Mixed Dialkylaluminum Chlorides and Mixed Trimethylorganoaluminates in Chemoselective 1,4 Addition Reactions to Alkylidene Malonic Acid Diethyl Ester

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Dedicated to Prof. Dr. R. R. Schmidt on the Occasion of his 65th Birthday

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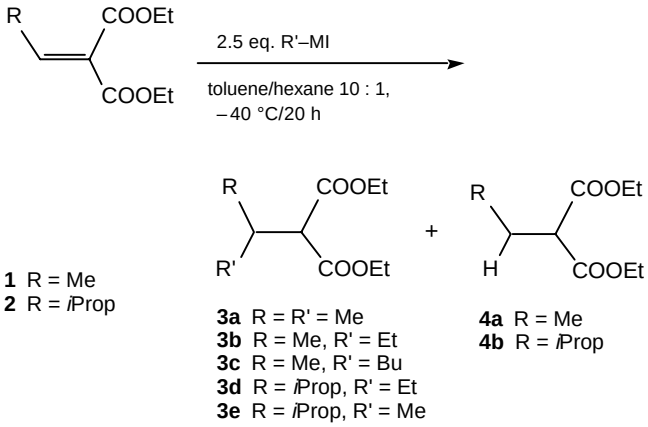
Abstract. Mixed alkyl-methyl- and aryl-methylorganoaluminum chlorides **6** were formed by reaction of methylaluminum dichloride with organolithium or Grignard compounds and used for chemoselective 1,4 addition of higher alkyl, aryl, alkenyl and alkinyl groups to alkylidine malonic esters **1** and **2**. As an alternative, mixed trimethylorganoaluminates **7** can also be applied for these Michael addition reactions. For conjugate addition of alkenyl groups to alkylidene malonates **1** and **2**, alkenyl diisopropylalanes **10** obtained from alkynes and diisopropylaluminum hydride proved the most efficient reagents. Using these novel mixed organoaluminum compounds, β-branched malonic (carboxylic) acid derivatives **3c**, **8**, **9** and **11** were obtained in good yields. The method offers a general access to β-branched carboxylic derivatives of quite diverse structure not dependent on the commercial availability of the organoluminum chlorides.

Trivalent organoaluminum reagents combine the properties of Lewis acidity with nucleophilic reactivity in their tetracoordinated complexes [1]. The conjugate additions of dimethylaluminum chloride and diethylaluminum chloride to alkylidene malonic acid derivatives was demonstrated an efficient access to β-methyl- and β-ethyl-branched carboxylic acid derivatives [2]. Dimethyl- and diethylaluminum chloride as well as diisobutylaluminum chloride are commercially available, while other dialkyl- (or diaryl)aluminum chlorides must be prepared prior to their use in such reactions. Dipropylaluminum chloride not reliably stable in solution can be prepared by comproportionation from aluminum trichloride and tripropylaluminum [3]. Diphenylaluminum chloride is accessible in a two step synthesis. First, triphenylaluminum is synthesized from diphenylmercury and aluminum and subjected to comproportionation with aluminum trichloride [4]. The synthesis of homologous organoaluminum chlorides requires similar exertion. This situation illustrates the need for a more general and simple access to organoaluminum reagents which can be used in 1,4 addition reactions to Michael acceptors. One option should consist of the application of mixed dialkylaluminum chlorides. So far, such compounds have not been described in the literature, obviously because they undergo exchange of substituents through dimeric or oligomeric aggregates. As a consequence, it is concluded that mixed dialkylaluminum chlorides should be generated *in situ* prior to their use in the conjugate addition to α,β-unsaturated carbonyl compounds.

Methodical Investigations

In order to classify the mode of reactions of organometallic reagents, diethyl ethylidene-malonate **1** and diethyl isobutylidenemalonate **2** have been used as the model substrates. The reactivity (in terms of conversion) and the chemoselectivity of the 1,4 addition versus the β-hydride transfer (Scheme 1) of the different reagents are shown in Table 1.



Scheme 1 Reaction of diethyl alkylidene malonates with organometallic reagents

All reactions were carried out under standard conditions at –40 °C in toluene using 2.5 equivalents of the organometallic reagent. The reaction time was 20 h. The crude products were determined by gas chromatography and identified by comparison of their retention times with those of reference compounds.

The results quoted in Table 1 show that a) the reactivity of dialkylalumium chlorides is generally higher than that of monoalkylaluminum dichlorides (entry 1 versus 2, entry 5 versus 6); b) the reactivity of ethylaluminum chlorides is higher than that of methylalumi-

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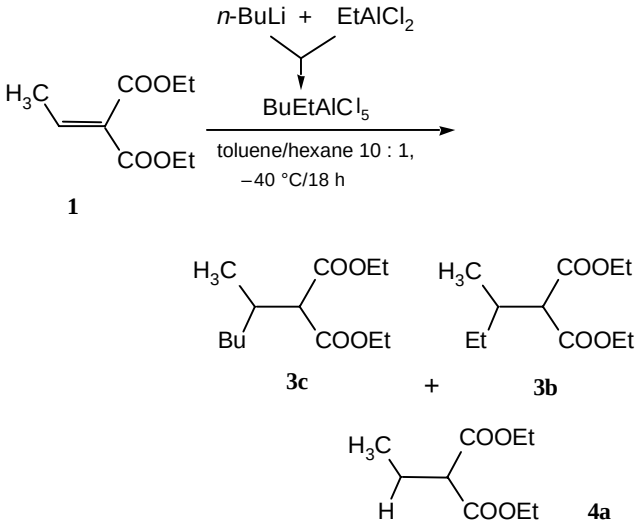
Table 1 Reaction of organometallic reagents with alkylidene malonic esters **1** and **2**

Entry	Educt	R' – M	Conversion (%)	Ratio [a]) **3** : **4**	Remark
1	**1**	Me_2AlCl	100	100 : 0	[2]
2	**1**	$MeAlCl_2$	82	100 : 0	–
3	**1**	$EtAlCl_2$	100	98 : 2	–
4	**1**	BuLi	100	88 : 12	and 3 polar products
5	**2**	Et_2AlCl	100	33 : 67	[2]
6	**2**	$EtAlCl_2$	75	79 : 21	–
7	**2**	$MeAlCl_2$	45	100 : 0	–

[a]) Determined from crude product by GC

num chlorides (entry 2 versus 3, entry 6 versus 7); this is in agreement with the markedly different reactivity of diethyl- and dimethylaluminum chloride towards α,β-unsaturated *N*-acyl oxazolidinones [5–7]); c) the slower reaction of ethylaluminum dichloride to isobutylidenemalonic ester **2** more selectively yields the 1,4 adduct compared to the reaction of diethylaluminum chloride which preferentially forms the hydride transfer product (entry 6 versus 5); butyllithium reacts with the acceptor to give polar products of 1,2 addition [8] besides the conjugate adducts.

As a first example of a mixed dialkylaluminum chloride we synthesized *n*-butyl-ethylaluminum chloride (**5**) from ethylaluminum dichloride (1M in *n*-hexane) and *n*-butyllithium (1.6M in *n*-hexane) in toluene at –40 °C. Immediate precipitation of lithium chloride indicates the formation of the mixed dialkylaluminum chloride **5**. After addition of ethylidene malonic ester **1** and 18 h at –40 °C, gaschromatographical analysis of the crude product showed the formation of three compounds (Scheme 2).

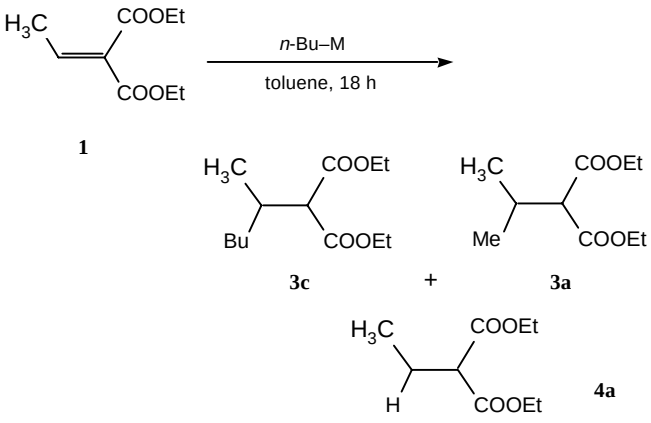


Scheme 2 Reaction of *in situ*-generated *n*-butyl-ethylaluminum chloride malonates

The hydride transfer product **4a** was the major component as was also observed in the reaction of **1** with diethylaluminum chloride (Table 1). Ethyl and *n*-butyl were transferred in almost equal extension as can be expected for a mixed dialkylaluminum chloride **5**.

In particular, polar components from 1,2 addition of butyllithium (see, Table 1) have not been detectable. It can be concluded from these results, that the reacting species are not the single components ethylaluminum dichloride and butyllithium, but the mixed butylethylaluminum chloride **5**.

The lower reactivity of methylaluminum reagents in conjugate addition reactions [1, 5–7] (see also Table 1) suggests that methyl containing mixed organoaluminum reagent should be more suitable than **5** for the 1,4-additon of higher alkyl, aryl and other groups to Michael acceptors. In this sense, *n*-butylmethylaluminum chloride **6a** was synthesized from *n*-butyllithium and methylaluminum dichloride and, subsequently, reacted with ethylidenemalonic ester **1** (Scheme 3, entry 1 in Table 2).



Scheme 3 1,4-Addition of *n*-butyl-methylaluminum reagents to ethylidene malonic ester **1**

In this reaction, the products of butyl transfer and methyl transfer (**3a**) were formed in a ratio of > 3:1 (ac-

cording to GC analysis). The reduced acceptor **4a** was obtained in amounts equal to those of the butyl substituted compound **3c**. In order to enhance the selectivity, the reaction was carried out at – 78 °C. At this temperature the ratio of butyl to methyltransfer increased to 8:1. However, the hydride transfer to give **4a** was not influenced (Table 2).

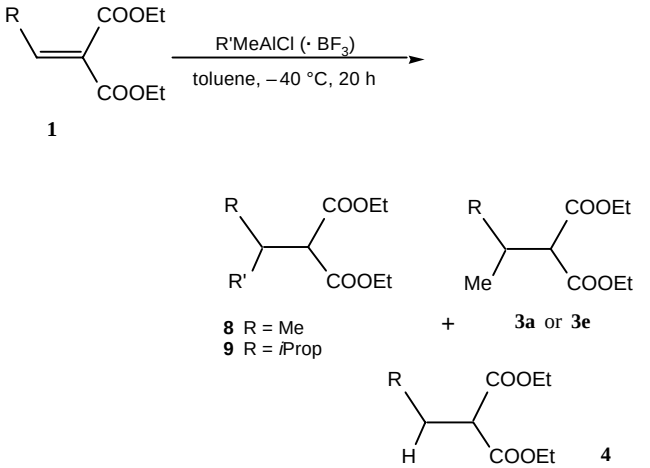
Table 2 Conjugate addition of mixed *n*-butyl-methylaluminum reagents to ethylidene malonic ester **1**

Entry	Bu-M	Temp (°C)	Ratio of Products [a] **3c** : **3a** : **4a**
1	BuMeAlCl **6a**	– 40 °C	42 : 13 : 45
2	BuMeAlCl **6a**	– 78 °C	47 : 6 : 47
3	Li^+BuMe_3Al **7**	– 40 °C	57 : 14 : 30
4	$BuMeAlCl{\cdot}BF_3$	– 40 °C	87 [b]) : 7 : 6

[a]) Determined from crude product by GC; [b]) yield: 74%

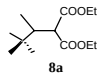
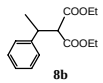
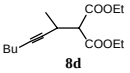
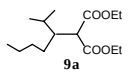
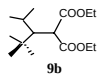
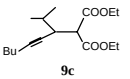
The reactivity of the mixed organoaluminum reagents can be modified either by enhancing their nucleophilicity or by combination with a Lewis acid [2]. Alanate complexes should exhibit enhanced nucleophilicity. Lithium *n*-butyltrimethylalanate **7a** reacted with acceptor **1** to form an increased amount of the 1,4-butyl addition product **3c**, although the butyl moiety is competing with three methyl groups in this reagent. The hydride transfer was slightly reduced. However, a selective and efficient 1,4 addition of the butyl group to the alkylidenemalonic ester was achieved when *n*-butylmethylaluminum chloride **6** was mixed with one equivalent of borontrifluoride prior to the 1,4 addition reaction [2]. Under these conditions the (1-methyl-pentyl)malonic acid ester **3c** was obtained with excellent selectivity and isolated in a yield of 74%. The products of methyl transfer **3a** and of hydride transfer **4a** were formed in only small amounts and could be separated from **3c** by flash-chromatography.

This efficient method was adopted for the 1,4 addition of other groups from mixed organomethylaluminum chlorides not only to **1**, but also to the isobutylidenemalonic ester **2** as an example of a sterically demanding Michael acceptor (Scheme 4).



Scheme 4 1,4-Addition of mixed organomethylaluminum chlorides to alkylidene malonates

Table 3 1,4-Addition of mixed organomethylaluminum chlorides to ethylidende- (**1**) and isobutylidene malonic ester **2** according to Scheme 4

Product	Reagent	Ratio of Products [a] **8** or **9** : **3** : **4**	Yield (%) [conversion (5)]
 **8a**	*t*BuMeAlCl·BF_3	92 : 2 : 6	66
 **8b**	MePheAlCl	95 : 5 : 0	71
 **8c**	MeVinylAlCl	100 : 0 : 0	35 (66)
 **8d**	HexinylMeAlCl	100 : 0 : 0	71
 **9a**	BuMeAlCl·BF_3	65 : 5 : 32	34 (84)
 **9b**	*t*BuMeAlCl·BF_3	89 : 8 : 3	77 (92)
 **9c**	HexinylMeAlCl	100 : 0 : 0	99

[a]) Determined from crude product by GC

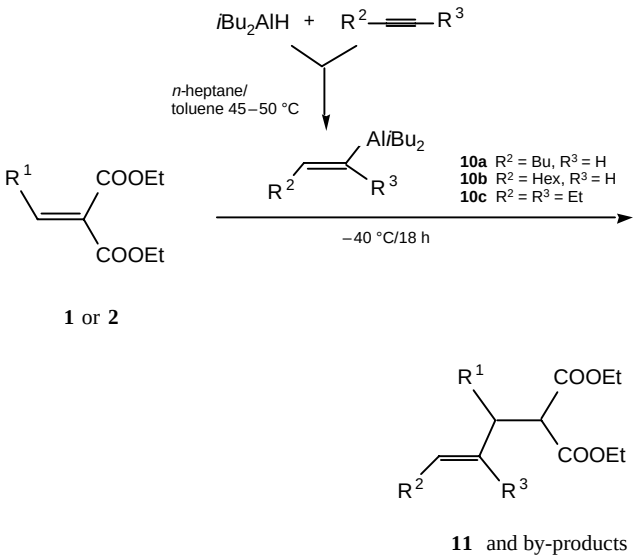
The reactions were performed in toluene at –40 °C within a reaction time of 18 h. In cases of competing hydride transfer, the mixed organoaluminum chloride was first treated with borontrifluoride prior to the addition reaction (Table 3). The results quoted in Table 3 give evidence that the 1,4 addition of mixed organomethylaluminum chlorides is of general use for the synthesis of β-branched carboxylic acid derivatives. While the reaction of *n*-butylmethylaluminum chloride **6a** (Scheme 3, Table 2) can be considered a typical example for the transfer of *n*-alkyl groups, the highly selective formation of **8a** from ethylidenemalonic ester **1** and *tert*-butylmethylaluminum chloride **6b**/borontrifluoride illustrates that sterically demanding branched groups can be added to the acceptor by this methodology.

During this reaction, a quaternary carbon is formed. The product **4a** of the hydride transfer was found in only small amounts. Transfer of a β-hydrogen is not expected in the 1,4 addition of methylphenylaluminum chloride **6c** to **1**. Therefore, precomplexation with boron trifluoride was not necessary. A highly selective transfer of the phenyl group was achieved to give adduct **8b** in high yield. The mixed methylvinylaluminum chloride **6d** synthesized from vinylmagnesium bromide and methylaluminum dichloride proved less reactive than **6a** and **6b**. Its reaction with **1** remained incomplete within the time of 18 h. However, the product **8c** of the 1,4-vinyl addition was obtained with complete selectivity. In contrast, 1-hexinylmethylaluminum chloride **6e** generated from 1-hexinyllithium and methylaluminum dichloride exhibits high reactivity and underwent completely selective 1,4 addition of the hexinyl group to **1** to furnish product **8d**.

It is expected and was shown for the 1,4 addition of diethylaluminum chloride [2] that extensive β-hydride transfer occurs with sterically hindered Michael acceptors. In order to estimate the limitations of the 1,4-addition of mixed organoaluminum chlorides to Michael acceptors, isobutylidenemalonic ester **2** was applied as the substrate. Selective 1,4-addition of the *n*-butyl group from butylmethylaluminum chloride **6a** to give the branched compound **9a** was accompanied by hydride transfer to form **4b** even in the presence of boron trifluoride. Surprisingly, the conjugate addition of the *tert*-butyl group from *tert*-butylmethylaluminum chloride **6b**/borontrifluoride proceeded with high selectivity, and the multiply branched product **9b** was isolated in high yield. Once again, complete selectivity was achieved in the 1,4 addition of the rod-like 1-hexinyl group from the reactive 1-hexinylmethylaluminum chloride **6e**. The branched carboxylic acid derivative **9c** was isolated in almost quantitative yield.

1,4 -Addition Reactions of Mixed Alkenyl Diisobutylalanes

As already outlined for the addition of methylvinylaluminum chloride to acceptor **1** (Table 3), the reactivity of the mixed alkenylaluminum chlorides is lower than that of the other reagents **6**. This resulted in incomplete conversions, *e.g.* in the formation of **8c**. Therefore, the use of alternative mixed alkenyl organoaluminum reagents in conjugate addition reactions to Michael acceptors was investigated. Organoaluminum hydrides readily undergo hydroalumination reactions [9–11]. There are no experiences reported on the conjugate addition of trialkylaluminum reagents to alkylidenemalonic derivatives. In addition, hydroaluminations of alkines often are accompanied by undesired side-reactions *e.g.* hydroalumination of the product or formation of the alkinylaluminum compound from terminal alkines, if reaction temperature and ratio of components are not optimized. In order to prevent such side reactions, the bulky diisobutylaluminumhydride was used for addition reactions to 1-hexine, 1-octine and 3-hexine in *n*-heptan/toluene at 45–50 °C to form the alkenyl diisobutylaluminum reagents **10** (Scheme 5). Hydroaluminations proceed with *cis*-stereoselectivity, to give *Z*-configured alkenylalanes (this was confirmed for the terminal alkenyl diisobutylalanes **10a** and **10b** by the coupling constants J = 15.1 Hz for the olefinic protons in the NMR spectra). To the solution of the mixed organoaluminum compounds **10** at –40 °C the alkylidenemalonic esters **1** or **2**, respectively, was added.



Scheme 5 1,4-Addition of mixed alkenyl diisobutylalanes to alkylidene malonates

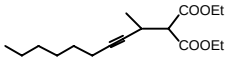
The conjugate addition reactions of the mixed 1-alkenyl organoalanes proceeded with high selectivity and gave the branched alkenylmalonic esters **11a–c** in high yield (Table 4).

Only small amounts of the β-alkinyl substituted derivatives **8d**, **8e**, **9c** formed from the corresponding alki-

Table 4 1,4-Additon of mixed alkenyl diisobutylalanes 10 to alkylidene malonic esters **1**/**2** to give substituted *C*-allylmalonic esters **11** (Scheme 5)

Product	R^1	R^2	R^3	Ratio [a]) of **11** : (by-product)	Yield of **11** (%)
11a	CH_3	*n*-C_4H_9	H	97 : 3 (**8d**)	84
11b	$CH(CH_3)_2$	*n*-C_4H_9	H	97 : 3 (**9c**)	74
11c	CH_3	*n*-C_6H_{13}	H	93 : 7 (**8e**) [b])	82
11d	CH_3	C_2H_5	C_2H_5	79 : 21 (**4a**)	43
11e	$CH(CH_3)_2$	C_2H_5	C_2H_5	80 : 20 (**4b**)	47

[a]) Determined by gas chromatography from crude product;

[b]) **8e**: 

nyl diisobutylalane as the by-product of the hydroalumination were detectable and could easily be removed by flash-chromatography.

The 1,4 addition of 3-hexenyl diisobutylalane **10c** to the acceptors **1**/**2** was accompanied by β-hydride transfer to give reduced acceptors **4**. Nevertheless, the 1,4 adducts **11d** and **11e** were the mayor product (ratio 4:1) and could be isolated in pure form and acceptable yield. The results show that mixed alkenyl diisobutylalanes are alternative reagents to the alkenyl methylaluminum chlorides. Their complementary use with the mixed alkylmethylaluminum chlorides, arylmethylaluminum chlorides and alkinyl methylaluminum chlorides in 1,4-additon reactions to alkylidene malonic esters constituents a general efficient method for the synthesis of β-branched carboxylic acid derivatives of diverse structure.

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Experimental

Toluene and heptane were dried before use by distillation from potassium benzophenone ketyl. Alkylidenemalonic diethyl esters **1** and **2** were synthesized according to published procedures [12]. Dimethyl- and diethylaluminum chloride as well as methyl- and ethylaluminum dichlorides and diisobutylaluminumhydride (1.5M, toluene) were purchased from Aldrich and used as 1M solutions in *n*-hexane. Petroleum ether refers to *b.p.* 40–70 °C. Flash-chromatography was carried out using silica gel 60 (Merck, Darmstadt, Germany), 0.04–0.063 nm. TLC was performed on silica gel (Kieselgel 60 F_{254}, Merck, Darmstadt, Germany). Gaschromatography was carried out with a fused silica-column (PERMABOND SE-30-DF-0.25, 25m × 0.32 mm ID, Machery & Nagel, Düren, Germany). ^1H and ^{13}C NMR-spectra were recorded on a Bruker AC 200 or on a Bruker AM 400 NMR spectrometer. All NMR spectra have been recorded in $CDCl_3$ using TMS as the standard. Satisfactory microanalyses were obtained for most of the new compounds and those incompletely characterized in the literature.

Methodical Investigations

For reactions of diethyl alkylidene malonates **1** and **2** with dimethyl- and diethylaluminum chlorides, see ref [2].

Reaction of Methyl- and Ethylaluminum Dichloride with Alkylidenemalonic Esters 1 and 2 (General Procedure)

A solution of methylaluminum dichloride or ethylaluminum dichloride (3 mmol, 3 ml of 1M solution in *n*-hexane) in dry toluene (50 ml) under argon atmosphere was stirred at –40 °C, and the diethyl alkylidenemalonate **1** or **2** (1.2 mmol) was added. The mixture was stirred at –40 °C for 20 h and then poured into sat. aqueous ammonium chloride solution (100 ml). The aqueous layer was extracted three times with dichloromethane (30 ml). The combined organic layers were washed with sat. ammonium chloride solution and dried with magnesium sulfate. After evaporation of the solvent *in vacuo*, the remaining crude products were analyzed by gaschromatography. Diethyl ethylmalonate **4a** and diethyl isobutylmalonate **4b** were identified by comparison with authentic material synthesized according to ref. [12]. The products of conjugate addition **3a**, **3b**, **3d** and **3e** were identified by comparison with authentic substances described in ref. [2] (see, Table 1).

Diethyl Isopropylmalonate (**3a**) [2, 5]

GC analysis: 80 °C (5 min) → 150 °C (5 °C/min): R_t = 6.73 min.

Diethyl (1-Methylpropyl)malonate (**3b**) [2, 13]

GC analysis: 80 °C (5 min) → 150 °C (5 °C/min): R_t = 5.08 min (**4a**); 9.58 min (**3b**).

Diethyl (1,2-Dimethyl-propyl)malonate (**3e**) [2, 5]

GC analysis: 100 °C (5 min) → 200 °C (5 °C/min): R_t = 7.27 min.

Diethyl (1-Ethyl-2-methyl-propyl)malonate (**3d**) [2, 14]

GC analysis: 100 °C (5 min) → 200 °C (5 °C/min): R_t = 5.05 min (**4b**); 9.23 min (**3d**). The reaction of diethyl ethylidenemalonate **1** (1.2 mmol) with *n*-butyllithium (3.0 mmol, 1.9 ml 1.6M in *n*-hexane) in toluene (50 ml) under conditions

as described in the general procedure for the reactions of the alkylaluminum dichloride gave a crude product that consisted of 5 components of which 2 could be determined by gas chromatography: 80 °C (5 min) → 150 °C (5 °C/min): R_t = 5.09 min (**4a**); 14.37 (**3c**, *vide infra*).

Mixed Organoaluminum Compounds (General Procedures)

Method A: Mixed dialkylaluminum chlorides **5** and **6**: In a dry two-neck flask under argon atmosphere dry toluene (50 ml) was cooled to –40 °C. Methyl- or ethylaluminum dichloride (*vide infra*, 1M solution in *n*-hexane) and the organolithium- or organomagnesium compound (*vide infra*) were added using a syringe through a septum. The mixture is stirred for 1 h. In the indicated cases (*vide infra*) 1 equivalent of boron trifluoride etherate is added and the mixture stirred for an additional hour.

Method B: Ate complex **7** To a solution of trimethylaluminum (2M in *n*-hexane) in dry toluene (50 ml) under argon atmosphere at –40 °C an equimolar amount of a solution of the organolithium compound (or Grignard compound) in an appropriate inert solvent was added. The solution was stirred at –40 °C for 1 hour prior to its use in the 1,4 addition reaction.

1,4 Addition Reaction of Mixed Organoaluminum Compounds with Diethyl Alkylidenemalonates 1/2 (General Procedure)

To the *in situ* generated solution of the mixed organoaluminum compound **5**, **6** or **7**, respectively, in toluene under argon atmosphere at –40 °C, the diethyl alkylidenemalonate was added. After stirring at –40 °C for 18–20 h, the mixture was poured into sat. aqueous ammonium chloride solution. The aqueous solution was extracted three times with dichloromethane (30 ml). The combined organic layers were washed with sat. aqueous ammonium chloride solution, dried with magnesium sulfate, and the solvent was evaporated. The remaining crude product was analyzed by gas chromatography and the components identified by comparison with authentic samples [2]. Products of the most efficient method were purified by flash-chromatography in petroleum ether/ethyl acetate (25:1) and characterized (see also Tables 2 and 3).

Diethyl (1-Methyl-pentyl)malonate (**3c**)

a) The product was formed in a mixture with the hydride transfer product **4a** (*vide supra*) and the 1,4 ethyl adduct **3b** according to method A from ethylaluminum dichloride (3 ml, 1M in *n*-hexane, 3.0 mmol), *n*-butyllithium (1.9 ml, 1.6M in *n*-hexane, 3.0 mmol) and diethyl ethylidenemalonate **1** (222 mg, 1.19 mmol). Yield 246 mg (crude product mixture), yellowish oil; GC analysis: 80 °C (5 min) → 150 °C (5 °C/min): R_t = 5.21 min (**4a**); 9.46 min (**3b**) and 14.31 min (**3c**); **4a**:**3b**:**3c** = 71:15:14.

b) By method A from methylaluminum dichloride (3 ml, 1M in *n*-hexane, 3.0 mmol), *n*-butyllithium (1.9 ml, 1.6M in *n*-hexane, 3.0 mmol) and diethyl ethylidenemalonate **1** (222 mg, 1.19 mmol). Yield 294 mg (crude product mixture), yellowish oil; GC analysis: 80 °C (5 min) → 150 °C (5 °C/min): R_t = 5.19 min (**4a**), 6.64 min (**3a**) and 14.39 min (**3c**). **4a**:**3a**:**3c** = 45:13:42.

c) analogous to b), however, reaction temperature –78 °C, reaction time 3 h: conversion 30%. Ratio of products see Table 2.

d) By method B from trimethylaluminum (1.5 ml, 2M in *n*-hexane, 3.0 mmol), *n*-butyllithium (1.9 ml, 1.6M in *n*-hexane, 3.0 mmol) and 222 mg (1.19 mmol) of diethyl ethylidenemalonate **1**. Yield 288 mg (crude product mixture), yellowish oil; GC analysis: R_t = 5.17 min (**4a**), 6.63 min (**3a**) and 14.42 min (**3c**). **4a**:**3a**:**3c** = 30:14:56.

e) Preparative synthesis by method A from methylaluminum dichloride (9.0 ml, 1M in *n*-hexane, 9.0 mmol), *n*-butyllithium (5.7 ml, 1.6M in *n*-hexane, 9.1 mmol) and borontrifluoride etherate (1.2 ml, 9.76 mmol) and then diethyl ethylidenemalonate (666 mg, 3.58 mmol). Yield 649 mg (74% pure, colourless oil, R_t = 0.75 (petroleum ether/ethyl acetate 10:1). (GC analysis: R_t = 5.07 min (**4a**), 6.58 min (**3a**), and 14.37 min (**3c**). **4a**:**3a**:**3c** = 6:7:87)). – ^{1}H NMR (200 MHz, $CDCl_3$): d/ppm = 4.11 (q, 4H, J = 7.0 Hz, CH_2O), 3.14 [d, 1H, J = 8.3 Hz, $CH(COOEt)_2$], 0.90 (d, 3H, J = 6.8 Hz, CH–C$\underline{H}_3$), 0.80 (t, 3H, J = 5.6 Hz, $(CH_2)_3C\underline{H}_3$). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 168.95, 168.77 (C=O), 61.00, 60.95 (CH_2O).

$C_{13}H_{24}O_4$	Calcd.: C 63.91 H 9.90
(224.3)	Found: C 63.81 H 9.87.

Diethyl (1,2,2-Trimethylpropyl)malonate (**8a**) [2]

This compound was synthesized according to method A from methylaluminum dichloride (3.0 ml, 1M in hexane, 3.0 mmol), *tert*-butyllitium (2.0 ml, 1.5M in *n*-pentane, 3.0 mmol), borontrifluoride etherate (0.36 ml, 2.9 mmol) and diethyl ethylidenemalonate **1** (222 mg, 1.19 mmol). GC analysis: 80 °C (5 min) → 150 °C (5 °C/min): R_t = 4.98 min (**4a**), 6.48 min (**3a**), and 13.12 min (**8a**). Ratio **4a**:**3a**:**8a** = 6:2:92. Yield 193 mg (66%), pure, colourless oil, R_f = 0.58 (petroleum ether/ethyl acetate 5:1). The product is identical with the one described in ref. [2].

Diethyl (1-Phenylethyl)malonate (**8b**) [2]

The compound was obtained by method A from methylaluminum dichloride (3 ml, 1M in hexane, 3.0 mmol), phenyllithium (1.9 ml, 1.6M in cyclohexane, 3.0 mmol) and diethyl ethylidenemalonate **1** (222 mg, 1.19 mmol). GC analysis of the crude product: 80 °C (5 min) → 150 °C (5 °C/min): R_t = 6.58 min (**3a**) and 19.28 min (**8b**). Ratio **3a**:**8b** = 5:95. Yield 222 mg (71%, pure), colourless oil, R_f = 0.45 (petroleum ether/ethyl acetate 5:1). The product is identical with the compound described in ref. [2].

Diethyl (1-Methylallyl)malonate (**8c**)

According to method A, the mixed methylvinylaluminum chloride was formed from methylaluminum dichloride (6 ml, 1M in *n*-hexane, 6 mmol) and vinylmagnesium bromide (6 ml, 1M in tetrahydrofuran, 6 mmol) and reacted with diethyl ethylidenemalonate **1** (444 mg, 2.4 mmol). GC analysis of the crude product (conversion 69%): 80 °C (5 min) M 150 °C (5 °C/min): R_t = 8.65 min (**8c**), see Table 3. Yield 178 mg (35%), colourless oil, R_f = 0.65 (petroleum ether/ethyl acetate 5:1). – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 5.47 (ddd, 1H, J_{trans} = 17.6 Hz, J_{cis} = 10.0 Hz, J_{vic} = 7.8 Hz, -CH=), 5.01 (m, 2H, CH_2=), 4.15 (q, 2H, J = 7.0 Hz, CH_2O), 4.11 (q, 2H, J = 7.2 Hz, CH_2O), 3.22 [d, 1H, J = 9.3 Hz,

$CH(COOEt)_2$]. – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 139.83 (-<u>C</u>H=), 115.33 (CH_2=), 61.24, 61.16 (CH_2O), 57.71 [<u>C</u>H$(COOEt)_2$].

$C_{11}H_{18}O_4$	Calcd.: C 61.66 H 8.47
(214.3)	Found: C 61.68 H 8.40.

Diethyl (1-Methyl-hept-2-ynyl)malonate (**8d**)

Obtained by method A from methylaluminum dichloride (3 ml, 1M in *n*-hexane, 3.0 mmol), 1-hexynyllithium (3.0 mmol, from 1-hexyne in toluene and 1.05 equiv. *n*-butyllithium) and diethyl ethylidenemalonate **1**. GC analysis of the crude product: 80 °C (5 min) → 150 °C (5 °C/min): R_t = 18.80 min (**8d**). Yield 200 mg (71%), colourless oil, R_f = 0.52 (petroleum ether/ethyl acetate 10:1). – ^1H NMR (200 MHz, $CDCl_3$): δ/ppm = 4.16, 4.15 2(q, 2H, J = 7.2 Hz, CH_2O), 3.29 [d, 1H, J = 9.3 Hz, $CH(COOEt)_2$], 3.14 (m, 1H, C<u>H</u>Me), 2.07 (dt, J = 6.6 Hz ^5J = 2.0 Hz, CH_2–C≡C). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 167.76, 167.62 (C=O), 82.32, 80.56 (C≡C), 58.17 [<u>C</u>H$(COOEt)_2$], 30.92 (CH_2), 26.40 (CHMe), 21.76 (CH_2). No correct elemental analysis was obtained, because a by-product < 5% formed during work up could not be separated.

Diethyl (1-Isopropyl-pentyl)malonate (**9a**)

Obtained by method A from methylaluminum dichloride (2.4 ml, 1M in *n*-hexane, 2.4 mmol), *n*-butyllithium (1.5 ml, 1.6M in *n*-hexane, 2.4 mmol), borontrifluoride etherate (0.3 ml, 2.44 mmol) and diethyl isobutylidenemalonate **2** (204 mg, 0.95 mmol). – GC analysis of the crude product mixture (conversion 84%): 100 °C (5 min) → 200 °C (5 °C/min): R_t = 5.04 min (**4b**), 7.16 min (**3e**, Scheme 1), 13.18 min (**9a**); ratio **4b**:**3e**:**9a** = 32:5:63. Yield 87 mg (34%, still contains < 3% of **4b**), colourless oil, R_f = 0.46 (petroleum ether/ethyl acetate). – ^1H NMR (200 MHz, $CDCl_3$): δ/ppm = 4.14 (q, 4H, J = 7.0 Hz, CH_2O), 3.37 [d, 1H, J = 7.8 Hz, $CH(COOEt)_2$], 1.76 (d sept., 1H, J = 6.8 Hz, J = 2.4 Hz, $CHMe_2$), 0.90 – 0.81 (m, 9H, $3CH_3$-). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 169.59, 169.42 (C=O), 44.10 (CHBu), 31.35 (CH_2), 29.74 (<u>C</u>HMe_2), 20.34, 18.50 [(<u>C</u>$H_3)_2$CH].

Diethyl (1-Isopropyl-2,2-dimethyl-propyl)malonate (**9b**)

This compound was synthesized by method A from methylaluminum dichloride (2.4 ml, 1M in *n*-hexane, 2.4 mmol), *tert*-butyllithium (1.6 ml, 1.5M in *n*-pentane, 2.4 mmol), borontrifluoride (0.3 ml, 2.44 mmol) and diethyl isobutylidenemalonate **2** (204 mg, 0.95 mmol). – GC analysis of the crude product (conversion 92%): 100 °C (5 min) → 200 °C (5 °C/min): R_t = 4.95 min (**4b**), 7.10 min (**3e**); 12.28 min (**9b**). Yield 199 mg (77%), colourless oil, R_f = 0.50 (petroleum ether/ethyl acetate 10:1). – ^1H NMR (200 MHz, $CDCl_3$): δ/ppm = 4.13, 4.12 (2 q, 2×2H, J = 7.0 Hz, J = 7.2 Hz, CH_2O), 2.14 (dd, 1H, J = 5.4 Hz, J = 2.0 Hz, CH*t*Bu), 2.08 (d sept., 1H, J = 7.1 Hz, J = 1.6 Hz, C<u>H</u>Me_2), 0.95 (s, 9H, $C(CH_3)_3$). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 170.55 (C=O), 61.24, 61.13 (CH_2O), 35.50 (CMe_3), 29.07 [C(<u>C</u>$H_3)_3$], 28.32 ($CHMe_2$).

$C_{15}H_{28}O_4$	Calcd.: C 66.14 H 10.36
(272.4)	Found: C 66.16 H 10.34.

Diethyl (1-Isopropyl-hept-2-ynyl)malonate (**9c**)

Obtained by method A from methylaluminum dichloride (2.4 ml, 1M in *n*-hexane, 2.4 mol), 1-hexynyllithium (2.4 mmol in toluene/*n*-hexane, see **8d**) and diethyl isobutylidenemalonate (204 mg, 0.95 mmol). – GC analysis: 100 °C (5 min) → 200 °C (5→°C/min): R_t = 17.06 min (**9c**). Yield 278 mg (99%), colourless oil, R_f = 0.43 (petroleum ether/ethyl acetate 10:1). – ^1H NMR (200 MHz, $CDCl_3$): δ/ppm = 4.16, 4.14 (2 q, 2×2H, J = 7.2 HZ, CH_2O), 3.07 (ddd, 1H, J = 10.9 Hz, J = 5.7 Hz, ^5J = 2.3 Hz, CH*i*Pr), 2.09 (dt, 2H, J = 6.7 Hz, ^5J = 2.3 Hz, CH_2C≡), 1.68 (d sept, 1H, J = 6.7 Hz, J = 3.6 Hz, $CHMe_2$). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 167.88, 167. 72 (C=O), 84.54, 76.61 (C≡C), 38.78 (CH*i*Pr), 28.86 ($CHMe_2$).

$C_{17}H_{28}O_4$	Calcd.: C 68.89 H 9.52
(296.4)	Found: C 69.14 H 9.54.

Generation and 1,4-Addition Reactions of Alkenyl Diisobutylalanes (10)

n-Heptane (10 ml) was distilled from potassium/benzophenone under argon atmosphere into a Schlenk tube. Through a septum, the alkyne (3 equivalents related on the alkylidene malonate to be reacted) and diisobutylaluminumhydride (also 3 equivalents, 1.5M in toluene) were added. In the case of terminale alkynes, the mixture was heated to 40 – 45 °C for 2 h. For reaction of 3-hexyne with diisobutylaluminumhydride, the mixture was heated to 50 °C for 3 h. Then, the solution was cooled to – 40 °C and the diethyl alkylidenemalonate (1 equivalent) was added. The reactions were conducted and work up was carried as described for the addition reactions with mixed dialkylaluminum chlorides (*vide supra*).

Diethyl (E-1-Methyl-hept-2-enyl)malonate (**11a**)

Obtained from 1-hexyne (0.6 ml, 5.33 mmol), diisobutylaluminumhydride (3.6 ml, 5.4 mmol) and diethyl ethylidenemalonate **1** (333 mg, 1.8 mmol). – GC analysis of the crude product: 80 °C (5 min) → 150 °C (5 °C/min): R_t = 18.28 min (**11a**), 18.55 min (**8d**). Yield 407 mg (84%, pure), colourless oil, R_f = 0.65 (petroleum ether/ethyl acetate 5:1). – ^1H NMR (200 MHz, $CDCl_3$): δ/ppm = 5.46 (dt, 1H, J_{trans} = 15.1 Hz, J = 6.4 Hz, CH_2–C<u>H</u>=CH), 5.28 (dd, 1H, J_{trans} = 15.4 Hz, J = 8.1 Hz, CH·C<u>H</u>=CH). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 131.70, 131.24 (HC=CH), 58.30 [$CH(COOEt)_2$].

$C_{15}H_{26}O_4$	Calcd.: C 66.64 H 9.69
(270.4)	Found: C 66.42 H 9.64.

Diethyl (E-1-Isopropyl-hept-2-enyl)malonate (**11b**)

Obtained from 1-hexyne (0.48 ml, 4.27 mmol), diisobutylaluminumhydride (2.9 ml, 4.35 mmol) and diethyl isobutylidenemalonate **2** (306 mg, 1.43 mmol). – GC analysis of the crude product: 100 °C (5 min) → 200 °C (5 °C/min): R_t = 16.64 min (**11b**), 16.78 (**9c**). Yield 352 mg (82%), colourless oil, R_f = 0.77 (petroleum ether/ethyl acetate 5:1). – ^1H NMR (200 MHz, $CDCl_3$): δ/ppm = 5.43 (dt, 1H, J_{trans} = 15.1 Hz, J = 6.6 Hz, CH_2C<u>H</u>=CH), 5.22 (dd, 1H, J = 15.4 Hz, J = 9.5 Hz, CHC<u>H</u>=CH), 1.67 (d sept., 1H, J = 6.8 Hz, J = 4.9 Hz, $CHMe_2$). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 135.02, 125.80 (CH=CH), 49.18 (<u>C</u>H*i*Pr), 29.16 ($CHMe_2$).

$C_{17}H_{30}O_4$	Calcd.: C 68.42 H 10.13
(298.4)	Found: C 68.51 H 10.27.

Diethyl (E-1-Methyl-non-2-enyl)malonate (**11c**)

Obtained from 1-octyne (0.89 ml, 5.42 mmol), diisobutylalu-

minumhydride (3.6 ml, 5.4 mmol) and diethyl ethylidenemalonate **1**. – GC analysis of the crude product: 80 °C (5 min) → 150 °C (5 °C/min): R_t = 22.61 min (**11c**), 22.69 min (**8c**, Table 4). Yield 396 mg (74%, pure), colourless oil, R_f = 0.68 (petroleum ether/ethyl acetate 5:1). – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 5.45 (dt, 1H, J_{trans} = 15.3 Hz, J = 6.5 Hz, C$\underline{H}_2$CH=CH), 5.27 (dd, 1H, J_{trans} = 15.1 Hz, J = 7.8 Hz, CHC$\underline{H}$=CH), 1.91–1.79 (m, 2H, C$\underline{H}_2$CH=C), 1.01 (d, 3H, J = 6.8 Hz, C$\underline{H}_3$–CH-). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 131.74, 131.23 (CH=CH), 37.32 ($\underline{C}$HMe$_2$).

$C_{17}H_{30}O_4$	Calcd.: C 68.42	H 10.13
(298.4)	Found: C 68.49	H 10.17.

Diethyl (E-2-Ethyl-1-methyl-pent-2-enyl)malonate (**11d**)

This compound was synthesized from 3-hexyne (0.61 ml, 5.37 mmol), diisobutylaluminumhydride (3.6 ml, 5.4 mmol) and diethyl ethylidenemalonate **1** (333 mg, 1.8 mmol). – GC analysis of the crude product: 80 °C (5 min) → 150 °C (5 °C/min): R_t = 5.04 min (**4a**), 17.30 min (**11d**). Yield 206 mg (43%), colourless oil, R_f = 0.66 (petroleum ether/ethyl acetate 5:1). – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 5.12 (t, 1H, J = 7.1 Hz, $CH_2C\underline{H}$=C), 2.83 (dq, 1H, J = 10.9 Hz, J = 6.8 Hz, C$\underline{H}$Me), 2.12–1.86 (m, 4H, C$\underline{H}_2$CH=CC$\underline{H}_2$-). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 141.62 ($\underline{C}$=CH), 127.57 ($\underline{C}$H=C), 22.62, 20.83 ($\underline{C}$HC=C$\underline{C}$H$_2$).

$C_{15}H_{26}O_4$	Calcd.: C 66.64	H 9.69
(270.4)	Found: C 66.64	H 9.56.

Diethyl (E-2-Ethyl-1-isopropyl-pent-2-enyl)malonate (**11e**)

The compound was obtained from 3-hexyne (0.49 ml, 4.31 mmol), diisobutylaluminumhydride (2.9 ml, 4.35 mmol) and diethyl isobutylidenemalonate **2** (306 mg, 1.43 mmol). – GC analysis of the crude product: 100 °C (5 min) → 200 °C (5 °C/min): R_t = 4.91 min (**4b**), 15.92 (**11e**). Yield 202 mg (47%), colourless oil, R_f = 0.70 (petroleum ether/ethyl acetate 5:1). – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 5.03 (t, 1H, J = 7.3 Hz, $CH_2\underline{C}$H=C), 2.74 (dd, 1H, J = 11.2 Hz, J = 4.9 Hz, CH*i*Pr), 2.45–1.67 (m, 5H, C$\underline{H}_2$CH=CC$\underline{H}_2$, CHMe$_2$). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 138.02 (C=), 129.95 (CH=), 50.29 (CH*i*Pr), 29.99 (CHMe$_2$). The product contained >5% of **4b**. ESI-MS: *m/z* = 321.4 (M+Na).

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