145. A Stereospecific Synthesis of (*E*, *Z*)-α,β-γ,δ-Diunsaturated Aldehydes, Ketones, and Esters Using the *Benary* Reaction

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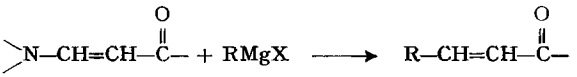
(15. V. 74)

Summary. The reaction between (*Z*)-1-alkenyllithium and (*E*)-β-(N,N-dialkylamino)-α,β-alkenals, (*E*)-β-(N,N-dialkylamino)-α,β-alkenones or (*E*)-β-(N,N-dialkylamino)-α,β-alkenoic esters yields mainly (*E*,*Z*)-α,β-γ,δ-diunsaturated aldehydes, ketones, or esters and is therefore highly stereospecific.

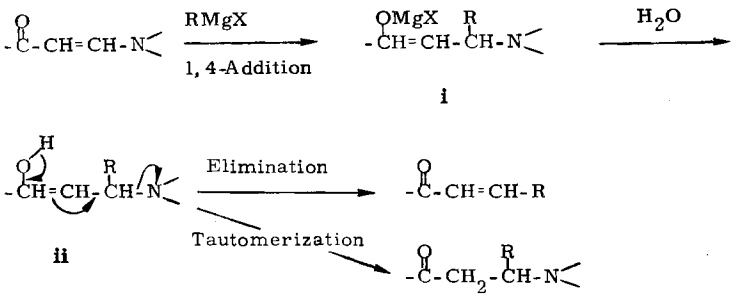
Introduction. – In 1931 *Benary* [1] discovered that β-(N,N-dialkylamino)-vinyl ketones react with *Grignard* reagents, under formal replacement of the amino group

Scheme 1



by R, to give α,β-unsaturated ketones. This reaction proved to be general and to offer an easy access not only to α,β-unsaturated ketones [1] [2] [4] [5] [9] [11] [14] but also to α,β-unsaturated aldehydes [3] [8] and α,β-unsaturated esters [10] as well as poly-unsaturated ketones and aldehydes [3–8] [12] [13] [15]. In the case of

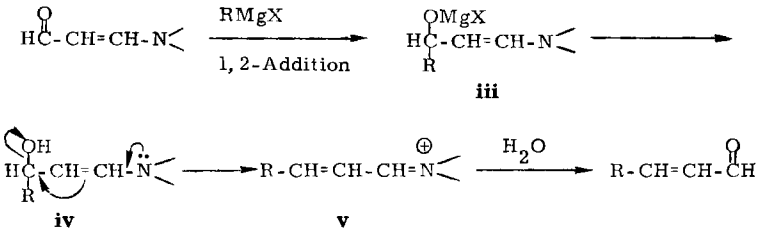
Scheme 2



β-amino vinyl ketones the reaction is believed [1] [5] [8] [9] to involve conjugate addition and yield the magnesium enolate **i** as intermediate; this is then hydrolyzed to give the amino enol **ii**. This unstable, second intermediate **ii**, can either decompose with elimination of a *sec* amine to give the α,β-unsaturated ketone, or tautomerize to produce a β-amino ketone.

β-Aminopropenals and δ-Amino-pentadienals, however, seem to react with organomagnesium or organolithium compounds mainly in a 1,2-fashion at the carbonyl group [7] [8] [12].

Scheme 3

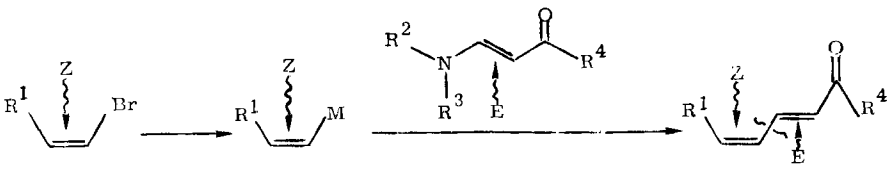


During work-up water is eliminated and an enimmonium compound is formed which can be isolated as such (see *e.g.* [7] [12]). Subsequent hydrolysis gives the α,β-unsaturated aldehyde.

Despite these mechanistic and preparative investigations, nothing is reported about the stereochemistry of the products.

In the present communication we report a facile access to some (*E,Z*)-α,β-γ,δ-diunsaturated aldehydes, ketones, and esters using the *Benary* reaction as outlined below.

Scheme 4



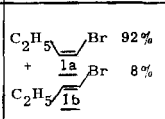
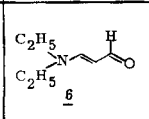
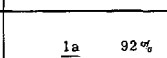
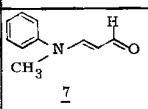
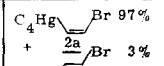
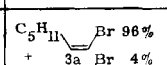
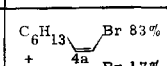
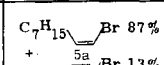
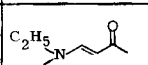
As we had expected on the basis of mechanistic considerations (see Discussion) the double bond geometry of the reactants remains mainly preserved in the product; this particular *Benary* type sequence is therefore highly *stereospecific*.

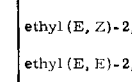
Among the aldehydes synthesized (*E,Z*)-2,4-decadienal (**12a**) has been shown to be present in tomatoes [16], bell-pepper [17], peanuts [18], potato chips [19], cooked apples [20], bread [21], cranberries [22] and tea [23]. (*E,Z*)-2,4-Nonadienal (**11a**) has been found in potato chips [19] and tea [23], and (*E,Z*)-2,4-heptadienal (**10a**) has been reported to be a constituent of tomatoes [16] [24], cranberries [22] and tea [25]. (*E,Z*)-3,5-Octadien-2-one (**15a**) has been identified in tea [23], and ethyl (*E,Z*)-2,4-decadienoate (**18a**)[1]) in *Bartlett* pears [27].

Results and Discussion. – (*Z*)-1-Alkenyl bromides were readily accessible by the general decarboxylative elimination reaction of 2,3-dibromoacids in the presence of sodium hydrogencarbonate and dimethyl formamide (DMF) at ~100–110° as described by *Norris* [28]. The yields range from 50 to 80% and the isomeric purity is better than 97% *Z*. However, the bromides undergo a slow isomerization at room temperature and finally reach thermodynamic equilibrium (for 1-propenyl bromide in neat liquid phase ~68% (*Z*) and ~32% (*E*) [29]); if they are not used immediately after preparation, they can be stored at −20° for several months. 1-Alkenyllithiums were obtained from 1-alkenyl bromides and granulated lithium (containing 1.5% of sodium) in diethyl ether at −8° to −15°, the double bond geometry being retained [30]. The corresponding vinyl *Grignard* compounds were prepared

[1]) For earlier syntheses see [26] [27c].

Table. *α,β,γ,δ-Diunsaturated Aldehydes, Ketones, and Esters* via *the* Benary *reaction*
(Scheme 4, M = Li)

Experiment No	Reactants Bromides, (Z)-(E)-distribution	Enamine	Products[2] distribution of isomers	Yield[2] of isomeric mixture
Aldehydes 3	 92% + 8%	 6	(E, Z)-2, 4-heptadienal (10a) 81% (E, E)-2, 4-heptadienal (10b) 19%	30%
4	 92% + 8%	 7	10a 65% 10b 35%	12%
5	 97% + 3%	6	(E, Z)-2, 4-nonadienal (11a) 84% (E, E)-2, 4-nonadienal (11b) 16%	25%
6	2a 97% + 2b 3%	7	11a 20% 11b 80%	32%
1a, 1b[3], 1c[4]	 96% + 4%	6	(E, Z)-2, 4-decadienal (12a) 87% (55%)[3] (45%)[4] (E, E)-2, 4-decadienal (12b) 13% (45%)[3] (55%)[4]	31% (19%)[3] (10%)[4]
2a, 2b[4]	3a 96% + 3b 4%	7	12a 14% (12%)[4] 12b 86% (88%)[4]	57% (35%)[4]
7	 83% + 17%	6	(E, Z)-2, 4-undecadienal (13a) 60% (E, E)-2, 4-undecadienal (13b) 40%	23%
8	4a 83% + 4b 17%	7	13a 12% 13b 88%	41%
9	 87% + 13%	6	(E, Z)-2, 4-dodecadienal (14a) 71% (E, E)-2, 4-dodecadienal (14b) 29%	14%
10	5a 87% + 5b 13%	7	14a 17% 14b 83%	50%
Ketones 11	1a 98% + 1b 2%	 8	(E, Z)-3, 5-octadien-2-one (15a) 98% (E, E)-3, 5-octadien-2-one (15b) 2%	45%

Experiment No	Reactants Bromides (Z)-(E)-distribution	Enamine	Products[2] distribution of isomers	Yield[2] of isomeric mixture
12	+ 4a 98% / 4b 2%	8	(E, Z)-3, 5-dodecadien-2-one (16a) 98% / (E, E)-3, 5-dodecadien-2-one (16b) 2%	40%
Esters 13	+ 2a 98% / 2b 2%	 9	ethyl (E, Z)-2, 4-nonadienoate (17a) 95% / ethyl (E, E)-2, 4-nonadienoate (17b) 5%	12%
14	+ 3a 98% / 3b 2%	9	ethyl (E, Z)-2, 4-decadienoate (18a) 89% / ethyl (E, E)-2, 4-decadienoate (18b) 11%	32%
15	+ 4a 98% / 4b 2%	9	ethyl (E, Z)-2, 4-undecadienoate (19a) 96% / ethyl (E, E)-2, 4-undecadienoate (19b) 4%	25%
16	+ 5a 97% / 5b 3%	9	ethyl (E, Z)-2, 4-dodecadienoate (20a) 95% / ethyl (E, E)-2, 4-dodecadienoate (20b) 5%	15%

from the bromides and magnesium turnings in tetrahydrofuran (THF) at 45–50°, again with retention of double bond configuration [31].

The enamino aldehydes **6** [8] and **7** [8], ketone **8** [5] and ester **9** [32] were prepared from the corresponding acetylenic carbonyl compounds and either diethylamine or N-methylaniline.

In all experiments described (see Table) the organometallic compounds were treated at −10° with the enamines (stochiometric quantities), and after the reaction mixture had been allowed to warm to 25° it was poured into ice/diluted H_2SO_4 and extracted with ether. If this acidic decomposition was carried out at 25°, stereospecifity and yields were much lower (see *e.g.* Exp. 1b, footnote 3). Not only the reaction conditions but also the nature of the reactants were most critical for stereochemistry and yield of the reaction. High stereospecifity was observed only with N,N-diethylamino compounds (see Exp. **1**, 3, 5, 7, 9), N-methylanilino derivatives showing a predilection for the thermodynamically most stable all-(*E*) isomer (see Exp. 2, 4, 6, 8, 10). Alkenyllithium compounds were superior to alkenyl *Grignard* reagents with regard to yields (see Exp. 1c and 2b, footnote 4).

The structures of the compounds obtained were established by NMR. in combination with $Eu(fod)_3$ shift agent [33]. The shifted spectra were of first order and could easily be analyzed (see Exper. Part).

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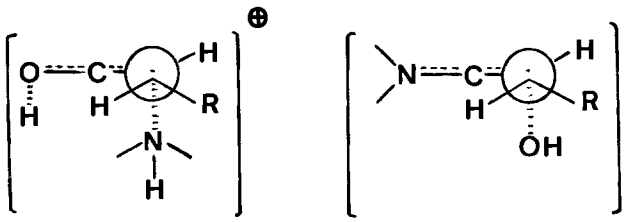
[2] Only the neutral reaction products have been isolated.

[3] Decomposition of reaction mixture at 25° instead at 0°.

[4] Using an organomagnesium compound in THF instead of an organolithium reagent in ether.

Mechanism. – In order to account for the overall stereochemistry observed, the formation of the two double bonds will be discussed separately. The α,β-double bond is formed during the aqueous acidic work up by an elimination process involving an intermediate of type **ii** (for β-amino-α,β-unsaturated ketones and esters) or type **iv** (for β-amino-α,β-unsaturated aldehydes).

In both cases a transition state having an antiperiplanar geometry of the large substituents, such as **ii**‡ and **iv**‡, and leading to an (*E*)-double bond, must be preferred for steric reasons.



ii‡ **iv**‡

The (*Z*)-γ,δ-double bond stems from the (*Z*)-1-alkenyllithium reagent which is known to undergo SE-type reactions with *retention* of the double bond geometry. The substituent R, *i.e.* 1-alkenyl, in **ii** and **iv** must therefore have (*Z*)-configuration which is *retained* during the α,β-double bond forming elimination step and during the isolation of the product (as in Exp. 1, 3, 5, 7, 9, 11–16).

Conclusion. – Although the yields are not very satisfactory, the present method offers a short and – under certain conditions – stereospecific access to a series of *unstable* and not *readily accessible* (*E,Z*)-α,β-γ,δ-diunsaturated aldehydes[5]), ketones[5]), and esters[6]).

Experimental Part[7])

(in collaboration with *R. Chappaz*)

1a) *Preparation of* (E,Z)-*2,4-decadienal* (**12a**) *and* (E,E)-*2,4-decadienal* (**12b**) *from bromides* **3a** *and* **3b** *and enamine aldehyde* **6** [8]. 1-Lithio-1-heptene was prepared from granulated lithium, containing 1.5% of sodium[8]) (0.7 g; 100 mmol), in abs. ether (20 ml) and 1-bromo-1-heptene (8.85 g; 50 mmol; **3a** 96% and **3b** 4%) in abs. ether (30 ml) at $-10°$. After the mixture had been stirred 2 h at $-8°$ to $-15°$, (*E*)-β-(N,N-diethylamino)acroleine (**6**) (6.35 g; 50 mmol) in abs. ether (50 ml) was added dropwise at $-10°$ during 15 min. The reaction mixture became doughy. Stirring was continued another 2 h while the temperature was allowed to rise to 20°. Excess of lithium was removed by filtration on glass wool, and the reaction mixture was poured onto an iced 20% aqueous H_2SO_4 solution. The product was extracted with ether, washed ($NaHCO_3$ and brine), dried ($MgSO_4$), concentrated and distilled. 2.47 g (31%) b.p. 102–107°/11 Torr. Analysis by GLPC.[9]) showed the presence of **12a** (87%) and **12b** (13%).

[5]) For a different method of preparation using a *Wittig* reaction see [26a].

[6]) For different methods of preparation see [26].

[7]) For general remarks see experimental section of [34]. The spectral data given are limited to one example of each class of homologues.

[8]) *Metallgesellschaft* AG, Frankfurt a.M.

1b) An experiment was made using the same conditions but the reaction mixture was poured onto 10% aqueous H_2SO_4 solution (100 ml) at 25°. 1.46 g (19%) b.p. 102–107°/11 Torr was obtained. Analysis by GLPC.[9]) showed the presence of **12a** (55%) and **12b** (45%).

1c) The corresponding vinyl *Grignard* compound was prepared from 1-bromo-1-heptene (4.42 g; 25 mmol; **3a** 96% and **3b** 4%) and magnesium turnings (0.6 g; 25 mmol) in abs. THF (25 ml) at 45–50° (see [35]). (*E*)-β-(N,N-diethylamino)acroleine (3.17 g; 25 mmol) in abs. THF (20 ml) was added dropwise at −10° during 10 min. Stirring was continued for 2 h while the temperature was allowed to rise to 20°. After work-up and bulb distillation 0.39 g (10%) b.p. 90–100°/0.01 Torr was obtained. Analysis by GLPC.[9]) showed the presence of **12a** (35%) and **12b** (65%).

Spectral data of **12a**: 90 MHz NMR.[10]): 0.92 (3 H, *t*, J = 6 Hz); 2.37 (2 H, $d \times t$, J = 6 Hz and 8 Hz, H (ε)); 6.04 (1 H, $d \times t$, J = 11 Hz and 8 Hz, H (δ)); 6.09 (1 H, $d \times d$, J = 8 Hz and 15 Hz, H (α)); 6.30 (1 H, $d \times d$, J = 11 Hz, H (γ)); 7.50 (1 H, $d \times d$, J = 11 Hz and 15 Hz, H (β)); 9.63 (1 H, *d*, J = 8 Hz, —C*H*O). After Eu(fod)$_3$ has been added (C(Eu/prod) = 0.33): 2.85 (2 H, $d \times t$, J = 6 Hz and 8 Hz, H (ε)); 6.35 (1 H, $d \times t$, J = 11 Hz and 8 Hz, H (δ)); 7.31 (1 H, $d \times d$, J = 11 Hz and 11 Hz, H (γ)); 8.92 (1 H, $d \times d$, J = 11 Hz and 15 Hz, H (β)); 10.20 (1 H, $d \times d$, J = 8 Hz and 15 Hz, H (α)); 12.73 (1 H, *d*, J = 8 Hz, —C*H*O). The assignment given above has further been corroborated by irradiating the shifted spectrum at —C*H*O (H(α): $(d \times d) \rightarrow d$) and at H (ε) (H (δ): $(d \times t) \rightarrow d$). – IR. ($CCl_4$): 3010, 2710, 1680, 1630, 1590, 985, 725. – MS.: 152 (M^+, 8) 123 (3), 109 (2), 95 (12), 81 (100), 67 (21), 55 (21), 41 (41), 29 (25).

Spectral data of **12b**: 90 MHz NMR.[10]): 0.92 (3 H, *t*, J = 6 Hz); 2.25 (2 H, *m*); 6.08 (1 H, $d \times d$, J = 8 Hz and 15 Hz, H (α)); 6.10–6.45 (2 H, *m*); 6.95–7.35 (1 H, *m*, H (β)); 9.54 (1 H, *d*, J = 8 Hz, —C*H*O). After Eu(fod)$_3$ has been added (C(Eu/prod) = 0.36): 2.73 (2 H, $d \times t$, J = 7 Hz and 7 Hz, H (ε)); 6.78 (1 H, $d \times t$, J = 15 Hz and 7 Hz, H (δ)); 7.40 (1 H, $d \times d$, J = 10 Hz and 15 Hz, H (γ)); 8.68 (1 H, $d \times d$, J = 10 Hz and 15 Hz, H (β)); 10.47 (1 H, $d \times d$, J = 15 Hz and 8 Hz, H (α)); 13.05 (1 H, *d*, J = 8 Hz, —C*H*O). The assignment given above has further been corroborated by irradiating the shifted spectrum at H (ε) (H (δ) $(d \times t) \rightarrow d$) and at −C*H*O (H (α) $(d \times d) \rightarrow d$). – IR. ($CCl_4$): 3015, 1685, 1640, 1600, 985. – MS.: 152 (M^+, 7) 123 (2), 109 (1), 95 (8), 81 (100), 67 (16), 55 (16), 41 (32), 29 (18).

2a) *Preparation of* (E,Z)-*2,4-decadienal* (**12a**) *and* (E,E)-*2,4-decadienal* (**12b**) *from bromides* **3a** *and* **3b** *and enamine aldehyde* **7** [8]. 1-Lithio-1-heptene was prepared from granulated lithium, containing 1.5% of sodium[8]) (0.7 g; 100 mmol), in abs. ether (20 ml) and 1-bromo-1-heptene (8.85 g; 50 mmol; **3a** 96% and **3b** 4%) in abs. ether (30 ml) at −10°. After the mixture had been stirred 2 h at −8° to −15° (*E*)-β-(N-methyl-N-phenylamino)-acroleine (**7**) (8.05 g; 50 mmol) in abs. ether (50 ml) was added dropwise at −10° during 15 min. The reaction mixture became doughy. Stirring was continued another 2 h while the temperature was allowed to rise to 20°. Excess of lithium was removed by filtration on glass wool, and the reaction mixture was poured onto an iced 20% aqueous H_2SO_4 solution. The product was extracted with ether, washed ($NaHCO_3$ and brine), dried ($MgSO_4$), concentrated and distilled. 4.32 g (57%) b.p. 57–61°/0.01 Torr. Analysis by GLPC.[9]) showed the presence of **12a** (14%) and **12b** (86%).

2b) The corresponding vinyl *Grignard* compound was prepared from 1-bromo-1-heptene (4.42 g; 25 mmol; **3a** 96% and **3b** 4%) and magnesium turnings (0.6 g; 25 mmol) in abs. THF (25 ml) at 45–50° (see [31]). (*E*)-β-(N-methyl-N-phenylamino)-acroleine (4.02 g; 25 mmol) in abs. THF (20 ml) was added dropwise at −10° during 10 min. Stirring was continued for 2 h while the temperature was allowed to rise to 20°. After work-up and bulb distillation at 95–105°/0.01 Torr 1.37 g (35%) was obtained. Analysis by GLPC.[9]) showed the presence of **12a** (12%) and **12b** (88%).

3) *Preparation of* (E,Z)-*2,4-heptadienal* (**10a**) *and* (E,E)-*2,4-heptadienal* (**10b**) *from bromides* **1a** *and* **1b** *and enamine aldehyde* **6**. Using the conditions described for experiment 1a) 1-bromo-1-butene (6.75 g; 50 mmol; **1a** 92% and **1b** 8%) gave, after distillation, 1.65 g (30% yield); b.p. 59–61°/10 Torr. Analysis by GLPC.[11]) showed the presence of **10a** (81%) and **10b** (19%).

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[9]) 5 mm × 2 m, 20% Carbowax 20 M, 200°.

[10]) $-CH_2(\varepsilon)-CH(\delta)=CH(\gamma)-CH(\beta)=CH(\alpha)-\overset{O}{\overset{\|}{C}}-$

[11]) 5 mm × 2 m, 20% Carbowax 20 M, 175°.

4) *Preparation of* (E,Z)-*2,4-heptadienal* (**10a**) *and* (E,E)-*2,4-heptadienal* (**10b**) *from bromides* **1a** *and* **1b** *and enamine aldehyde* **7**. Using the conditions described for the experiment 2a) 1-bromo-1-butene (6.75 g; 50 mmol; **1a** 92% and **1b** 8%) gave, after distillation, 0.65 g (12%); b.p. 58–62°/10 Torr. Analysis by GLPC.[11]) showed the presence of **10a** (65%) and **10b** (35%).

5) *Preparation of* (E,Z)-*2,4-nonadienal* (**11a**) *and* (E,E)-*2,4-nonadienal* (**11b**) *from bromides* **2a** *and* **2b** *and enamine aldehyde* **6**. Using the conditions described for the experiment 1a) 1-bromo-1-hexene (3.26 g; 20 mmol; **2a** 97% and **2b** 3%) gave, after distillation, 0.70 g (25%); b.p. 91–94°/10 Torr. Analysis by GLPC.[11]) showed the presence of **11a** (84%) and **11b** (16%).

6) *Preparation of* (E,Z)-*2,4-nonadienal* (**11a**) *and* (E,E)-*2,4-nonadienal* (**11b**) *from bromides* **2a** *and* **2b** *and enamine aldehyde* **7**. Using the conditions described for the experiment 2a) 1-bromo-1-hexene (3.26 g; 20 mmol; **2a** 97% and **2b** 3%) gave, after distillation, 0.89 g (32%); b.p. 93–95°/10 Torr. Analysis by GLPC.[11]) showed the presence of **11a** (20%) and **11b** (80%).

7) *Preparation of* (E,Z)-*2,4-undecadienal* (**13a**) *und* (E,E)-*2,4-undecadienal* (**13b**) *from bromides* **4a** *and* **4b** *and enamine aldehyde* **6**. Using the conditions described for the experiment 1a) 1-bromo-1-octene (3.82 g; 20 mmol; **4a** 83% and **4b** 17%) gave, after distillation, 0.75 g (23%); b.p. 61–66°/0.01 Torr. Analysis by GLPC.[9]) showed the presence of **13a** (60%) and **13b** (40%).

8) *Preparation of* (E,Z)-*2,4-undecadienal* (**13a**) *and* (E,E)-*2,4-undecadienal* (**13b**) *from bromides* **4a** *and* **4b** *and enamine aldehyde* **7**. Using the conditions described for the experiment 2a) 1-bromo-1-octene (3.82 g; 20 mmol; **4a** 83% and **4b** 17%) gave, after distillation, 1.36 g (41%); b.p. 63–65°/0.01 Torr. Analysis by GLPC.[9]) showed the presence of **13a** (12%) and **13b** (88%).

9) *Preparation of* (E,Z)-*2,4-dodecadienal* (**14a**) *and* (E,E)-*2,4-dodecadienal* (**14b**) *from bromides* **5a** *and* **5b** *and enamine aldehyde* **6**. Using the conditions described for the experiment 1a) 1-bromo-1-nonene (10.25 g; 50 mmol; **5a** 87% and **5b** 13%) gave, after distillation, 1.37 g (14%); b.p. 70–80°/0.01 Torr. Analysis by GLPC.[9]) showed the presence of **14a** (71%) and **14b** (29%).

10) *Preparation of* (E,Z)-*2,4-dodecadienal* (**14a**) *and* (E,E)-*2,4-dodecadienal* (**14b**) *from bromides* **5a** *and* **5b** *and enamine aldehyde* **7**. Using the conditions described for the experiment 2a) 1-bromo-1-nonene (10.25 g; 50 mmol; **5a** 87% and **5b** 13%) gave, after distillation, 4.94 g (50%); b.p. 72–83°/0.01 Torr. Analysis by GLPC.[9]) showed the presence of **14a** (17%) and **14b** (83%).

11) *Preparation of* (E,Z)-*3,5-octadien-2-one* (**15a**) *and* (E,E)-*3,5-octadien-2-one* (**15b**) *from bromides* **1a** *and* **1b** *and enamine ketone* **8** [5]. Using the conditions described for the experiment 1a) 1-bromo-1-butene (4.72 g; 30 mmol; **1a** 98% and **1b** 2%) and (*E*)-*β*-(N,N-diethylamino)-vinyl ketone **8** (4.22 g; 30 mmol) gave, after distillation, 1.74 g (45%); b.p. 71–73°/11 Torr. Analysis by GLPC.[12]) showed the presence of **15a** (98%) and **15b** (2%).

Spectral data of **15a**: 90 MHz NMR.[10]): 1.06 (3 H, *t*, J = 8 Hz); 2.31 (3 H, *s*); 2.38 (2 H, $d \times q$, J = 7 Hz and 8 Hz, H (ε)); 5.92 (1 H, $d \times t$, J = 10 Hz and 7 Hz, H (δ)); 6.14 (1 H, $d \times d$, J = 10 Hz and 10 Hz, H (γ)); 6.16 (1 H, *d*, J = 15 Hz, H (α)); 7.48 (1 H, $d \times d$, J = 10 Hz and 15 Hz, H (β). After Eu(fod)$_3$ has been added (C(Eu/prod) = 0.24): 1.27 (3 H, *t*, J = 8 Hz); 2.80 (2 H, $d \times q$, J = 8 Hz and 8 Hz, H (ε)); 5.21 (3 H, *s*); 6.24 (1 H, $d \times t$, J = 8 Hz and 10 Hz, H (δ)); 6.92 (1 H, $d \times d$, J = 10 Hz and 10 Hz, H (γ)); 8.75 (1 H, *d*, J = 15 Hz, H (α)); 9.68 (1 H, $d \times d$, J = 15 Hz and 10 Hz, H (β)). The assignment given above has further been corroborated by irradiating the shifted spectrum at H (β) (H(γ): $(d \times d) \rightarrow d$; and H ($\alpha$): $d \rightarrow$ '*s*') and at H (ε) (H (δ): $(d \times t) \rightarrow d$). – IR. (liq.): 3015, 1685, 1665, 1625, 1575, 1355, 1250, 990, 955. – MS.: 124 (M^+, 30) 109 (19), 95 (100), 81 (66), 65 (7), 53 (29), 43 (78), 27 (21).

12) *Preparation of* (E,Z)-*3,5-dodecadien-2-one* (**16a**) *and* (E,E)-*3,5-dodecadien-2-one* (**16b**) *from bromides* **4a** *and* **4b** *and enamine ketone* **8**. Using the conditions described for the experiment 1a) 1-bromo-1-octene (6.15 g; 30 mmol; **4a** 98% and **4b** 2%) and (*E*)-*β*-(N,N-diethylamino)-vinyl ketone **8** (4.22 g; 30 mmol) gave, after distillation, 2.2 g (40%); b.p. 58–59°/0.01 Torr. Analysis by GLPC.[13]) showed the presence of **16a** (98%) and **16b** (2%).

13) *Preparation of ethyl* (E,Z)-*2,4-nonadienoate* (**17a**) *and ethyl* (E,E)-*2,4-nonadienoate* (**17b**) *from bromides* **2a** *and* **2b** *and enamine ester* **9** [32]. Using the conditions described for the experiment 1a) 1-bromo-1-hexene (10.5 g; 64 mmol; **2a** 98% and **2b** 2%) and ethyl (*E*)-*β*-(N,N-diethylamino)-

[12]) 5 mm × 2 m, 5% Carbowax 20 M, 140°.

[13]) 5 mm × 2 m, 5% Silicone, 170°.

acrylate **9** (11.0 g; 64 mmol) gave, after distillation, chromatography on 40 g silica gel (elution with hexane: ether 95:5), and bulb distillation 1.4 g (12%); b.p. 80–90°/0.03 Torr. Analysis by GLPC.[14]) showed the presence of **17a** (95%) and **17b** (5%).

14) *Preparation of ethyl* (E,Z)*-2,4-decadienoate* (**18a**) *and ethyl* (E,E)*-2,4-decadienoate* (**18b**) *from bromides* **3a** *and* **3b** *and enamine ester* **9**. Using the conditions described for the experiment 1a) 1-bromo-1-heptene (5.66 g; 32 mmol; **3a** 98% and **3b** 2%) and ethyl (*E*)-β-(N,N-diethylamino)-acrylate **9** (5.47 g; 32 mmol) gave, after distillation, 2.09 g (32%); b.p. 66–76°/0.01 Torr. Analysis by GLPC.[14]) showed the presence of **18a** (89%) and **18b** (11%).

Spectral data of **18a**: 90 MHz NMR.[10]): 0.90 (3 H, *t*, $J = 6$ Hz); 1.30 (3 H, *t*, $J = 7$ Hz); 2.27 (2 H, $d \times q$, $J = 8$ Hz and 6 Hz, H (ε)); 4.21 (2 H, *q*, $J = 7$ Hz); 5.86 (1 H, $d \times t$, $J = 10$ Hz and 7 Hz, H (δ)); 5.88 (1 H, *d*, $J = 15$ Hz, H (α)); 6.14 (1 H, $d \times d$, $J = 10$ Hz and 11 Hz, H (γ)); 7.62 (1 H, $d \times d$, $J = 11$ Hz and 15 Hz, H (β)). – IR. (CCl_4): 3020, 1715, 1710, 1635, 1600, 990. – MS.: 196 (M^+, 36) 167 (3), 151 (40), 139 (3), 125 (77), 108 (22), 97 (71), 81 (100), 67 (83), 55 (44), 41 (60), 29 (97). – UV. (95% EtOH): λ_{max} 265 nm ($\varepsilon = 24.800$).

15) *Preparation of ethyl* (E,Z)*-2,4-undecadienoate* (**19a**) *and ethyl* (E,E)*-2,4-undecadienoate* (**19b**) *from bromides* **4a** *and* **4b** *and enamine ester* **9**. Using the conditions described for the experiment 1a) 1-bromo-1-octene (42.8 g; 224 mmol; **4a** 98% and **4b** 2%) and ethyl (*E*)-β-(N,N-diethylamino)-acrylate **9** (38.3 g; 224 mmol) gave, after distillation, 11.5 g (25%); b.p. 80–85°/0.02 Torr. Analysis by GLPC.[14]) showed the presence of **19a** (96%) and **19b** (4%).

16) *Preparation of ethyl* (E,Z)*-2,4-dodecadienoate* (**20a**) *and ethyl* (E,E)*-2,4-dodecadienoate* (**20b**) *from bromides* **5a** *and* **5b** *and enamine ester* **9**. Using the conditions described for the experiment 1a) 1-bromo-1-nonene (13 g; 64 mmol; **5a** 97% and **5b** 3%) and ethyl (*E*)-β-(N,N-diethylamino)- acrylate **9** (11.0 g; 64 mmol) gave, after distillation, chromatography on 250 g silica gel (elution with hexane: ether 92:8), and bulb distillation 2.1 g (15%); b.p. 115–125°/0.08 Torr. Analysis by GLCP.[14]) showed the presence of **20a** (95%) and **20b** (5%).

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146. Regiospecific Acylation, Alkylation, and Aldol Condensation Using Magnesium Enolates Resulting from the Conjugate Addition of *Grignard* Reagents to α,β-Unsaturated Ketones

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(15. V. 74)

Summary. The magnesium 3,3-dimethylcyclohex-1-enolate **11**, formed in the copper catalyzed addition of methylmagnesium iodide to 3-methylcyclohex-2-enone, has been subjected to regiospecific electrophilic reactions such as acylation, alkylation, and aldol condensation in order to find a new access to the damascones, ionones and carotenoids. By way of illustration a new synthesis of γ-damascone is described.

Introduction. – Regioselective substitution of non-symmetrical ketones at the α-position is a frequent problem in organic synthesis, and several sophisticated methods have been developed for those cases where the usual substitution leads to the wrong isomer or to an isomeric mixture[1]).

This problem can readily be solved by generating the desired enolate anion and then trapping it with an electrophile under non-equilibrating, kinetically controlled conditions.

Stork was the first to alkylate enolate anions which had been specifically generated from α,β-unsaturated ketones with lithium in liquid ammonia [2]. Since then, specific alkylation experiments have been reported in which enolate anions were generated either by reduction of

[1]) See *e.g.* [1], pp. 492 and 734.