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-Damascenone[1])

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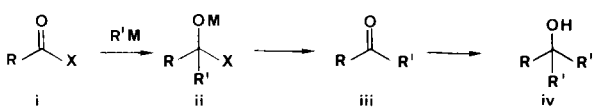
The novel reagents formed by combination of allylmagnesium chloride and a strong non-nucleophilic lithium base ($LiNR_2$) convert non- or slowly enolizable carboxylic esters or carboxamides into 2-propenyl ketones which are protected from further reaction by their *in situ* conversion into enolates. 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.* X = 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



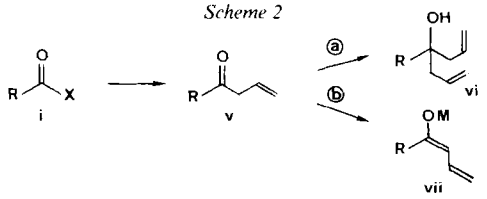
In many cases, application of one or the other of these two methods is successful. However, the highly reactive allylic *Grignard* reagents are known to give predominantly the tertiary alcohol **iv** even with acid chlorides at −78° [2] (method 1: activation of substrate) and the procedures that take 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].

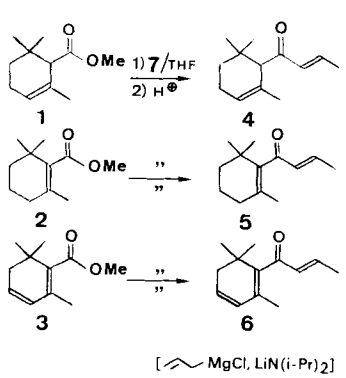
Scheme 2



Although it is known that *Grignard* reactions in polar solvents favor enolate formation (HMPA [8], Et_3N [9]), application of these conditions to our systems was unsuccessful. In certain cases, an excess of allyllithium has been shown to effect the desired transformation **i**→**vii** [10] by acting at first as the nucleophile and then as the base. However, this makes it difficult to predict the outcome of the reaction (competition between path ⓐ and ⓑ, *Scheme 2*)[3]).

Results. – We now report that the new reagent **7**, a combination of the nucleophilic *Grignard* reagent (CH_2=CH–CH_2MgCl) and the powerful non-nucleophilic lithium base LiN(i-Pr)$_2$, converts the readily available esters **1, 2**, and **3** [12] into α-damascone (**4**), β-damascone (**5**), and β-damascenone (**6**) with high selectivity[4]) *(Scheme 3)*.

Scheme 3



	Selectively[4])	Yield[5]) [%]
1 → **4**	98:2	85
2 → **5**	> 90:10[6])	80
3 → **6**	96:4	76

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Thus, under these conditions, deprotonation of the 2-propenyl ketones competes successfully with nucleophilic attack of a second allyl-*Grignard* reagent on the ketone carbonyl group. To gain more insight into the course of this reaction, we selected the ester **8** [7] [13] and the amide **9**, which bear no H-atom in the α-position, as test substrates *(Scheme 4)*.

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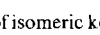
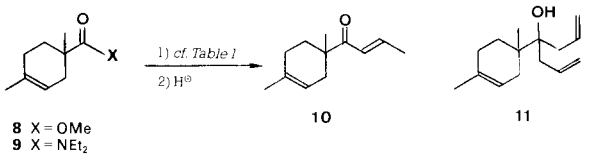
[3]) For very recent ketene-to-ketone-enolate conversions, see [11].

[4]) The selectivity refers to the reaction of the intermediate ketone **v** along either path ⓑ or ⓐ *(Scheme 2)*.

[5]) The products **4, 5, 6, 10, 14**, and **18** contain 5–10% of isomeric ketones  and  . Application of *Reetz*'s isomerization conditions (neutral alumina) [4] give (*E*)-1-propenyl ketones of higher purity, but in somewhat lower yield.

[6]) Reaction temperature 0–5°. The reaction is more selective at 35° (95:5), but gives a lower yield (60%).

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 observed[7]).

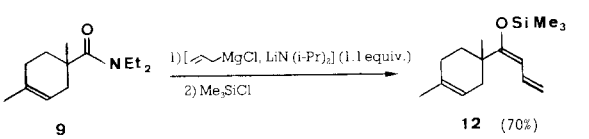
Table 1. *Formation of* **10**/**11** *from* **8** *or* **9**

Entry	Substrate	Reaction conditions	**10**/**11**[a])
1	**8**	MgCl (2 equiv.)	14:86
2	**8**	[MgCl, $LiN(i\text{-}Pr)_2$] (1.3 equiv.)	67:33
3	**8**	[Li,$ClMgN(i\text{-}Pr)_2$] (1.4 equiv.)	70:30
4	**8**	Li[b]) (2 equiv.)	(30:70)[c])
5	**9**	MgCl (2 equiv.)	50:50
6	**9**	[MgCl, $LiN(i\text{-}Pr)_2$] (1.1 equiv.)[d])	92:8 (99:1)[c])
7	**9**	[MgCl, $LiN(i\text{-}Pr)_2$] (1.1 equiv.)[d])	95:5 (99:1)[c])
8	**9**	Li[b])	94:6 (95:5)[c])
9	**9**	[$MgClNEt_2$] (2 equiv.)	56:44

[a]) Yield of **10** + **11** *ca.* 85%.
[b]) Prepared according to *Eisch* [14]; contains LiOPh.
[c]) Ratios in brackets refer to incomplete conversion (70–80%).
[d]) The same result is obtained when $LiNEt_2$ is used instead of $LiN(i\text{-}Pr)_2$. However, with $LiNEt_2$, 2 equiv. of *Grignard* reagent are required for full conversion.

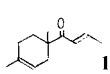
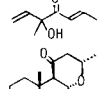
In addition, quenching the reaction mixture (*Entry 6*) with Me_3SiCl affords silylenol-ether **12**[8]) in high yield, providing further evidence for the presence of an enolate (*Scheme 5*).

Scheme 5



[7]) The diethylamides corresponding to esters **1**–**3** are unreactive.
[8]) $(E)/(Z) \approx 9:1$. 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**	MgCl(1.7), $LiN(i\text{-}Pr)_2$ (1.05)	 **4**		(85)	98:2	28:72
2	 **2**	MgCl(1.5), $LiN(i\text{-}Pr)_2$ (1.5)	 **5**		(80)	≥ 90:10	15:85
3	 **3**	MgCl(1.45), $LiN(i\text{-}Pr)_2$ (1.65)	 **6**		(76)	≥ 96:4	15:85
4	 **8**	MgCl(1.3), $LiN(i\text{-}Pr)_2$ (1.3)	 **10**		(60)	67:33	14:86
5	 **9**	MgCl(1.3), $LiN(i\text{-}Pr)_2$ (1.3)	**10**		(78)	92:8 (99:1[d])	50:50
6	 **8**	1) $LiNEt_2$ (1.15) 2) MgCl (1.3), $LiN(i\text{-}Pr)_2$ (1.3)	**10**		(77)	92:8	–
7	 **13**	MgCl(1.5), $LiN(i\text{-}Pr)_2$ (1.5)	 **14**	+	 **15**	20:80	2:98
8	 **16**	MgCl(1.05), $LiN(i\text{-}Pr)_2$ (1.05)	**14** (77)	+	**15**	80:20	17:83
9	 **13**	1) $LiNEt_2$ (1.05) 2) MgCl (1.05), $LiN(i\text{-}Pr)_2$ (1.05)	**14** (66)	+	**15**	80:20	–
10	 **17**	1) $LiN(i\text{-}Pr)_2$ (1.0) 2) MgCl(1.3), $LiN(i\text{-}Pr)_2$ (1.3)	 **18**		(65)	92:8	5:95
11	 **19**	1) $LiN(i\text{-}Pr)_2$ (1.0) 2) MgCl(1.15), $LiN(i\text{-}Pr)_2$ (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 $CH_2=CH\text{–}CH_2MgCl$ alone.
[d]) Incomplete conversion (≈ 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 = NEt_2 more favorable than OMe; *ii*) added base: effective bases: $LiNEt_2 \approx LiN(i\text{-}Pr)_2 \gg ClMgN(i\text{-}Pr)_2$; ineffective bases: *t*-BuOK, KH, NaH, LiH, $LiNH_2$; *iii*) temperature: higher temperatures favor enolatization.

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 $LiN(i\text{-}Pr)_2$. Larger amounts of $LiN(i\text{-}Pr)_2$ led to a slightly improved selectivity, but the side products also become more important (presumably resulting from concurrent condensation reactions). Possibly, allylmagnesium chloride and $LiN(i\text{-}Pr)_2$ form a 1:1 aggregate containing amide and allylunits bonded to Mg and Li together with variable amounts of 'free' $LiN(i\text{-}Pr)_2$. 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 = NR_2), thus, imparting to the whole transformation (nucleophilic attack of allylmetal derivative, elimination of 'R_2NM' and deprotonation of the ketone **v**) some intramolecular character[11]).

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* reagent[12])[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.

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[10]) For a discussion about non-stoichiometric effects with organolithium derivatives, see [17] [18]; for a recent example of a mixed diethylmagnesiumethyllithium 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}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 hexane[14]) (45.25 ml, 2.55N, 115.4 mmol) was added at 0° to a stirred soln. of $(i\text{-}Pr)_2NH$ (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 sample[5])[15]).

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 $(i\text{-}Pr)_2NH$ (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 sample[5])[15]).

β-Damascenone (= *(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), $(i\text{-}Pr)_2NH$ (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%)[5]), identical to an authentic sample[15]) 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}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 $LiN(i\text{-}Pr)_2$ (13.0 mmol, prepared from $(i\text{-}Pr)_2NH$ (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 solution[16]). 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%)[5]), 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 $LiN(i\text{-}Pr)_2$ (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.

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

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

[16]) Alternative procedure: addition of **1** to a soln. of $LiNEt_2/LiN(i\text{-}Pr)_2$ 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. ^{1}H-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. 1 H); 5.37 (*d*, *J* = 11, 1 H); 6.51 (*d't'*, *J* ≈ 10, 17, 1 H). 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. NH_4Cl soln./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 to give **13** (26.17 g, 71%). B.p. 75°/4 Torr. IR: 2970, 1720, 1640, 1470, 1140. ^{1}H-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. NH_4Cl 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 CH_2Cl_2. IR ($CDCl_3$): 2960, 1680, 1620, 1440, 980. ^{1}H-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 ($CDCl_3$): 2970, 1610, 1415, 1060. ^{1}H-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-butenoate* (**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. ^{1}H-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).

(3RS, 4a*SR*, 6a*RS*, 10a*RS*, 10b*SR*)-*3,7,7-10a-Tetramethylperhydronaphtho[2,1-b]pyran-1 one* (**20**). A soln. of *methyl 2-hydroxy-5,5,8a-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*, 4a*SR*, 8a*SR*)-1-(2-hydroxy-5,5,8a-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 (Et_2O/$NaHCO_3$) afforded **20** (1.72 g, 95%). M.p. 85–90°. IR ($CDCl_3$): 2920, 1700, 1085. ^{1}H-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).

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