-3), 51.2 (d; CHN_2), 82.1 (s; C-2), 97.0 (d; C-5), 149.0 (s; C-6), 197.7 (s; CO). - MS: m/z (%) = no M^+, 152 (M - N_2, 22), 137 (13), 109 (100), 95 (35), 81 (38).

1,5-Dimethyl-8-oxatricyclo[3.2.1.$0^{2,7}$]octan-6-one (6)

According to ref.[22] 0.29 g (2% by weight) of $[Rh(OAc)_2]_2$ and 0.29 g of K_2CO_3 were suspended in 60 ml of CH_2Cl_2. To this stirred suspension at r.t. was added slowly a solution of 14.4 g (80 mmol) of 5 in 120 ml of CH_2Cl_2. Stirring was continued for 2 h. Then 100 ml of CH_2Cl_2 were added, and the mixture was extracted five times with 50 ml of 5% aqueous Na_2CO_3. After drying over K_2CO_3 and removal of the solvent, KRD in presence of some Na_2CO_3 gave 10.7 g (88%) of 6, b.p. 85-95°C/5 Torr. - IR: 1740 cm^{-1} (CO). - ^1H NMR ($CDCl_3$): δ = 1.21 (s; 1-Me), 1.65 (s; 5-Me), 1.73, 2.01 (ABdd, J = 13; 10; 5 Hz; 4-H_2), 1.81 (ddd, J = 9; 2.5; 2.5 Hz; 2-H), 1.91 (d, J = 9 Hz; 7-H), 2.13 (mc; 3-H_2). - ^{13}C NMR ($CDCl_3$): δ = 16.8 (t; C-3), 18.3, 19.0 (2 q; 1-, 5-Me), 33.3, 34.1 (2 d; C-2, -7), 35.0 (t; C-4), 70.9 (s; C-1), 80.2 (s; C-5), 211.5 (s; C-6). - MS: m/z (%) = 152 (M^+, 16), 124 (29), 110 (27), 109 (53), 96 (100), 95 (61), 81 (78).

Reaction of ketone 6 with RMgX/CuI, general procedure

From 50 mmol of alkyl halide (see table 1a) and 1.1 g (45 mmol) of Mg turnings in 30 ml of ether a Grignard solution was prepared. At -25°C 30 ml of THF and 0.21 g of CuI were added dropwise in such a manner that the temp. was maintained from -75 to -70°C. Stirring was continued at -75°C for 30 min and then at -5°C to 0°C for 4.5 h. The mixture was poured into 150 ml of cooled sat. NH_4Cl solution. Work-up (5 times 25 ml of ether), KRD and FC (PE/ether 20:1) gave the ketones 8-15 (1. fraction) and the alcohols 17-20, 22-24 (2. fraction).

Wolff-Kishner reduction of ketones 8-15, general procedure

A mixture of 10 mmol of ketone 8-15, 4.4 g of K_2CO_3, 4.2 g of hydrazine hydrate, and 50 ml of triethylene glycol was heated at reflux for 1.5 h. After replacing the condenser by a distillation head, the temp. was raised to 200°C. After 1.5 h the residue was refluxed at 250°C for 3 h, cooled, diluted with 100 ml of water, and extracted five times with ether. The ether phases and the distillate were combined, washed with 10% HCl, water and brine. The solvent was removed through a 20 cm Vigreux column. After KRD the mixture was separated by FC to give the ethers 2, 26-32 (1. fraction) and the alcohols 33-40 (2. fraction). The ethers were further purified by chromatography on 15 g of Florisil® (0.15-0.25 mm) with pentane/ether (50:1).

Table 1a. Yields, b.p., and IR[a] of 3-Alkyl-1,3-dimethyl-2-oxabicyclo[2.2.2]octan-6-ones 8 - 15

Alkyl	Halide used	Cpd. no.	Yield (%)	b.p. (°C/Torr)	m.p. (°C)
Ethyl	Br	8	67	120-125/5	30
Propyl	I	9	69	145-150/5	
1-Methylethyl	Br	10	73	140-145/5	
Butyl	Br	11	65	100-105/0.06	47
2-Methylpropyl	Br	12	82	100-105/0.06	
4-Methylpentyl	I	13	50	110-115/0.06	
2-Ethylbutyl	Br	14	85	120-125/0.06	
4-Methyl-3-pentenyl	Br	15	76	110-115/0.06	

cont. Table 1b.

Table 1b. Yields, m.p., and IR of exo-6-Alkyl-1,5-dimethyl-8-oxatricyclo[3.2.1.$0^{2,7}$]octan-endo-6-ols (16-20, 22-25)

Alkyl	Cpd. no.	Yield (%)	m.p.[b] (°C)	IR (OH) (cm^{-1})
Methyl[c]	16	46	oily	3620, 3490
Ethyl	17	15	35	3630, 3490
Propyl	18	15	60	3590, 3450
1-Methylethyl	19	8	61	3620, 3490
Butyl	20	20	70	3630, 3490
4-Methylpentyl	22	39	oily	3640, 3400
2-Ethylbutyl	23	4	oily	3630, 3480
4-Methyl-3-pentenyl	24	10	oily	3640, 3570
Ethenyl[d]	25	67	85	3670, 3500

a) 1740 cm^{-1}. — b) From PE. — c) For comparison, prepared according to ref.[8]. - d) Only product with H_2C=CH-MgBr.

Table 2. ^{1}H NMR data of alcohols 16 - 20 and 22 - 25 $CDCl_3$, 400 MHz, δ-values, J[a], for numbering see formula

No.	1-Me s	7-Me s	3-H d	4-H ddd	5-H_{endo} dddd	5-H_{exo} ddd	6-H_{endo} ddd	6-H_{exo} ddd	2-R[b]
16	1.43	1.06	1.16	0.81	2.11	2.05	1.80	1.46	1.26 s
17	1.43	1.05	1.31	0.82	2.14	2.05	1.83	1.44	1.04 t (7), 1.55, 1.59 ABq (15;7)
18	1.43	1.05	1.30	0.81	2.16	2.05	1.82	1.44	0.98 t (7)
19	1.42	1.11	1.24	0.87	2.15	2.06	1.85	1.42	1.02, 1.05 2 d (7), 1.89 qq (7;7)
20	1.43	1.05	1.31	0.81	2.14	2.06	1.83	1.44	0.94 t (7), 1.37 sext (7)
22	1.43	1.04	1.32	0.82	2.09	2.06	1.82	1.44	0.98, 0.99 2 d (7), 1.59 non (7)
23	1.44	1.04	1.39	0.80	2.09	2.06	1.83	1.44	0.88 t (7), 1.30, 1.39 2 sept (7)
24	1.44	1.05	1.34	0.82	2.12	2.05	1.82	1.43	1.65, 1.75 2 s,br., 2.21 dt,br. (7;7), 5.19 tqq (7;1;1)
25	1.49	0.99	1.23	0.88	2.19	2.07	1.85	1.50	5.17 dd (11;1.5), 5.24 dd (17.5; 1.5), 5.96 dd (17.5; 11)

a) J [Hz]: 3,4 = 8; 4,5_{endo} = 2; 4,5_{exo} = $5_{exo}6_{endo}$ = 3.5; $5_{endo}6_{endo}$ = $5_{exo}6_{exo}$ = 11; $5_{endo}5_{exo}$ = $6_{endo}6_{exo}$ = 14; $5_{endo}6_{exo}$ = 6.5. — b) Significant signals only.

Table 3a. Yield, b.p. and ^{1}H NMR data[a] of 3-Alkyl-1,3-dimethyl-2-oxa-bicyclo[2.2.2]octanes (2, 26-32)

No.	Alkyl	Yield (%)	b.p. (°C/5 Torr)	1-Me	3-Me	3-R
2[b]	4-Methyl-3-pentenyl	80	90—94[c]	1.15	1.29	1.63, 1.73 2 s,br., 5.30 t,br. (7)
26	Ethyl	70	65—70	1.15	1.23	0.85 t (7.5), 1.68, 1.69 ABq (15;7.5)
27	Propyl	75	68—72	1.15	1.26	0.95 t (7.5)
28	1-Methylethyl	73	67—68	1.14	1.10	0.75, 1.17 2 d (7), 2.06 qq (7;7)
29	Butyl	76	82—88	1.16	1.27	0.95 t (7)
30	2-Methylpropyl	78	85—90	1.13	1.29	0.97, 1.12 2 d (7), 1.47 dd (14;5), 1.65 dd (14;7), 1.79 qqdd (7;7;7;5)
31	4-Methylpentyl	70	90—95	1.16	1.29	0.93, 0.94 2 d (7), 1.56 qqt (7;7;7)
32	2-Ethylbutyl	75	95-100	1.13	1.29	0.92, 0.99 2 t (7), 1.55 ttt (7;7;7)

[a] C_6D_6, 400 MHz, δ-values, significant signals only, J (Hz). — [b] Assignment of Me-groups vice versa to ref.[3]. — [c] Ref.[3] b.p. 120°C/0.1 Torr.

Table 3b. Yield and ^{1}H NMR data[a] of 2-(4-Methylcyclohex-3-en-1-yl)-.....2-ols (33-40) [b]; for numbering see formula.

No.	Name	Yield (%)	1-Me s,br.	2-H mc	7-Me s	7-R
33	..butan-	22	1.64	5.37 [5.40]	1.08 [1.11]	0.91 t, 1.50 q (7.5)
34	..pentan-	10	1.64	5.39 [5.37]	1.12 [1.09]	0.92 t (7)
35	..3-methylbutan-	13	1.65	5.37 [5.41]	1.02 [1.05]	0.89, 0.91[c] [0.87, 0.92]
36	..hexan-	15	1.65	5.37 [5.40]	1.09 [1.12]	0.91 [0.92] t (7)
37	..4-methylpentan-	10	1.65	5.37 [5.40]	1.11 [1.13]	0.96 [0.95] t (7.5)
38	..6-methylheptan-	trace				
39	..4-ethylhexan-	12	1.65	5.37 [5.40]	1.10 [1.12]	0.87 t (7)
40	..6-methyl-5-hepten-[d]	9				

[a] $CDCl_3$, 400 MHz, δ-values, significant signals only, J (Hz), [minor isomer]. — [b] IR: ~ 3600, 3480 cm^{-1}. — [c] 2 d (7), 1.82 qq (7;7). — [d] α-Bisabolol, spectra identical with those of authentic material.

Table 4. ^1H NMR data of ketones 7, 8a-15a [characteristic values for 8b-15b, if detectable]; C_6D_6, 400 MHz, δ-values, J (Hz); for numbering see formula

No.	1-Me s	7-Me s	3-H_{endo} [a] dd	3-H_{exo} [b] ddd	4-H [c]	6-H_{endo} [d,e] ddd	7-R [f]
7 [g]	1.32	1.03	1.85	2.54	1.67	1.2-1.3 m	1.15 s
$CDCl_3$	1.38	1.14	2.21	2.78	1.99 mc	1.64 (14;11.5;2.5)	1.23 s
8	1.32 [1.32]	0.98 [1.15]	1.86 [1.81]	2.51 [2.47]	1.42 dddd	1.26 (14;12;2.5)	0.72 [0.65] t (7.5) 1.47, 1.49 ABq (15;7.5)
9	1.34 [1.34]	1.00 [1.15]	1.87 [1.83]	2.53	1.44 dddd	1.27 (14;12;2.5)	0.89 [0.80] t (7.5)
10	1.31 [1.31]	0.85 [0.99]	1.85	2.54 [2.51]	1.53 dddd	1.26 (12;12; 1)	0.62, 1.06 [0.53, 1.00] 2 d (7), 1.85 qq (7;7)
11	1.34 [1.34]	1.02 [1.16]	1.88 [1.85]	2.54	1.46 dddd	1.27 (15;13; 2)	0.91 [0.86] t (7.5)
12 [h]	1.32	1.03	1.86	2.56	1.42 dddd	1.26 (13;11; 2)	0.89, 1.04 2 d (7), 1.34 dd (14;5), 1.52 dd (14;7)
13 [h]	1.34	1.04	1.89	2.54	1.47 mc	1.29 (14;12; 2)	0.93, 0.94 2 d (7)
14	1.32 [1.32]	1.04 [1.20]	1.87 [1.84]	2.58	1.41 dddd	1.26 (14;12; 2)	0.87, 0.92 [0.82, 0.87] 2 t (7.5), 1.48, 1.64 ABd (14;7)
15	1.33 [1.33]	1.04 [1.19]	1.87 [1.85]	2.53 [2.58]	1.46 [1.51] mc	1.26 (12;11; 2)	1.59, 1.72 [1.55, 1.68] 2 d (1), 5.31 [5.21] tqq (7;1;1)

a) J = 19;3. — b) J = 19;3;3. — c) J = 3.5;3;3;2.5. — d) 5-H_{endo}: 0.9-1.0 m; 5-H_{exo}: 1.2-1.3 m. — e) 6-H_{exo}: 1.5-1.7 m. — f) Significant signals only. — g) See ref.[23,24]. h) < 3% of isomer b.

Table 5. ^{13}C NMR data (C_6D_6, δ-values) of ethers 2, 26 - 32; for numbering see formula.

No.	C-1 s	C-2+ t	C-6+ t	C-3° t	C-5° t	C-4 d	C-7 s	1-Me q	7-Me q	7-R
2 [a]	69.1	32.0	32.1	23.0	23.2	31.0	75.4	27.9	26.0	17.6 q, 25.8 q, 23.8 t, 42.3 t, 125.6 d, 130.7 s
26	68.4	31.3	31.4	22.1	22.4	29.5	74.9	27.1	24.5	8.4 q, 33.9 t
27	69.1	32.0	32.2	22.9	23.2	30.8	75.3	30.8	25.9	15.2 q, 18.2 t, 44.9 t
28	69.1	31.9	32.0	22.4	23.5	30.0	77.2	27.9	18.7+	16.8+q, 18.3+q, 35.7 d
29	69.1	32.0	32.2	23.0	23.2	30.8	75.4	27.9	26.0	14.3 q, 23.9 t, 27.3 t, 42.2 t
30	69.0	31.8	32.1	23.1	23.3	32.3	75.6	27.9	26.1	24.8 q, 25.3 q, 24.8 d, 50.4 t
31	69.1	32.0	32.2	23.0	23.2	30.9	75.4	27.9	26.0	22.8 q, 22.8 t, 28.2 d, 40.1 t, 42.6 t
32	69.0	31.8	32.1	23.2	23.4	32.6	75.8	27.8	26.1	10.6 q, 11.3 q, 27.5 t, 26.8 t, 36.6 d, 44.3 t

+, ° exchangeable values. — [a] In agreement with ref.[3].

Table 6. ^{13}C NMR data ($CDCl_3$, δ-values) of ketones 7, 8a - 15a

No.	C-1 s	C-2 s	C-3 t	C-4 d	C-5 t	C-6 t	C-7 s	1-Me q	7-Me q	7-R
7 [a,b]	75.6	208.1	40.9	36.5	21.9	28.9	73.9	19.9	27.9	28.6 q
8	75.3	210.2	40.4	33.2	21.6	29.0	76.7	19.5	24.9	8.6 q, 33.0 t
9	75.2	210.5	40.7	34.1	21.4	28.8	76.3	19.5	24.8	14.8 q, 18.5 t, 44.2 t
10	75.2	210.6	41.1	34.1	21.0	28.9	78.2	19.5	18.6	17.7 q, 16.5 q, 35.6 d
11	75.3	210.4	40.7	34.1	21.4	29.0	76.3	19.5	24.8	14.0 q, 23.3 t, 27.4 t, 41.5 t
12	75.1	210.4	41.0	35.7	21.7	28.7	76.5	19.4	24.8	24.4 q, 25.0 q, 24.8 d, 49.7 t
13 [a]	75.3	208.3	40.9	34.4	21.6	29.1	76.0	20.0	23.1	22.7 q, 28.1 d, 24.7 t, 39.9 t, 42.2 t
14 [a]	75.2	208.2	41.2	36.4	21.8	28.7	76.3	19.9	24.8	10.4 q, 11.2 q, 26.4 t, 27.2 t, 36.7 d, 43.8 t
15 [a]	75.3	208.2	40.9	34.6	21.6	29.0	75.8	20.0	24.6	17.6 q, 25.8 q, 24.1 t, 42.0 t, 124.9 d, 131.2 s

[a] In C_6D_6. — [b] In agreement with ref.[23].

Table 7. ^{13}C NMR data ($CDCl_3$, δ-values) of alcohols 16 - 20, 22 - 25, 33 - 37 and 39[a)]

No.	C-1	C-2	C-3	C-4	C-5	C-6	C-7	1-Me	7-Me	2-R
	s	s	d	d	t	t	s	q	q	
16	80.6	78.8	30.9	18.3	16.1	28.0	62.8	20.0	19.1	24.6 q
17	81.0[+]	81.4[+]	27.1	18.3	16.2	29.0	63.2	19.8	19.1	7.8 q, 29.4 t
18	81.3	80.7	27.5	18.3	16.1	28.8	63.2	19.8	19.1	14.8 q, 16.6 t, 39.3 t
19	82.6	83.2	24.7	18.6	16.6	30.9	63.9	19.4	18.8	18.1 q, 33.4 d
20	81.4	80.8	27.6	18.4	16.1	28.8	63.2	19.8	19.1	14.1 q, 23.4 t, 25.5 t, 36.7 t
22	81.4	80.8	27.6	18.4	16.1	28.9	63.2	19.9	19.1	22.4 q, 22.8 q, 21.1 t, 27.9 d, 37.2 t, 39.6 t
23	81.6	81.6	27.1	18.0	16.0	28.4	63.1	19.8	19.0	10.7 q, 11.1 q, 27.3 t, 27.5 t, 35.9 d, 39.4 t
24	80.8	81.3	27.4	18.4	16.1	28.7	63.2	19.9	19.1	17.7 q, 25.7 q, 22.2 t, 36.7 t, 124.5 d, 132.2 s
25	81.3	81.8	29.7	18.6	16.0	28.2	63.4	20.9	19.0	112.5 t, 141.4 d
	s	d	t	d	t	t	s	q	q	7-R
33	134.1	120.5	26.8	42.3	23.2	31.1	74.2	23.3	22.8	7.5 q, 32.6 t
34	133.8	120.7	26.0	42.8	23.2	31.0	74.2	23.3	24.1	14.7 q, 16.7 t, 41.9 t
35	134.2	120.7	26.9	40.7	22.9	31.0	75.7	23.3	19.2	16.4 q, 17.3 q, 33.9 d
36	134.1	120.6	26.9	42.7	23.3	31.0	74.2	23.3	23.4	14.1 q, 24.2 t, 25.4 t, 40.1 t
37	134.1	120.6	27.0	43.7	23.3	31.0	74.9	23.3	23.7	24.9 q, 23.8 d, 48.7 t
39	134.1	120.6	27.0	44.1	23.5	31.1	75.0	23.3	23.6	10.7 q, 10.8 q, 27.1 t, 27.2 t, 35.6 d, 43.1 t

a) For numbering see formula.

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