

25. Synthesis of (*E*)-1-Propenyl Ketones from Carboxylic Esters and Carboxamides by Use of Mixed Organolithium-Magnesium Reagents

Synthesis of α -Damascone, β -Damascone, and β -Damascenone¹⁾

by Charles Fehr* and José Galindo

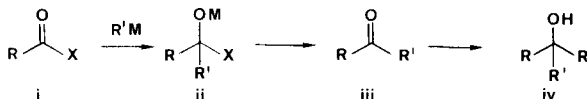
Firmenich SA, Research Laboratories, CH-1211 Geneva 8

(22.XI.85)

The novel reagents formed by combination of allylmagnesium chloride and a strong non-nucleophilic lithium base (LiNR_2) convert non- or slowly enolizable carboxylic esters or carboxamides into 2-propenyl ketones which are protected from further reaction by their *in situ* conversion into enolates. This modified *Grignard* reaction is applied to efficient syntheses of α -damascone, β -damascone, β -damascenone, and various other (*E*)-1-propenyl ketones.

Introduction. – In general, the reaction of carboxylic esters **i** with a *Grignard* reagent predominantly leads to tertiary alcohols **iv** because the intermediate ketones **iii** are more reactive than the substrate **i** (*Scheme 1*). Nevertheless, ketones can be obtained when the reactivity of the substrate **i** is increased (e.g. $\text{X} = \text{Cl}$) [2] [3]. Another method for favoring ketone formation is based on the survival of the addition product **ii** prior to hydrolysis (e.g. low temperatures, sterically uncrowded intermediate **ii**, strong O-M bond and X-M chelation [4]²⁾).

Scheme 1



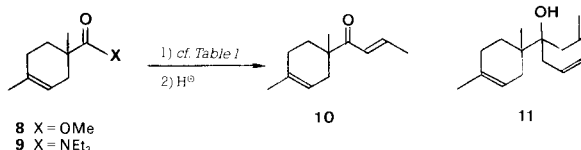
In many cases, application of one or the other of these two methods is successful. However, the highly reactive allylic *Grignard* reagents are known to give predominantly the tertiary alcohol **iv** even with acid chlorides at -78° [2] (method 1: activation of substrate) and the procedures that take advantage of the stabilization of intermediate **ii** (method 2) are not appropriate for highly substituted systems.

With the goal being a direct approach to the precious rose ketones **4–6** [6] as well as the perfumistically interesting ketone **10** [7], we required an efficient method for converting a carboxylic esters or carboxamide into a (*E*)-1-propenyl ketone. We reasoned that for substrate esters or amides **i** with a low tendency to enolize, the presence of a strong external base would protect the intermediate 2-propenyl ketone **v** from further reaction (to **vi**) by rapid deprotonation into its enolate **vii** (*Scheme 2*).

¹⁾ This work was presented at the Swiss Chemical Society Meeting in Berne, October 14, 1983. For a preliminary account, see [1].

²⁾ For a special (intramolecular) case, see [5].

Scheme 4



As illustrated in Table 1, the presence of a lithiumdialkylamide greatly favors the formation of ketone **10** (cf. Entries 1 and 2). When the same reaction is effected with the carboxamide **9**, the selectivity for *mono-Grignard* reaction is excellent (Entries 6 and 7), only traces of *tert*-alcohol **11** being observed⁷⁾.

Table 1. Formation of **10/11** from **8** or **9**

Entry	Substrate	Reaction conditions	10/11 ^{a)}
1	8	MgCl (2 equiv.)	14:86
2	8	[MgCl, LiN(i-Pr) ₂] (1.3 equiv.)	67:33
3	8	[Li, LiMgN(i-Pr) ₂] (1.4 equiv.)	70:30
4	8	Li ^{b)} (2 equiv.)	(30:70) ^{c)}
5	9	MgCl (2 equiv.)	50:50
6	9	[MgCl, LiN(i-Pr) ₂] (1.1 equiv.) ^{d)}	92:8 (99:1) ^{c)}
7	9	[MgCl, LiN(i-Pr) ₂] (1.1 equiv.) ^{d)}	95:5 (99:1) ^{c)}
8	9	Li ^{b)}	94:6 (95:5) ^{c)}
9	9	[MgCl, LiMgNEt ₂] (2 equiv.)	56:44

^{a)} Yield of **10** + **11** ca. 85%.

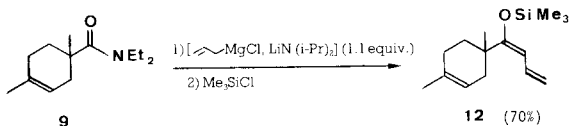
^{b)} Prepared according to *Elsch* [14]; contains LiOPh.

^{c)} Ratios in brackets refer to incomplete conversion (70–80%).

^{d)} The same result is obtained when LiNEt₂ is used instead of LiN(i-Pr)₂. However, with LiNEt₂, 2 equiv. of *Grignard* reagent are required for full conversion.

In addition, quenching the reaction mixture (Entry 6) with Me₃SiCl affords silylenol-ether **12**⁸⁾ in high yield, providing further evidence for the presence of an enolate (Scheme 5).

Scheme 5



⁷⁾ The diethylamides corresponding to esters **1–3** are unreactive.

⁸⁾ (*E*)/(*Z*) ≈ 9:1. We assume that the major silylenol ether **12** formed has the (*E*)-configuration (see [15]).

Table 2. Reactions of Various Carboxylic Esters and Carboxamides to Yield (E)-1-Propenyl Ketones

Entry	Substrate	Reagents (equiv.)	Product (yield [%]) ^{a)}	Selectivity ^{b)}	No Li reagent ^{c)}	
1	 1	$\text{CH}_2=\text{CH}-\text{MgCl}$ (1.7), $\text{LiN}(\text{i-Pr})_2$ (1.05)	 4	(85)	98:2	28:72
2	 2	$\text{CH}_2=\text{CH}-\text{MgCl}$ (1.5), $\text{LiN}(\text{i-Pr})_2$ (1.5)	 5	(80)	$\geq 90:10$	15:85
3	 3	$\text{CH}_2=\text{CH}-\text{MgCl}$ (1.45), $\text{LiN}(\text{i-Pr})_2$ (1.65)	 6	(76)	$\geq 96:4$	15:85
4	 8	$\text{CH}_2=\text{CH}-\text{MgCl}$ (1.3), $\text{LiN}(\text{i-Pr})_2$ (1.3)	 10	(60)	67:33	14:86
5	 9	$\text{CH}_2=\text{CH}-\text{MgCl}$ (1.3), $\text{LiN}(\text{i-Pr})_2$ (1.3)	10	(78)	92:8 (99:1) ^{d)}	50:50
6	 8	1) LiNEt_2 (1.15) 2) $\text{CH}_2=\text{CH}-\text{MgCl}$ (1.3), $\text{LiN}(\text{i-Pr})_2$ (1.3)	10	(77)	92:8	–
7	 13	$\text{CH}_2=\text{CH}-\text{MgCl}$ (1.5), $\text{LiN}(\text{i-Pr})_2$ (1.5)	 14 +  15		20:80	2:98
8	 16	$\text{CH}_2=\text{CH}-\text{MgCl}$ (1.05), $\text{LiN}(\text{i-Pr})_2$ (1.05)	14 (77) + 15		80:20	17:83
9	 13	1) LiNEt_2 (1.05) 2) $\text{CH}_2=\text{CH}-\text{MgCl}$ (1.05), $\text{LiN}(\text{i-Pr})_2$ (1.05)	14 (66) + 15		80:20	–
10	 17	1) $\text{LiN}(\text{i-Pr})_2$ (1.0) 2) $\text{CH}_2=\text{CH}-\text{MgCl}$ (1.3), $\text{LiN}(\text{i-Pr})_2$ (1.3)	 18	(65)	92:8	5:95
11	 19	1) $\text{LiN}(\text{i-Pr})_2$ (1.0) 2) $\text{CH}_2=\text{CH}-\text{MgCl}$ (1.15), $\text{LiN}(\text{i-Pr})_2$ (1.15)	 20	(55)	99:1	80:20

^{a)} After acid treatment (TsOH , see *Exper. Part*); see *Footnote 5*.^{b)} See *Footnote 2*; GC ratios, no calibration.^{c)} Selectivity with $\text{CH}_2=\text{CH}-\text{CH}_2\text{MgCl}$ alone.^{d)} Incomplete conversion ($\approx 75\%$).

The examples presented in *Table 2* illustrate the general applicability of this new approach and show that carboxamides react in a more selective manner than the corresponding carboxylic esters (*cf.* **8** and **9**, *Entries 4* and *5*; **13** and **16**, *Entries 7* and *8*). In addition, we have found that these amides can be prepared *in situ* from the corresponding esters by treatment with 1 equiv. of LiNEt_2 (*Entries 6* and *9*)⁹⁾.

Discussion. – Although there is apparently no doubt concerning the formation of stable enolates which serve as protecting groups for the intermediate 2-propenyl ketones **v**, several factors influence the outcome of the reaction: *i*) leaving group X of substrate

⁹⁾ For other examples of this method, see [16] and references cited therein.

i: $X = \text{NEt}_2$ more favorable than OMe ; ii) added base: effective bases: $\text{LiNEt}_2 \approx \text{LiN}(\text{i-Pr})_2 \gg \text{ClMgN}(\text{i-Pr})_2$; ineffective bases: $t\text{-BuOK}$, KH , NaH , LiH , LiNH_2 ; iii) temperature: higher temperatures favor enolization.

The experiments performed with **8** and **9** as substrates (*Table 1*) lead us to believe that allylmagnesium chloride and the lithiumdialkylamide are interacting to form a mixed aggregate **7** of characteristic reactivity. Indeed, in a cross-over experiment, the mixture of allyllithium and chloromagnesium diisopropylamide (as compared to **7**) showed the same reactivity towards **8** (*Table 1*, compare *Entries 2* and *3*)¹⁰). In most cases, a good chemoselectivity was obtained using equimolar amounts of allylmagnesium chloride and $\text{LiN}(\text{i-Pr})_2$. Larger amounts of $\text{LiN}(\text{i-Pr})_2$ led to a slightly improved selectivity, but the side products also become more important (presumably resulting from concurrent condensation reactions). Possibly, allylmagnesium chloride and $\text{LiN}(\text{i-Pr})_2$ form a 1:1 aggregate containing amide and allylunits bonded to Mg and Li together with variable amounts of 'free' $\text{LiN}(\text{i-Pr})_2$. The fact that the constitution of the reacting species is almost certainly modified during the reaction makes the complete understanding of the *mono-Grignard* reaction even more difficult. We postulate that the mixed aggregate also undergoes complexation with the substrate **i** (especially, when $X = \text{NR}_2$), thus, imparting to the whole transformation (nucleophilic attack of allylmethyl derivative, elimination of ' R_2NM ' and deprotonation of the ketone **v**) some intramolecular character¹¹).

In addition to the constitutional factors, the nature of the metal also plays an important role. In comparison with allylmagnesium chloride the electropositive lithium renders the reagent **7** more basic, stable lithium enolates are obtained and moreover, the decreased *Lewis*-acid character of the reaction medium reduces activation of the ketone carbonyl group for further attack by the *Grignard* reagent¹²)¹³).

In conclusion, the aforementioned procedure for the preparation of sterically hindered (*E*)-1-propenyl ketones represents an efficient solution to the long standing problem of direct *mono*-addition of allyl-*Grignard* reagents to sterically crowded carboxylic esters and carboxamides. In continuation of our work in this field, we are presently investigating other allylic and non-allylic organo-metallic reagents.

We would like to thank Prof. D. Seebach for interesting discussions on mechanistic aspects of our results.

¹⁰) For a discussion about non-stoichiometric effects with organolithium derivatives, see [17] [18]; for a recent example of a mixed diethylmagnesiummethylithium reagent, see [19].

¹¹) For interactions between lithium enolates and secondary amines, see [18], for interactions between organolithium compounds and esters or ketones, see [20].

¹²) The presence of MgBr_2 is known to suppress the formation of enolates [21].

¹³) The reactions with **13** and **16** (*Table 2*, *Entries 7*, *8*, and *9*) gave no cyclic products. Nevertheless, we cannot exclude a single-electron transfer (SET) taking place during the *Grignard* reaction. For discussions concerning SET or non-SET mechanisms in organometallic reactions containing LiNR_2 , see [22].

Experimental Part

(with the valuable collaboration of M. Pittet)

General. TLC was performed on *F* 254 plates (Merck); the spots were revealed using EtOH/anisaldehyde/ H_2SO_4 18:1:1. GC was carried out on a Carlo Erba Fractovap 2350 or a Hewlett Packard 5890. IR: Perkin-Elmer 297 spectrometer; band positions in cm^{-1} . $^1\text{H-NMR}$: Varian EM 360 (60 MHz) or Bruker WH 360 (360 MHz); chemical shifts in δ are reported in ppm relative to TMS as internal standard. MS: Finnigan MAT 1020/4021 (70 eV).

α -Damascone (= (E)-1-(2,6,6-Trimethyl-2-cyclohexenyl)-2-buten-1-one; **4**). A soln. of BuLi in toluene or hexane¹⁴⁾ (45.25 ml, 2.55N, 115.4 mmol) was added at 0° to a stirred soln. of (i-Pr)₂NH (11.76 g (165 ml), 116 mmol) in THF (145 ml). After complete addition, the clear yellow soln. was allowed to attain 20° and treated with a soln. of allylmagnesium chloride in THF (75.0 ml, 2.50 N, 187 mmol). The resulting grey soln. was heated at 33°, and a soln. of methyl α -cyclogeraniate (= methyl 2,6,6-trimethyl-2-cyclohexene-1-carboxylate; **1**) [12] (20.0 g, 110 mmol) in THF (26 ml) was added dropwise during 5 min at 35°. After 45 min, the grey-green soln. was quenched with aq. NH_4Cl /ice and extracted with Et_2O . The org. phase was washed with aq. 5% HCl, aq. sat. NaHCO_3 and aq. sat. NaCl soln. dried (Na_2SO_4), evaporated and distilled (60–70°/0.05 Torr). A soln. of the distillate (20.44 g) and TsOH (400 mg) in toluene (25 ml) was stirred at 20° for 15 h, poured into aq. 10% Na_2CO_3 soln., and the product was extracted (Et_2O). Distillation (60–70°/0.05 Torr) afforded **4** (17.95 g (85%)), identical to an authentic sample¹⁵⁾.

β -Damascone (= (E)-1-(2,6,6-Trimethyl-1-cyclohexenyl)-2-buten-1-one; **5**). A soln. of BuLi in hexane (56.8 ml, 1.45N, 82.4 mmol) was added at –10 to 0° to a stirred soln. of (i-Pr)₂NH (8.59 g (120 ml), 85.1 mmol) in THF (60 ml). After complete addition, the clear yellow soln. was treated with a soln. of allylmagnesium chloride in THF (32.9 ml, 2.50N, 82.3 mmol) at 0°, and methyl β -cyclogeraniate (= methyl 2,6,6-trimethyl-1-cyclohexene-1-carboxylate; **2**) [12] (10.0 g, 54.9 mmol) was added to the grey soln. at 0–5°. The mixture was stirred at 0° for 1 h and at 20° for 2 h. Workup and isomerization (TsOH) as described above gave, after filtration through silica gel (50 g; cyclohexane/ AcOEt 98:2, **5** (8.42 g (80%)), identical to an authentic sample¹⁵⁾.

β -Damasconone (= (E)-1-(2,6,6-Trimethyl-1,3-cyclohexadienyl)-2-buten-1-one; **6**). It was proceeded as described for **5**, but after complete addition of methyl β -safranate (= methyl 2,6,6-trimethyl-1,3-cyclohexadiene-1-carboxylate; **3**) [12], the red brown mixture was stirred at 5° for 2 h. Reagents used: BuLi/hexane (100.6 ml, 1.60N, 161 mmol), (i-Pr)₂NH (16.82 g (23.56 ml), 166 mmol), allylmagnesium chloride (73.1 ml, 2.50N, 183 mmol), **3** (20.0 g, 111 mmol) [12], and THF (40 ml). Workup and isomerization (TsOH (400 mg), no solvent) afforded **6** (16.05 g, 76%¹⁵⁾), identical to an authentic sample¹⁵⁾ and recovered **3** (1.52 g, 7%).

N,N-Diethyl-1,4-dimethyl-3-cyclohexene-1-carboxamide (**9**). A soln. of BuLi in hexane (15.9 ml, 1.45N, 23.0 mmol) was added at 0° to a stirred soln. of Et_2NH (1.75 g (2.46 ml), 24.0 mmol) in THF (30 ml). After 30 min, the soln. was cooled to –10°, and methyl 1,4-dimethyl-3-cyclohexene-1-carboxylate (**8**) [13] (3.36 g, 20 mmol) in THF (10 ml) was added in 2 min. The temp. rose to 10°. After 10 min, amide **9** was extracted (Et_2O /aq. sat. NH_4Cl soln.) and distilled in a bulb-to-bulb apparatus (oven temp. 150°/5 Torr). Yield: 3.50 g (84%). IR (neat): 2940, 1630, 1420, 1380, 1280, 1100. $^1\text{H-NMR}$ (60 MHz): 1.12 (t, J = 7, 6 H); 1.17 (s, 3 H); 1.68 (br. s, 3 H); ~1.60–2.20 (m, 5 H); 2.58 (d, J = 16, 1 H); 3.42 (q, J = 7, 4 H); 5.34 (m, 1 H). MS: 209 (20, M^+), 109 (74), 108 (100), 100 (60), 93 (49), 72 (66).

(E)-1-(1,4-Dimethyl-3-cyclohexenyl)-2-buten-1-one (**10**) (Table 2, Entry 6). Ester **8** [13] (1.68 g, 10.0 mmol) in THF (10 ml) was added at 0° to a soln. of LiNEt_2 (11.5 mmol), prepared from Et_2NH (876 mg (1.23 ml), 12.0 mmol) in THF (25 ml) and BuLi in hexane (7.18 ml, 1.60N, 11.5 mmol) at 0°. After 10 min, a mixture of $\text{LiN}(\text{i-Pr})_2$ (13.0 mmol, prepared from (i-Pr)₂NH (1.36 g (1.91 ml), 13.5 mmol) in THF (25 ml) and BuLi in hexane (8.12 ml, 1.60N, 13.0 mmol) at 0°, and allylmagnesium chloride in THF (5.65 ml, 2.30N, 13.0 mmol) was added at 20° in 3 min to the solution¹⁶⁾. Stirring was continued for 30 min. Workup, thermal isomerization (160°/3 h), and bulb-to-bulb distillation (oven temp. 110°/3 Torr) gave **10** (1.37 g, 77%¹⁵⁾), identical to an authentic sample [6].

(E)-1-(1,4-Dimethyl-3-cyclohexenyl)-1-(trimethylsilyloxy)-1,3-butadiene (**12**). A soln. of **9** (2.09 g, 10 mmol) in THF (30 ml) was treated at 20° with a mixture of $\text{LiN}(\text{i-Pr})_2$ (12.0 mmol) and allylmagnesium chloride (12.0 mmol) in THF/hexane (35 ml) as described above. After 30 min, the soln. was cooled to –70° and treated with Me_3SiCl (3.22 g (3.75 ml), 30.0 mmol). The cooling bath was removed and stirring was continued at 20° for 15 h.

¹⁴⁾ With BuLi in hexane, 4% of diallylated product was formed.

¹⁵⁾ α -Damascone (**4**), β -damascone (**5**) (or Dorinone beta*), and β -damasconone (**6**) (or Doricenone*) are manufactured by Firmenich SA.

¹⁶⁾ Alternative procedure: addition of **1** to a soln. of $\text{LiNEt}_2/\text{LiN}(\text{i-Pr})_2$ and treatment of the resulting soln. with allylmagnesium chloride (see [1]).

Evaporation and filtration (*Celite*, pentane) afforded **12**⁸) (1.75 g, 70%). IR (neat): 2970, 1620, 1260, 1090, 850. ¹H-NMR (360 MHz): 0.50 (s, 9 H); 1.40–2.30 (m, 9 H [max. 1.64]); 4.84 (dd, *J* = 2, 10, 1H); 5.02 (dd, *J* = 2, 17, 1H); 5.30 (br. 1H); 5.37 (*d*, *J* = 11, 1H); 6.51 (*d*′, *J* ≈ 10, 17, 1H). MS: 250 (23, *M*⁺), 235 (54), 194 (27), 167 (52), 73 (100).

Ethyl 2,2-Dimethyl-5-hexenoate (13). A soln. of ethyl 2-methylpropionate (25.17 g, 217 mmol) in THF (100 ml) was added dropwise at −78° to a soln. of LiN(*i*-Pr)₂ (228 mmol) in THF/hexane (400 ml). After 2 h, 4-bromobutene (29.26 g (22.2 ml), 217 mmol) in THF (50 ml) was added dropwise at −78° to the above soln. The mixture was allowed to attain 20° (2 h). After 13 h at 20°, the mixture was poured into aq. NH₄Cl soln./ice and extracted with Et₂O. The org. phase was washed with aq. 5% HCl, aq. sat. NaHCO₃ and aq. sat. NaCl soln., dried (Na₂SO₄), evaporated, and distilled to give **13** (26.17 g, 71%). B.p. 75°/4 Torr. IR: 2970, 1720, 1640, 1470, 1140. ¹H-NMR (60 MHz): 1.17 (s, 6 H); 1.27 (*t*, *J* = 7, 3 H); 1.40–2.25 (m, 4 H); 4.10 (*q*, *J* = 7, 2 H); 4.75–5.15 (m, 2 H); 5.45–6.15 (m, 1 H). MS: 170 (0.4, *M*⁺), 116 (77), 97 (40), 88 (67), 73 (22), 55 (100).

(*E*)-5,5-Dimethyl-2,8-nonadien-4-one (**14**) from N,N-Dimethyl-2,2-dimethyl-5-hexeneamide (**16**) (Table 2, Entry 8). A soln. of **16** (see below) (1.50 g, 90% pure, 6.85 mmol) in THF (5 ml) was added, at 30–40°, to a soln. of LiN(*i*-Pr)₂ (7.20 mmol) and allylmagnesium chloride (7.20 mmol) in THF/hexane (30 ml). After 90 min, the soln. was quenched with aq. NH₄Cl soln./ice and the product extracted in the usual manner. Bulb-to-bulb distillation (oven temp. 100–160°/2 Torr) afforded a 80:20 mixture (1.29 g) of **14** (and isomers) and 4-allyl-5,5-dimethyl-1,8-nonadien-4-ol (**15**). Isomerization (TsOH (20 mg), toluene (30 ml), 70°, 4 h), extractive isolation, and bulb-to-bulb distillation (oven temp. 100–150°/0.05 Torr) gave a 80:20 mixture **14/15** (1.14 g, 96% pure, yield of **14** ≈ 77%)⁵. A pure sample of **14** was obtained by chromatography (silica gel) with CH₂Cl₂. IR (CDCl₃): 2960, 1680, 1620, 1440, 980. ¹H-NMR (60 MHz): 1.10 (s, 6 H); 1.50–2.10 (m, 7 H [max. 1.92 (*d*, *J* = 6, 3 H)]); 4.80–5.20 (m, 2 H); 5.30–6.20 (m, 1 H); 6.50 (br. *d*, *J* = 15, 1 H); 6.94 (*dq*, *J* = 6, 15, 1 H). MS: 112 (54), 97 (19), 69 (100), 55 (91).

Ketone 14 from Ethyl 2,2-Dimethyl-5-hexenoate (13) (Table 2, Entry 9). Following the procedure described for **10**, ester **13** (1.50 g, 8.82 mmol) was converted via **16** into a 80:20 mixture **14/15** (1.29 g, 94% pure, yield of **14** ≈ 66%).

Amide 16. Following the procedure described above, **13** (8.14 g, 47.88 mmol) was converted into **16** (90% pure, 9.21 g, 88%) after bulb-to-bulb distillation (oven temp. 100–150°/4 Torr). IR (CDCl₃): 2970, 1610, 1415, 1060. ¹H-NMR (60 MHz): 1.13 (*t*, *J* = 7, 6 H); 1.28 (s, 6 H); 1.50–2.20 (m, 4 H); 3.40 (*q*, *J* = 7, 4 H); 4.80–5.20 (m, 2 H); 5.50–6.30 (m, 1 H). MS: 197 (2, *M*⁺), 143 (39), 100 (100), 97 (28), 72 (77), 58 (39), 55 (85).

(*E*)-3-Hydroxy-3-methyl-1,5-heptadien-4-one (**18**). A soln. of butyl 2-hydroxy-2-methyl-3-butenolate (**17**)¹⁷) (5.0 g, 29.07 mmol) in THF (30 ml) was treated at −10° with LiN(*i*-Pr)₂ (29.07 mmol) in THF/hexane (50 ml). The resulting soln. was added at 30–40° to a soln. of LiN(*i*-Pr)₂ (37.77 mmol) and allylmagnesium chloride (37.77 mmol) in THF/hexane (70 ml). After 90 min, the product was isolated in the usual manner and distilled in a bulb-to-bulb apparatus (oven temp. 100–140°/2 Torr) to afford an oil (2.99 g, mainly **18** and isomers), which was treated with TsOH (60 mg) in toluene (10 ml) at 20° for 70 h. Extractive isolation and bulb-to-bulb distillation (oven temp. 100–150°/2 Torr) afforded **18** (2.95 g, 90% pure, 65%)⁵. A pure sample of **18** was obtained by distillation. B.p. 65–70°/2 Torr. IR (neat): 3450, 2980, 1690, 1625, 1440, 1290, 1060, 920. ¹H-NMR (60 MHz): 1.34 (s, 3 H); 1.85 (dd, *J* = 2, 6, 3 H); 3.80 (br. s, 1 H); 5.15 (dd, *J* = 2, 11, 1 H); 5.40 (dd, *J* = 2, 17, 1 H); 5.85 (dd, *J* = 11, 17, 1 H); 6.35 (dd, *J* = 2, 15, 1 H); 7.06 (*dq*, *J* = 6, 15, 1 H). MS: 140 (0.3, *M*⁺), 125 (3), 122 (2), 97 (10), 71 (75), 69 (100).

(3*RS*, 4*aSR*, 6*aRS*, 10*aRS*, 10*bSR*)-3,7,7-10*a*-Tetramethylperhydronaphtho[2,1-*b*]pyran-1 one (**20**). A soln. of methyl 2-hydroxy-5,5,8*a*-trimethylperhydronaphthalene-1-carboxylate (**19**) [23] (3.0 g, 11.81 mmol) in THF (30 ml) was treated at −10° with LiN(*i*-Pr)₂ (11.81 mmol) in THF/hexane (20 ml). The resulting soln. was added at 35–40° to a soln. of LiN(*i*-Pr)₂ (13.6 mmol) and allylmagnesium chloride (13.6 mmol) in THF/hexane (30 ml). After 1 h, the product was isolated in the usual manner. Chromatography (silica gel) with cyclohexane/AcOEt 98:2→95:5 gave (1*RS*, 2*RS*, 4*aSR*, 8*aSR*)-1-(2-hydroxy-5,5,8*a*-trimethylperhydronaphthyl)-3-buten-1-one (1.81 g, 58%), which underwent isomerization and cyclization when heated in toluene/THF 1:1 (10 ml) and TsOH (50 mg) at 80° for 4 h. Extraction (Et₂O/NaHCO₃) afforded **20** (1.72 g, 95%). M.p. 85–90°. IR (CDCl₃): 2920, 1700, 1085. ¹H-NMR (360 MHz): 0.82 (s, 3 H); 0.87 (s, 3 H); 1.07 (s, 3 H); 1.22 (*d*, *J* = 7, 3 H); 0.90–1.80 (m, 9 H); 1.95 (*d*, *J* = 10, 1 H); 2.10 (m, 1 H); 2.15 (dd, *J* = 3, 14, 1 H); 2.46 (*d*, *J* = 14); 2.74 (dd, *J* = 7, 14); 3.96 (*dt*, *J* = 4, 10); 4.47 (*d*, *quint.*, *J* = 3, 7). MS: 264 (6, *M*⁺), 139 (74), 126 (21), 113 (100), 95 (32), 81 (23), 69 (27), 55 (21), 41 (23).

¹⁷) Obtained from BASF AG, Ludwigshafen.

REFERENCES

- [1] C. Fehr (*Firmenich SA*), Eur. Pat. Al 0093 840 (prior. 20.4.1982); *Chem. Abstr.* **1984**, 100, 102816w.
- [2] F. Sato, M. Inoue, K. Oguro, M. Sato, *Tetrahedron Lett.* **1979**, 20, 4303; J. Berluenga, M. Yus, J. M. Concellon, P. Bernad, *J. Org. Chem.* **1983**, 48, 609.
- [3] Recent examples: R. A. Grey, *J. Org. Chem.* **1984**, 49, 2288; V. Fiandanese, G. Marchese, V. Martina, L. Ronzini, *Tetrahedron Lett.* **1984**, 25, 4805; E. Negishi, V. Bagheri, S. Chatterjee, F. Luo, J. A. Miller, A. T. Stoll, *ibid.* **1983**, 24, 5181; N. Jabri, A. Alexakis, J. F. Normant, *ibid.* **1983**, 24, 5081; J. W. Labadie, D. Tueting, J. K. Stille, *J. Org. Chem.* **1983**, 48, 4634; G. Cahiez, A. Alexakis, J. F. Normant, *Synth. Commun.* **1979**, 9, 639 and ref. cited in [3] and [4].
- [4] M. T. Reetz, B. Wenderoth, R. Urz, *Chem. Ber.* **1985**, 118, 348; S. Wattanasin, F. G. Kathawala, *Tetrahedron Lett.* **1984**, 25, 811; G. A. Olah, G. K. S. Prakash, M. Arvanaghi, *Synthesis* **1984**, 228; T. Fujisawa, S. Ida, H. Uehara, T. Sato, *Chem. Lett.* **1983**, 1267; S. Kim, J. I. Lee, *J. Org. Chem.* **1983**, 48, 2608; T. Fujisawa, T. Mori, T. Sato, *Tetrahedron Lett.* **1982**, 23, 5059; M. W. Anderson, R. C. F. Jones, J. Saunders, *J. Chem. Soc., Chem. Commun.* **1982**, 283; M. Onaka, Y. Matsuoka, T. Mukaiyama, *Chem. Lett.* **1981**, 531; S. Nahm, S. M. Weinreb, *Tetrahedron Lett.* **1981**, 22, 3815; T. Mukaiyama, M. Araki, H. Takei, *J. Am. Chem. Soc.* **1973**, 95, 4763; N. F. Scilly, *Synthesis* **1973**, 160; M. J. Jorgenson, *Org. React.* **1970**, 18, 1; J. Klein, *Tetrahedron* **1964**, 20, 465; P. T. Izzo, S. R. Safir, *J. Org. Chem.* **1959**, 24, 701 and ref. cited in [3] and [4].
- [5] C. Fehr, *Helv. Chim. Acta* **1983**, 66, 2512.
- [6] E. Demole, P. Enggist, U. Säuberli, M. Stoll, E. sz. Kovats, *Helv. Chim. Acta* **1970**, 53, 541; E. Demole, D. Berthet, *ibid.* **1971**, 54, 681; W. Renold, R. Näf-Müller, U. Keller, B. Willhalm, G. Ohloff, *ibid.* **1974**, 57, 1301. For some other preparatively useful syntheses: G. Büchi, J. C. Vederas, *J. Am. Chem. Soc.* **1972**, 94, 9128; G. Ohloff, V. Rautenstrauch, K. H. Schulte-Elte, *Helv. Chim. Acta* **1973**, 56, 1503; S. Isoe, S. Katsumura, T. Sakan, *ibid.* **1973**, 56, 1514; S. Torii, K. Uneyama, H. Ichimura, *J. Org. Chem.* **1979**, 44, 2292; R. L. Snowden, B. L. Muller, K. H. Schulte-Elte, *Tetrahedron Lett.* **1982**, 23, 335.
- [7] A. F. Thomas, F. Näf (*Firmenich SA*), Jpn. Kokai, Tokyo Koho 8270, 831 (1.5.1982), *Chem. Abstr.* **1982**, 97, 162450b; A. F. Thomas, M. Lander-Schouwey, *Helv. Chim. Acta* **1984**, 67, 191.
- [8] F. Huet, G. Emptoz, A. Jubier, *Tetrahedron* **1973**, 29, 479; F. Huet, M. Pellet, A. Lechevallier, J.-M. Conia, *J. Chem. Res. (S)* **1982**, 246.
- [9] I. Kikkawa, T. Yorifuji, *Synthesis* **1980**, 877.
- [10] G. Büchi, H. Wüest, *Helv. Chim. Acta* **1971**, 54, 1767.
- [11] L. M. Baigrie, H. R. Seiklay, T. T. Tidwell, *J. Am. Chem. Soc.* **1985**, 107, 5391; R. Häner, T. Laube, D. Seebach, *ibid.* **1985**, 107, 5396.
- [12] K. H. Schulte-Elte, H. Strickler, F. Gautschi, W. Pickenhagen, M. Gadola, J. Limacher, B. L. Muller, F. Wuffli, G. Ohloff, *Liebigs Ann. Chem.* **1975**, 484; K. H. Schulte-Elte, B. L. Muller, B. Egger (*Firmenich SA*), Eur. Pat. appl. 46606 (prior. 26.8.1980); *Chem. Abstr.* **1982**, 97, 24036v.
- [13] W. Kreiser, P. Below, L. Ernst, *Liebigs Ann. Chem.* **1985**, 194.
- [14] J. J. Eisch, A. M. Jacobs, *J. Org. Chem.* **1963**, 28, 2145.
- [15] E. J. Corey, A. W. Gross, *Tetrahedron Lett.* **1984**, 25, 495.
- [16] D. Seebach, A. K. Beck, J. Goliński, J. N. Hay, T. Laube, *Helv. Chim. Acta* **1985**, 68, 162.
- [17] D. Seebach, Proceedings of The Robert A. Welch Foundation Conferences on Chemical Research 1984, p. 93.
- [18] T. Laube, J. D. Dunitz, D. Seebach, *Helv. Chim. Acta* **1985**, 68, 1373.
- [19] H. G. Richey, Jr., J. Farkas, Jr., *Tetrahedron Lett.* **1985**, 26, 275.
- [20] M. A. Al-Aseer, B. D. Allison, S. G. Smith, *J. Org. Chem.* **1985**, 50, 2715.
- [21] H. O. House, D. D. Traficante, *J. Org. Chem.* **1963**, 28, 355.
- [22] M. Newcomb, M. T. Burchill, *J. Am. Chem. Soc.* **1984**, 106, 8276 and ref. cited therein.
- [23] P. A. Stadler, A. Nechvatal, A. J. Frey, A. Eschenmoser, *Helv. Chim. Acta* **1957**, 40, 1373; M. Liapis, V. Ragoussis, N. Ragoussis, *J. Chem. Soc., Perkin Trans. I* **1985**, 815.