A Convenient Protocol for the Stereocontrolled Synthesis of Olefins with a Homoallylic Type of Functionality

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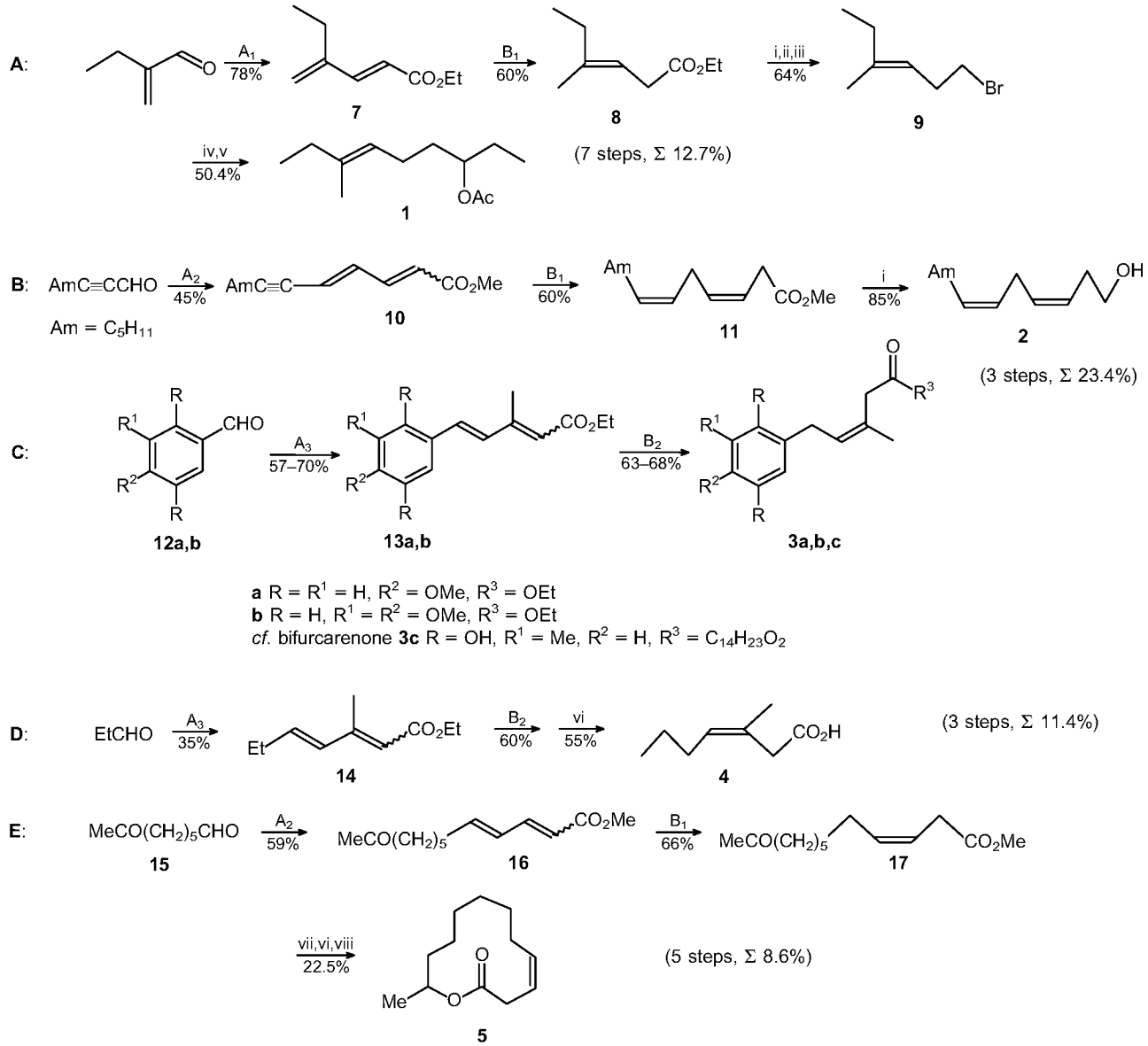
A combination of the Horner–Emmons synthesis of alkyl 2,4-dienoates with their hydrogenation over complex L·Cr(CO)$_3$ catalysts (L = arene or 3CO) provides a versatile, stereocontrolled approach to olefins with a homoallylic pattern of functional substitution, such as certain insect pheromones or (*Z*)-prenylated arenes analogous to the "left-side" moiety of bifurcarenone.

Olefins with a homoallylic pattern of functionalization are not uncommon among natural products. Here we propose a simple approach to such systems based on a two-stage sequence which unites the Horner–Emmons synthesis of the appropriately substituted alkyl 2,4-dienoates[1] and the increasingly popular 1,4-*cis* addition of H_2 to conjugated dienes catalysed by L·Cr(CO)$_3$ complexes, where L = arene or (CO)$_3$.[2,3]

By varying the nature of the aldehydes and phosphonates employed in the synthesis of alkyl 2,4-dienoates (stage A) one can obtain the (*E*)-trisubstituted alkenes (*cf.* ref. 4), skipped (*Z*,*Z*)-disubstituted diolefins (*cf.* ref. 5) and (*Z*)-prenylated arenes (*cf.* ref. 6), the yields of which can be optimized by selecting the appropriate conditions of hydrogenation (stage B) for various types of diene substrates. The alkyl dienoates derived from alkanals and allylic phosphonates uniformly give the (*Z*)-configurated di- and trisubstituted olefins, the geometrical purity of the latter being somewhat higher. Application of this protocol to the preparation of configurationally pure olefins is illustrated by Scheme 1 (entries A–E) which depicts the syntheses of quadrilure **1**, the



Scheme 1 *Reagents and conditions*: A_1, $(EtO)_2P(O)CH_2CO_2Et/K_2CO_3$–$H_2O$, 20 °C; A_2, $(EtO)_2P(O)CH_2CH{=}CHCO_2Me/NaNH_2$–THF, r.t.; A_3, $(EtO)_2P(O)CH_2C(Me){=}CHCO_2Et$/KOH (2 equiv.)/18-C-6 (0.1 equiv.)/PhH, r.t.; B_1, H_2 (80 atm)/(η-$PhCO_2Me$)$Cr(CO)_3$ (0.05 equiv.)/Me_2CO, 120 °C; B_2, H_2 (50 atm)/$Cr(CO)_6$ (~ 0.1 equiv.)/hexane, 160–180 °C; i, $LiAlH_4/Et_2O$; ii, TsCl/Py; iii, NaBr/DMF; iv, Mg/Et_2O, then EtCHO; v, Ac_2O/Py; vi, KOH/H_2O–MeOH (1:3, v/v), r.t., then HCl aq.; vii, $NaBH_4/EtOH_{aq}$; viii, (α-$C_5H_4NS)_2$-PPh_3/MeCN, r.t., then $AgClO_4$/xylene, 140 °C.

aggregation pheromone of the square-necked grain beetle,[7] (*Z,Z*)-3,6-decadien-1-ol **2**, a potent mimic of the trail pheromone of subterranean termites *Reticulitermes flavipes* and *R.virginicus,*[8] ethyl (*Z*)-5-aryl-3-methylpent-3-enoates **3a**,**b**, the close analogues of the non-chiral "left-side" moiety of bifurcarenone **3c**, an antimitotic agent from brown algae,[9] (*Z*)-3-methylhept-3-enoic acid **4**, a component of the sex pheromone of the bean beetle *Callosobruchus maculatus,*[10] and ferrulactone II **5**, the aggregation pheromone of the rusty grain beetle.[11] Earlier[3] this strategy was used in the synthesis of (*Z*)-3-decenoic acid **6**, the aggregation pheromone of the furniture carpet beetle *Anthrenus flavipes;*[12] the yield of **6** over three steps of synthesis from hexanal (including the lipase-catalysed hydrolysis of the pH-sensitive methyl ester of **6**) was 12.3%.

The olefination of 2-ethylpropenal with triethyl phosphonacetate (A_1) followed by hydrogenation of the resulting diene **7** over (η-$PhCO_2Me$)$Cr(CO)_3$ in acetone (B_1) and subsequent transformation of the ester **8** afforded the homoallylic bromide **9** of more than 98% geometrical purity (g.p.) which was easily converted to racemic **1**. Previously[7] the formation of the (*E*)-configurated olefinic moiety of **1** required somewhat more tedious procedures.

The reaction of 2-octynal with methyl 4-(diethylphosphonyl)but-2-enoate (A_2) gave the conjugated dienyne **10**[†] which was subjected to hydrogenation (B_1) to yield the skipped (*Z,Z*)-diene **11** of equally high g.p. Although the clean hydrogenation of alkynes to (*Z*)-alkenes over (η-arene)$Cr(CO)_3$ complexes has been reported,[5] we are not aware of the extention of this technique to the synthesis of skipped (*Z,Z*)-dienes prior to this work.

The olefination of anisaldehyde **12a** and veratraldehyde **12b** with ethyl 4-(diethylphosphonyl)-3-methylbut-2-enoate (A_3) afforded the respective ethyl dienoates, **13a** or **13b**, which were hydrogenated over $Cr(CO)_6$ at somewhat higher temperature (B_2) to give ethyl (*Z*)-5-aryl-3-methylpent-3-enoates, **3a** or **3b**. This sequence, if extended to the properly substituted benzaldehyde, might be a promising overture to the synthesis of bifurcarenone **3c**. Similarly, starting from propanal and the same C_5-phosphonate we obtained the diene **14**; the following hydrogenation over $Cr(CO)_6$ (stage B_2) and the hydrolysis of the resulting ester gave the pheromone **4** of nearly 100% g.p.

Finally, the olefination (A_2) of the keto aldehyde **15**[‡] followed by hydrogenation (B_1) led to methyl (*Z*)-11-oxododec-3-enoate **17** of nearly 99% g.p. The latter was converted to the racemic pheromone **5** in three conventional steps.

Thus, operational simplicity and configurational versatility of the disclosed synthetic protocol make it a method of choice for the stereocontrolled synthesis of olefins.

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[†] A 7:3 mixture of two stereoisomers. All other dienes had a 2*E*/2*Z* ratio between 85:15 and 90:10.

[‡] Prepared in five steps from tetrahydropyran in 32% yield overall.

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