Novel [1,*N*]-Carbon to Carbon Rearrangement of an Ester Group via Organotitanium Intermediates Wherein the *N* Varies from 2 to 5. Full Scope and Limitation Leading Predominantly to the Rearrangement

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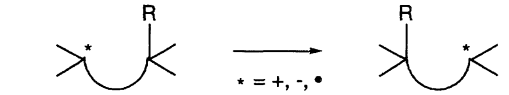
(Received February 16, 1998)

Malonates and methanetricarboxylates having an unsaturated side chain such as **2**, **12**, **20**, **22**, **24**, **31**, or **37** underwent a new ester rearrangement reaction promoted by (η^2-propene)Ti(O-*i*-Pr)$_2$ to afford the succinate derivative **4** or α,β-unsaturated ester **17**, **21**, **23**, **25**, **34**, or **38** via the migration of the ester group from its original bis- or tris-ester position to the acetylene- or olefin-titanium complex. It has been found that the side reactions competing with the desired migration are dealkylation of the side chain of the ester and a simple cyclization. The substrates and conditions which allow the ester migration a preferential path were determined as well as the scope and limitation of this reaction.

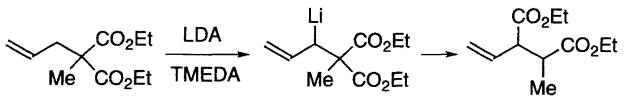
Rearrangement reactions, categorized into one of the most fundamental patterns of organic reactions,[1] could embody an ideal process: reorganization of the structure of an easily available precursor having all necessary carbons and/or functional groups into the target molecule, the preparation of which is otherwise a tedious process.[2] The reactions, which involve the migration of an organic group from one carbon to another, illustrated in Eq. 1, are useful for regio- and stereoselective carbon–carbon bond formation, and are also an interesting method for the scission of a carbon–carbon bond at a specified position. This type of rearrangement has been reported to occur under cationic, anionic, radical, or sigmatropic conditions.[1] Herein described is the migration of an ester group under anionic conditions via titanium intermediates (Eq. 2), which is best characterized by its operational simplicity and broad applicability to [1,2]- to [1,5]-migrations.



(1)

(2)

Migrations of an acyl group from carbon to a carbanionic moiety in the same molecule are frequently utilized.[3—5] However, the *carbon-to-carbon* rearrangements of the simplest fragment "CO_2R," as shown in Eq. 2, are less common and only a few examples have been reported. Equation 3 shows a [1,2]-migration of an ester group to the allyllithium moiety,[4a] while a [1,4]-migration mentioned as a side reaction in the tin-mediated reaction is shown in Eq. 4.[5] In these known examples, the value of *n* in [1,*n*]-rearrangement seems to be fixed. In conjunction with the study of (η^2-propene)Ti(O-*i*-Pr)$_2$ (**1**)-mediated reactions of unsaturated ester,[6—9] we experienced ester migration in an attempted cyclization of propargylmalonates (propargyl = 2-propynyl), as shown in Eq. 5.[10] Although this migration looked like a new entry of some synthetic value, we were, at the same time, hampered by becoming aware that a few side reactions inevitably accompany the desired reaction. In order to determine what substrates or conditions are suitable for the selective progress of the desired ester migration, we initiated a systematic investigation. In general, the migration requires one or two more anion-stabilizing ester group(s) at the carbon bearing the migrating ester group (that is, R^1 and/or R^2 should be CO_2R in Eq. 2) obviously arising from the importance of stabilization of the anionic charge left after migration of the ester group.[11] Accordingly, the scope and limitation of the ester rearrangement reaction starting from unsaturated malonates and methanetricarboxylates were examined.



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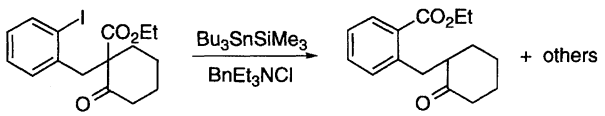

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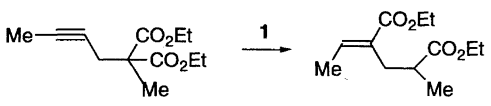
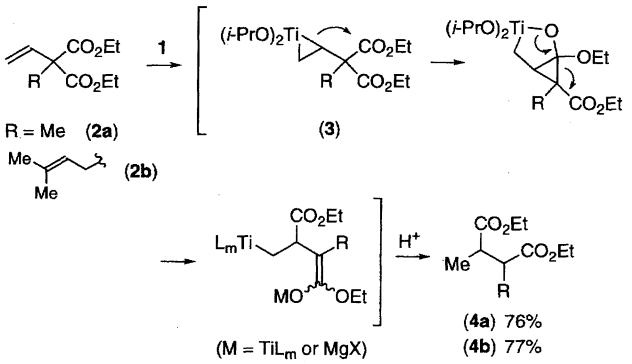


(5)

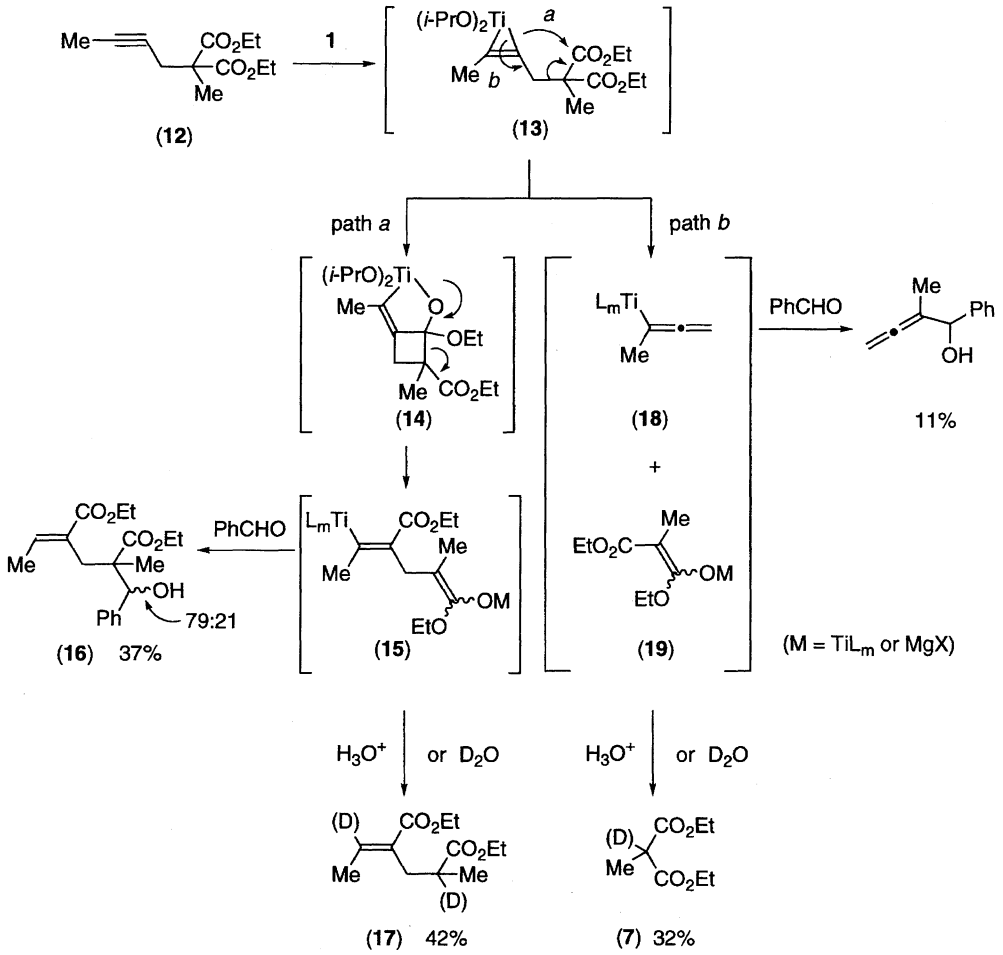
Results and Discussion

1,2-Rearrangement. The requisite organotitanium intermediate shown in Eq. 2 was readily generated in situ by treatment of unsaturated esters with **1**,[12–14] as illustrated in Eqs. 6 and 7. Diethyl methyl(vinyl)malonate (**2a**) and prenyl(vinyl)malonate (**2b**) (prenyl = 3-methyl-2-butenyl), which are readily prepared by the deconjugative alkylation of the lithium enolate of ethylidenemalonate,[15] underwent smooth migration of the ester group to the titanated position to give the succinate derivatives **4a** (a 5 : 1 mixture of diastereoisomers) and **4b** (a 3 : 1 mixture), but free of other side products after an aqueous workup (Eq. 6). The latter substrate demonstrated the chemoselectivity between olefins: The initial titanation took place preferentially at the terminal olefin rather than at the trisubstituted one. We did not attempt to determine the structure of the intermediate titanium species by deuterolysis in these cases, because a ^{1}H NMR analysis of the deuterated positions seemed to be difficult due to the presence of diastereoisomers as well as the considerably overlapping peaks on the spectra. However, we propose that the reaction proceeds in an analogous way to that shown in path *a* of Scheme 1 (vide infra).

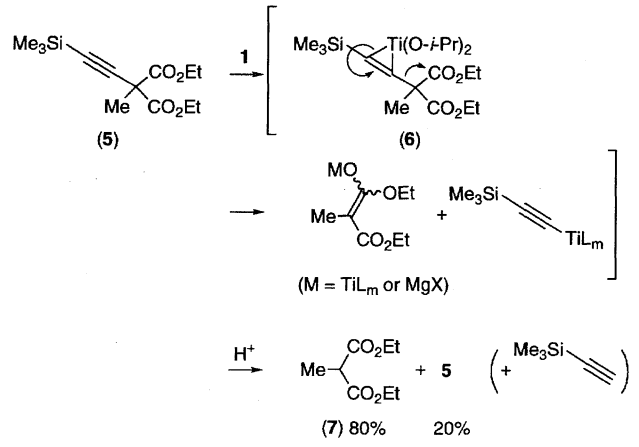


(6)

In stark contrast, the same treatment of the acetylene counterpart **5**[16] showed a completely different outcome to afford no desired product; however, the dealkynylated methylmalonate **7** presumably formed via β-elimination of the malonate anion from the intermediate acetylene–titanium complex **6**[14b,17] (Eq. 7). The choice of the kind of unsaturation (either olefin or acetylene) seems to be a critical factor for the success of the desired migration, which is repeatedly mentioned in the following sections.

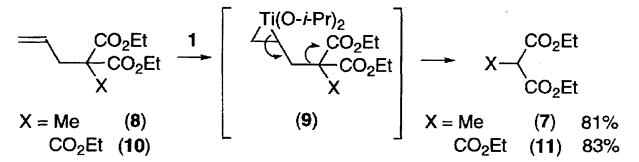


Scheme 1. Reaction path of [1,3]-rearrangement of the ester group.



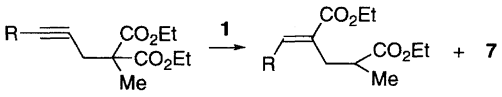
(7)

1,3-Rearrangement. In contrast to the successful 1, 2-rearrangement of vinylmalonates, as shown in Eq. 6, a variety of homologous allylmalonates only resulted in the deallylation, which is exemplified in the conversion **8**→**7** in Eq. 8.[6] The exclusive β-elimination of the malonate anion from the intermediate **9** should account for this observation. The corresponding triethyl 3-butene-1,1,1-tricarboxylate (**10**), readily prepared by the allylation of commercially available triethyl methanetricarboxylate (allyl bromide, NaH, DMF–C_6H_6, 80 °C),[18] behaved similarly only to suffer deallylation to revert to **11**.



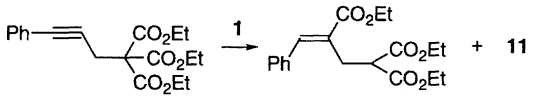
(8)

However, the treatment of diethyl methyl(propargyl)-malonate (**12**) with **1** gave the rearrangement product **17** along with depropargylation product **7** (Scheme 1). The stereochemistry of the carbon–carbon double bond of **17** was determined to be exclusively *E* by an NOE study of ^{1}H NMR spectroscopy. In order to propose the most likely reaction course, we performed some additional experiments (Scheme 1). One of the two ester groups of the malonate rearranged to the vinyltitanium portion in **13**[14b,17] to give **14**, which collapsed to bis-metallated α,β-unsaturated ester **15** (path *a*), which was, in fact, identified by deuterolysis to give bis-deuterated **17** (in>99% deuterium incorporation at each position) in place of a simple hydrolytic workup. Alternatively, β-elimination of the malonate anion through path *b* yielded the metallated **18** and **19**, the former of which could be trapped with benzaldehyde (vide infra) and the latter of which was identified by deuterolysis to give the deuterated **7** (again in>99% d) in a separate run as above. The metallated intermediate **15** could be intercepted with a carbonyl compound, providing a method for further carbon–carbon bond formation. For instance, treatment of the reaction mixture with benzaldehyde at −40 to 0 °C over 1 h selectively afforded the aldol product **16** as a mixture of diastereoisomers after hydrolysis[9,19] together with the product arising from **18** (Scheme 1). We did not detect any of the allylic alcohol derivatives resulting from the vinyltitanium moiety of **15** and the aldehyde in a crude reaction mixture, even when excess benzaldehyde (1.5 mol amt. to **12**) was employed under these reaction conditions. Two more substrates, such as **20** and **22**, having different acetylenic substituents also afforded **21** and **23** in comparable yields (Eq. 9). In these and the reactions in Scheme 1, the ratio of the desired rearrangement to the depropargylation always falls in a range of around 6 : 4 irrespective of the acetylene substituents.



(9)

Triethyl 3-butyne-1,1,1-tricarboxylate, readily available in a similar way to the synthesis of **10**, afforded the desired product **25** of the *E*-olefinic geometry along with **11** under the same reaction conditions as above (Eq. 10). To our satisfaction, the composition of the migration product vs. the depropargylated product was improved to 75 : 25 in the present triester case as compared to the ratio of approximately 6 : 4 recorded for the aforementioned malonate substrates **12**, **20**, and **22**.



(10)

1,4-Rearrangement. Having surveyed the 1,3-rearrangement, we expected that malonates having an unsaturated side chain other than the allyl or propargyl type should afford the ester transfer product as the sole product (thus, in much higher yields), because the dealkylation of the side chain is now intrinsically negotiated. However, we were not able to obtain the desired product from malonates having two methylene groups between the ester and the olefinic or acetylene moiety. Thus, only a complicated mixture was recovered from the olefinic substrates, such as **26** and **27** (Fig. 1), whilst the simple intramolecular nucleophilic acyl substitution reaction giving a cyclic α,β-unsaturated ketone **30** was found to be an exclusive path for the acetylenic malonate **28** (Eq. 11).[8] The last observation clearly shows that the ester rearrangement calls for the formation of a strained intermediate, like the 4-membered ring of **14** in Scheme 1, which is prone to break up towards the rearrangement reaction. The 5-membered intermediate **29** assumed in Eq. 11 must be stable enough to remain unchanged at this stage

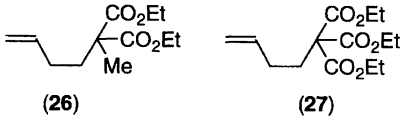
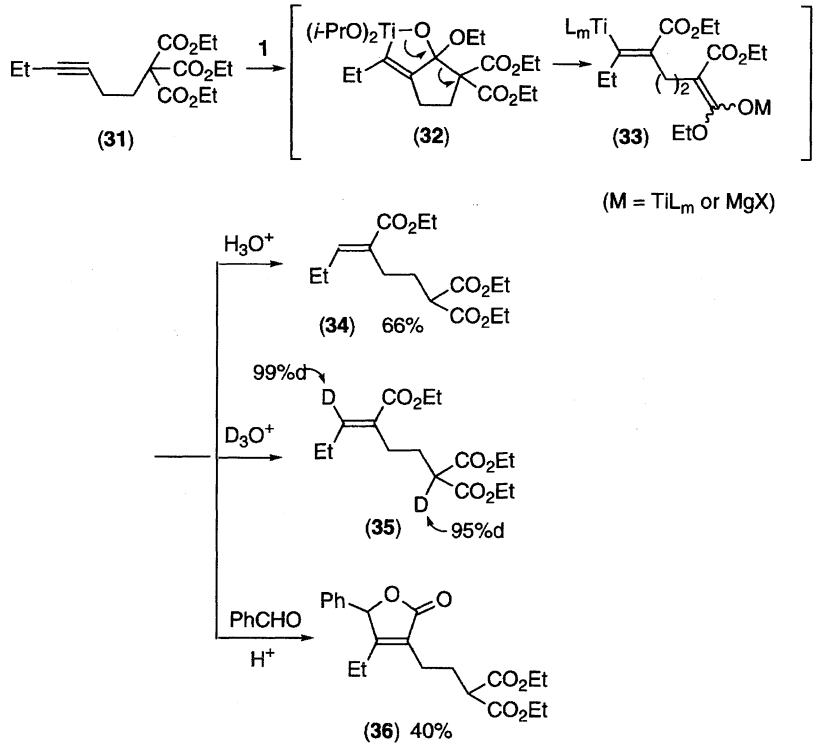
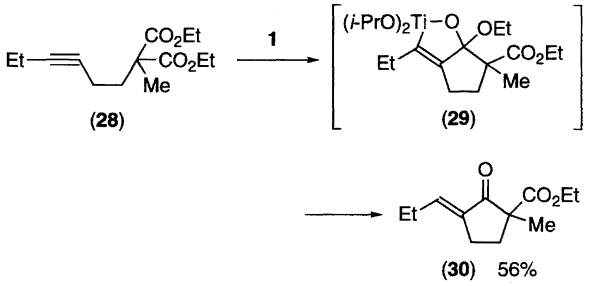


Fig. 1.



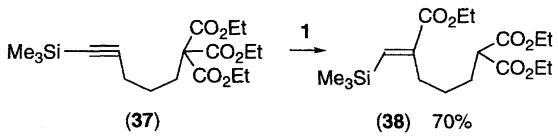
Scheme 2. [1,4]-Migration of the ester group.

to give **30** after hydrolysis. However, gratifyingly, the ester rearrangement starting from the (homopropargyl)methanetricarboxylate[18] did proceed well to give the desired product **34** having exclusively an *E* double bond as the sole isolable constituent after an aqueous workup (Scheme 2). The feasibility of the rearrangement apparently comes from the release of the very stable malonate anion, which is a sufficient driving force to make the reaction proceed beyond the 5-membered cyclic intermediate **32** to **33**. In addition to deuterolysis (to give **35**) that confirmed the presence of the bis-metallated intermediate like **33**, the addition to benzaldehyde took place selectively at the vinyltitanium moiety at −40 to 0 °C over 1 h to give the adduct **36**.[19,20] The formation of the lactone confirmed the stereochemistry of the tetra-substituted double bond.



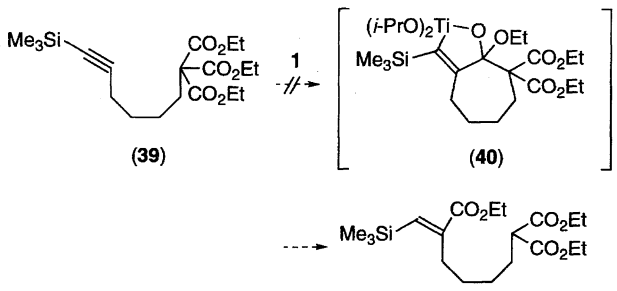
(11)

1,5-Rearrangement. The substrate-dependent feasibility of the 1,5-rearrangement resembles the tendency of the aforementioned 1,4-rearrangement. Thus, acetylenic triester **37** is the substrate of choice for the rearrangement, which underwent clean migration of one ester group to give the desired product **38** in good yield (Eq. 12).



(12)

Attempted 1,6-migration starting from triethyl 6-alkyne-1,1,1-tricarboxylate (**39**) has so far proved unsuccessful, resulting in the recovery of messy products (Eq. 13). This should arise from the unfavorable formation of the transient 7-membered ring in the intermediate **40**.

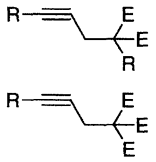
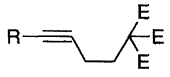
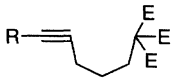
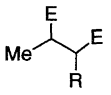
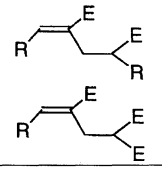
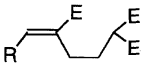
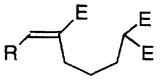


(13)

Conclusion

The ester rearrangement reported herein shows wide applicability to cover a full lineup involving [1,2]-, [1,3]-, [1,4]-, and [1,5]-rearrangements by a proper choice of the substrate, as summarized in Table 1. From a synthetic point of view, this reaction could provide a useful method for a regio- and stereoselective manipulation of unsymmetrical acetylenes by taking advantage of the intramolecular delivery of the ester fragment. The anionic nature of this rearrangement furnished a metallated species after migration, which may be utilized

Table 1. The Feasibility of [1,*n*]-Carbon-to-carbon Ester Rearrangements Mediated by **1**

n =	2	3	4	5
Suitable substrates (E = CO_2Et)				
Product				

for further synthetic elaboration. Since all the starting materials are readily prepared, this ester migration reaction may find applications in organic synthesis, which will be reported in due course.

Experimental

General. Infrared (IR) spectra were recorded on a JASCO FT/IR-230 spectrometer and are reported in wavenumbers (cm^{-1}). ^1H NMR spectra were measured on a Varian Gemini-2000 spectrometer (300 MHz) with $CDCl_3$ as solvent and their chemical shifts (δ values) are reported in parts per million downfield shift from Me_4Si (δ = 0 ppm) or residual $CHCl_3$ (δ = 7.26 ppm) as an internal standard. ^{13}C NMR spectra were measured on a Varian Gemini-2000 spectrometer (75 MHz) with $CDCl_3$ as a solvent and referenced to the center line of the solvent peaks (δ = 77.00 ppm). Diethyl ether and THF were distilled from sodium benzophenone ketyl. Ti(O-*i*-Pr)$_4$ was distilled and stocked under an argon atmosphere. Isopropylmagnesium chloride was prepared in Et_2O as a 1.0—1.5 M (1 M = 1 mol dm^{-3}) solution from isopropyl chloride and magnesium turnings by the usual procedure, titrated, and stocked under an argon atmosphere. All other reagents available from commercial sources were purified or dried in a standard manner, if necessary. All reactions were carried out under an argon atmosphere.

General Procedure for the Rearrangement of Malonic Ester Derivatives. To a mixture of Ti(O-*i*-Pr)$_4$ (0.213 g, 0.75 mmol) and an acetylenic or olefinic substrate (0.50 mmol) in ether (3.6 ml) was added *i*-PrMgCl (1.10 ml, 1.36 M in ether, 1.50 mmol) dropwise at −50 °C. The resulting yellow solution was stirred for 1 h at −45—−40 °C, after which time the color of the mixture turned brown.

Hydrolysis. After the addition of 1 M HCl (5 ml) at −40 °C, the mixture was gradually allowed to warm to room temperature and stirred for 15 min. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel, hexane–ether).

Deuterolysis. The reaction mixture was quenched with D_2O (1.0 ml) and stirred at room temperature for 30 min. The resultant yellow gelatinous mixture was filtered off through Celite, and the insoluble matter was washed with ether a few times. The combined ether filtrates were treated as above to afford the deuterated product.

Diethyl Methyl(vinyl)malonate (2a). ^1H NMR ($CDCl_3$) δ = 1.25 (t, J = 7.2 Hz, 6H, $CO_2CH_2CH_3$), 1.55 (s, 3H, Me), 4.20 (q, J = 7.2 Hz, 4H, CO_2CH_2), 5.20 (d, J = 17.7 Hz, 1H, *trans* CH_2=C), 5.26 (d, J=10.5 Hz, 1H, *cis* CH_2=C), 6.30 (dd, J = 10.5, 17.7 Hz, 1H, CH_2=C*H*); ^{13}C NMR ($CDCl_3$) δ = 13.86, 19.45, 56.12, 61.54, 116.06 (C=C), 136.14 (C=C), 171.16 (C=O); IR (neat) 2983, 2939, 1736 (C=O), 1637 (C=C), 1460, 1373, 1261 (C–O), 1190, 1126, 1024, 928, 860, 773 cm^{-1}. Found: C, 59.85; H, 8.27%. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05%.

Diethyl 2,3-Dimethylbutanedioate (4a). This is a known compound.[21] Spectral data for major isomer: ^1H NMR ($CDCl_3$) δ = 1.13—1.16 (m, 6H, Me), 1.243 (t, J = 7.2 Hz, 6H, $CO_2CH_2CH_3$), 2.73 (symmetric m, 2H, MeC*H*), 4.129 (q, J = 7.2 Hz, 2H, one of CO_2CH_2), 4.133 (q, J = 7.2 Hz, 2H, one of CO_2CH_2); ^{13}C NMR ($CDCl_3$) δ = 14.11, 14.78, 42.59, 60.51, 174.82 (C=O).

Spectral data for minor isomer (characteristic peaks): ^1H NMR ($CDCl_3$) δ = 1.235 (t, J = 7.2 Hz, 6H, $CO_2CH_2CH_3$), 2.78 (symmetric m, 2H, MeC*H*), 4.119 (q, J = 7.2 Hz, 4H, CO_2CH_2); ^{13}C NMR ($CDCl_3$) δ = 13.57, 41.64, 60.51, 175.47 (C=O); IR (neat) for a 5 : 1 mixture of diastereoisomers: 2981, 2840, 1734 (C=O), 1458, 1377, 1261 (C–O), 1193, 1157, 1078, 1032, 860 cm^{-1}.

Diethyl (Prenyl)(vinyl)malonate (2b). ^1H NMR ($CDCl_3$) δ=1.24 (t, J = 7.2 Hz, 6H, $CO_2CH_2CH_3$), 1.60 (s, 3H, *cis* Me), 1.66 (d, J = 0.9 Hz, 3H, *trans* Me), 2.76 (d, J = 7.2 Hz, 2H, C=CHCH_2), 4.19 (q, J = 7.2 Hz, 4H, CO_2CH_2), 5.00 (tt, J = 1.2, 7.2 Hz, 1H, C=C*H*), 5.17 (d, J = 17.7 Hz, 1H, *trans* CH_2=C), 5.29 (d, J = 11.1 Hz, 1H, *cis* CH_2=C), 6.29 (dd, J = 11.1, 17.7 Hz, 1H, CH_2=C*H*); ^{13}C NMR ($CDCl_3$) δ = 13.87, 17.84, 25.81, 33.60, 60.06, 61.35, 116.70 (C=C), 117.80 (C=C), 135.01 (C=C), 135.36 (C=C), 170.49 (C=O); IR (neat) 2982, 2928, 1733 (C=O), 1672 (C=C), 1638 (C=O), 1445, 1367, 1310, 1279, 1235 (C–O), 1212 (C–O), 1180, 1115, 1096, 1067, 1028, 990, 922, 860, 775 cm^{-1}. Found: C, 66.26, H, 8.76%. Calcd for $C_{14}H_{22}O_4$: C, 66.12; H, 8.72%.

Ethyl 2,6-Dimethyl-3-(ethoxycarbonyl)-5-heptenoate (4b). Spectral data for major isomer: ^1H NMR ($CDCl_3$) δ = 1.13 (d, J=6.9 Hz, 3H, Me), 1.23 (t, J = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.26 (t, J=7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.58 (s, 3H, *cis* Me), 1.67 (d, J = 1.2 Hz, 3H, *trans* Me), 2.10—2.19 (m, 1H, one of C–CHCH_2), 2.28—2.38 (m, 1H, one of C=CHCH_2), 2.63—2.76 (m, 2H, MeC*H*(CO_2Et)C*H*), 4.12 (symmetric m, 2H, CO_2CH_2), 4.14 (symmetric m, 2H, CO_2CH_2), 5.01—5.07 (m, 1H, C=C*H*); ^{13}C NMR ($CDCl_3$) δ = 14.07, 14.11, 14.68, 17.59, 25.65, 29.02, 41.46, 48.62, 60.31, 60.49, 120.63 (C=C), 134.19 (C=C), 173.93 (C=O), 175.06 (C=O).

Spectral data for minor isomer (characteristic peaks): ^1H NMR

($CDCl_3$) δ = 1.17 (d, J = 6.9 Hz, 3H, Me), 2.73—2.81 (m, 2H, MeC*H*(CO_2Et)C*H*); IR (neat) for a 3 : 1 mixture of diastereoisomers: 2979, 2933, 1736 (C=O), 1448, 1377, 1314, 1255 (C–O), 1157, 1109, 1036, 858, 770, 734 cm^{-1}. Found for a 3 : 1 mixture of diastereoisomers: C, 65.73; H, 9.45%. Calcd for $C_{14}H_{24}O_4$: C, 65.60; H, 9.44%.

Diethyl (2-Butynyl)(methyl)malonate (12). To a suspension of NaH (0.633 g, 55% in oil, 14.5 mmol) in THF (35 ml) was added diethyl methylmalonate (2.30 g, 13.2 mmol) dropwise at 0 °C. The reaction mixture was stirred at room temperature for 1 h. 1-Bromo-2-butyne (2.11 g, 15.8 mmol) was added and the resulting solution was stirred overnight. After the addition of water (70 ml) and extraction with ether, the organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel, hexane–ether) to afford the title compound (2.35 g, 79% yield); ^{1}H NMR ($CDCl_3$) δ = 1.24 (t J = 7.1 Hz, 6H, $CO_2CH_2CH_3$), 1.51 (s, 3H, Me), 1.75 (t, J = 2.6 Hz, 3H, $CH_3C{\equiv}C$), 2.71 (q, J = 2.6 Hz, 2H, $C{\equiv}CCH_2$), 4.189 (q, J = 7.1 Hz, 2H, one of CO_2CH_2), 4.193 (q, J = 7.1 Hz, 2H, one of CO_2CH_2); ^{13}C NMR ($CDCl_3$) δ = 3.32 ($CH_3C{\equiv}C$), 13.90, 19.67, 26.03, 53.33, 61.40, 73.78, (C≡C), 78.55 (C≡C), 171.38 (C=O); IR (neat) 2983, 2939, 2219 (C≡C), 1736 (C=O), 1458, 1377, 1294, 1246 (C–O), 1196, 1109, 1022, 862 cm^{-1}. Found: C, 63.57; H, 8.02%. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02%.

2,4-Bis(ethoxycarbonyl)-2-methyl-1-phenyl-4-(*E*)-hexenol (16). Spectral data for major isomer: ^{1}H NMR ($CDCl_3$) δ = 0.94 (s, 3H, Me), 1.19 (t, J = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.23 (t, J = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.61 (s, 1H, O*H*), 1.63 (d, J = 7.2 Hz, 3H, MeC*H*=C), 2.48 (d, J = 14.1 Hz, 1H, one of C=CCH_2), 2.96 (d, J = 14.1 Hz, 1H, one of C=CCH_2), 3.93 (q, J = 7.2 Hz, 1H, one of CO_2CH_2), 3.95 (q, J = 7.2 Hz, 1H, one of CO_2CH_2), 4.16 (q, J = 7.2 Hz, 2H, CO_2CH_2), 4.82 (s, 1H, PhC*H*), 6.90 (q, J = 7.2 Hz 1H, C*H*=C), 7.15–7.18 (m, 3H, Ph), 7.27—7.36 (m, 2H, Ph); ^{13}C NMR ($CDCl_3$) δ = 13.74, 14.02, 14.82, 17.26, 30.83, 51.98, 60.73, 60.80, 76.07, 127.24, 127.70, 128.11, 129.84, 140.08, 141.06, 168.98 (C=O), 176.04 (C=O); IR (neat) 3487 (OH), 3030 (Ph), 2981, 1720 (C=O), 1710 (C=O), 1639, 1458, 1383, 1271 (C–O), 1230 (C–O), 1140, 1107, 1090, 1053, 1030, 702 cm^{-1}. Found: C, 68.02, H, 7.74%. Calcd for $C_{19}H_{26}O_5$: C, 68.24; H, 7.84%.

Spectral data for minor isomer (characteristic peaks): ^{1}H NMR ($CDCl_3$) δ = 1.70 (d, J = 7.2 Hz, 3H, *Me*C=C), 4.98 (s, 1H, PhC*H*), 6.93 (q, J = 7.2 Hz, 1H, C*H*=C). The diastereomeric ratio was determined by the integration of the peaks for the benzylic position of each isomer, δ = 4.82 for the major isomer and δ =4.98 for the minor (79 : 21).

Ethyl 4-(Ethoxycarbonyl)-2-methyl-4-(*E*)-hexenoate (17). ^{1}H NMR ($CDCl_3$) δ = 1.17 (d, J = 7.5 Hz, 3H, Me), 1.28 (t, J = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.32 (t, J = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.84 (d, J = 7.5 Hz, 3H, CH_3C=C), 2.42 (dd, J = 8.3, 15.7 Hz, 1H, one of C=CCH_2), 2.70 (m, 2H, one of C=CCH_2, C=CCH_2C*H*), 4.10 (q, J = 7.1 Hz, 2H, CO_2CH_2), 4.19 (q, J = 7.1 Hz, 2H, CO_2CH_2), 6.96 (q, J = 7.5 Hz, 1H, C*H*=C); ^{13}C NMR ($CDCl_3$) δ = 14.13, 14.17, 14.42, 16.73, 30.23, 38.80, 60.17, 60.32, 130.77 (C=C), 139.09 (C=C), 167.37 (C=O), 176.19 (C=O); IR (neat) 2979, 2937, 1734 (C=O), 1710 (C=O), 1649 (C=C), 1460, 1377, 1275, 1221 (C–O), 1178, 1140, 1113, 1055, 856, 748 cm^{-1}. Found: C, 62.99; H, 8.75%. Calcd for $C_{12}H_{20}O_4$: C, 63.14; H, 8.83%. Irradiation of proton at δ =1.84 (CH_3C=C) showed 1% NOE to that at δ =2.70 (one of C=CCH_2).

Diethyl Methyl(2-nonynyl)malonate (20). ^{1}H NMR ($CDCl_3$) δ = 0.88 (t, J = 6.9 Hz, 3H, CH_3CH_2), 1.24 (t, J = 7.2 Hz, 6H, $CO_2CH_2CH_3$), 1.29 (m, 6H, alkyl), 1.42 (m, 2H, alkyl), 1.51 (s, 3H, Me), 2.10 (tt, J = 2.4, 7.2 Hz, 2H, $CH_2CH_2C{\equiv}C$), 2.74 (t, J = 2.4 Hz, 2H, $C{\equiv}CCH_2$), 4.184 (q, J =7.1 Hz, 2H, one of CO_2CH_2), 4.188 (q, J = 7.1 Hz, 2H, one of CO_2CH_2); ^{13}C NMR ($CDCl_3$) δ = 13.91 (3 carbons, alkyl-Me and $CO_2CH_2CH_3$), 18.52, 19.67, 22.45, 26.06, 28.34, 28.75, 31.24, 53.42, 61.37, 74.66 (C≡C), 83.39 (C≡C), 171.37 (C=O); IR (neat) 2979, 1733 (C=O), 1645, 1460, 1369, 1246 (C–O), 1176, 1095, 1034, 862 cm^{-1}. The correct elemental analysis was difficult to obtain for this compound. However, after hydrolysis and decarboxylation of this sample (KOH, EtOH), the resultant 2-methyl-4-undecynoic acid did afford the correct value: ^{1}H NMR ($CDCl_3$) δ = 0.88 (t, J = 6.9 Hz, 3H, *Me*CH_2), 1.25—1.37 (m, 6H, alkyl), 1.39—1.50 (m, 2H, alkyl), 1.59 (s, 3H, Me), 2.13 (tt, J = 2.4, 7.2 Hz, 2H, $CH_2CH_2C{\equiv}C$), 2.79 (t, J = 2.4 Hz, 2H, $C{\equiv}CCH_2$). Found: C, 65.11; H, 8.36%. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39%.

Ethyl 4-(Ethoxycarbonyl)-2-methyl-4-(*E*)-undecenoate (21). ^{1}H NMR ($CDCl_3$) δ = 0.86 (t, J = 6.8 Hz, 3H, CH_3CH_2), 1.12 (d, J = 6.1 Hz, 3H, Me), 1.28 (t, J = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.30 (t, J = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.30 (m, 6H, alkyl), 1.42 (m, 2H, alkyl), 2.17 (q, J = 7.2 Hz, 2H, CH_2CH=C), 2.41 (dd, J = 8.4, 16.0 Hz, 1H, one of CH=CCH_2), 2.61—2.74 (m, 2H, one of CH=CCH_2, $CHCH_3$), 4.08 (q, J=7.2 Hz, 2H, CO_2CH_2), 4.19 (q, J=7.2 Hz, 2H, CO_2CH_2), 6.84 (t, J=7.2 Hz, 1H, C*H*=C); ^{13}C NMR ($CDCl_3$) δ = 13.99, 14.06, 14.21, 16.72, 22.51, 28.74 (2 carbons, alkyl), 29.05, 30.61, 31.61, 38.85, 60.18, 60.37, 129.53 (C=C), 144.75 (C=C), 167.58 (C=O), 176.24 (C=O); IR (neat) 2929, 2858, 1736 (C=O), 1647 (C=C), 1460, 1377, 1281 (C–O), 1217, 1178, 1097, 858 cm^{-1}. Found: C, 68.18; H, 10.01%. Calcd for $C_{17}H_{30}O_4$: C, 68.42; H, 10.13%.

Diethyl Methyl(3-phenyl-2-propynyl)malonate (22). ^{1}H NMR ($CDCl_3$) δ = 1.27 (t, J = 7.1 Hz, 6H, $CO_2CH_2CH_3$), 1.60 (s, 3H, Me), 3.01 (s, 2H, $C{\equiv}CCH_2$), 4.18—4.26 (m, 4H, CO_2CH_2), 7.26—7.29 (m, 3H, Ph), 7.34—7.38 (m, 2H, Ph); ^{13}C NMR ($CDCl_3$) δ = 13.89, 19.80, 26.64, 53.40, 61.50, 83.27 (C≡C), 84.74 (C≡C), 123.35 (Ph), 127.95 (Ph), 128.22 (Ph), 131.66 (Ph), 171.11 (C=O); IR (neat) 2983, 2939, 2200 (C≡C), 1734 (C=O), 1599 (Ph), 1491, 1444, 1379, 1292, 1244 (C–O), 1196, 1109, 1022, 860, 758, 692 cm^{-1}. Found: C, 70.52; H, 7.00%. Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99%.

Ethyl 4-(Ethoxycarbonyl)-2-methyl-5-phenyl-4-(*E*)-pentenoate (23). ^{1}H NMR ($CDCl_3$) δ = 1.10 (d, J = 6.6 Hz, 3H, Me), 1.18 (t, J = 7.2 Hz, 3H, CH_2CH_3), 1.35 (t, J = 7.2 Hz, 3H, CH_2CH_3), 2.71 (dd, J = 7.4, 12.5 Hz, 1H, one of C=CCH_2), 2.79 (sextet, J = 7 Hz, 1H, C*H*CO_2), 2.95 (dd, J = 6.2, 12.5 Hz, 1H, one of C=CCH_2), 4.03 (m, 2H, C=CCO_2CH_2), 4.28 (q, J = 7.2 Hz, 2H, CO_2CH_2), 7.30—7.36 (m, 2H, Ph), 7.38 (d, J = 3.9 Hz, 3H, Ph), 7.74 (s, 1H, PhC*H*); ^{13}C NMR ($CDCl_3$) δ = 13.99, 14.15, 16.52, 30.82, 38.54, 60.26, 60.86, 128.48, 128.59, 129.27, 131.13, 135.56, 140.65, 168.24 (C=O), 176.08 (C=O); IR (neat) 3059 (Ph), 2979, 2935, 1734 (C=O), 1709 (C=O), 1631 (C=C), 1576 (Ph), 1448, 1375, 1259, 1225, 1201, 1124, 1022, 935, 858, 760, 702 cm^{-1}. Found: C, 70.51; H, 7.83%. Calcd for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64%.

General Procedure for the Rearrangement of Tricarboxylates. To a mixture of Ti(O-*i*-Pr)$_4$ (0.213 g, 0.75 mmol) and a triethyl alkynetricarboxylate (0.50 mmol) in ether (3.6 ml) was added *i*-PrMgCl (1.10 ml, 1.36 M in ether, 1.50 mmol) dropwise at −50 °C. The resulting yellow solution was stirred for 1 h at −45—−40 °C. The color of the mixture turned brown. After the addition of 1 M HCl (5 ml) at −40 °C, the mixture was gradually allowed to warm to room temperature and stirred for 15 min. The

organic layer was separated and the aqueous layer was extracted with ether. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel, hexane-ether) to afford the corresponding ester migration product.

Triethyl 4-Phenyl-3-butyne-1,1,1-tricarboxylate (24). ^{1}H NMR ($CDCl_3$) δ=1.29 (t, J=6.9 Hz, 9H, $CO_2CH_2CH_3$), 3.23 (s, 2H, C≡CCH_2), 4.29 (q, J=6.9 Hz, 6H, CO_2CH_2), 7.24—7.27 (m, 3H, Ph), 7.34—7.37 (m, 2H, Ph); ^{13}C NMR ($CDCl_3$) δ=13.70, 24.01, 62.29, 64.94, 82.59 (C≡C), 84.36 (C≡C), 123.35 (Ph), 127.87 (Ph), 128.11 (Ph), 131.59 (Ph), 165.93 (C=O); IR (neat) 3040 (Ph), 2983, 2939, 2906, 2240 (C≡C), 1743 (C=O), 1599 (Ph), 1491, 1444, 1367, 1273, 1201 (C–O), 1097, 1066, 1010, 860, 692 cm^{-1}. Found: C, 65.63; H, 6.47%. Calcd for $C_{19}H_{22}O_6$: C, 65.88; H, 6.40%.

Diethyl [2-(Ethoxycarbonyl)-3-phenyl-2-(*E*)-propenyl]malonate (25). ^{1}H NMR ($CDCl_3$) δ=1.15 (t, J=7.1 Hz, 6H, Me), 1.29 (t, J=7.1 Hz, 3H, Me), 3.20 (d, J=7.4 Hz, 2H, C=CCH_2), 3.79 (t, J=8.1 Hz, 1H, $CH(CO_2Et)_2$), 4.00—4.13 (m, 2H, C=CCO_2CH_2), 4.23—4.29 (m, 4H, CO_2CH_2), 7.32—7.34 (m, 2H, Ph), 7.38 (d, J=4.5 Hz, 3H, Ph), 7.77 (s, 1H, PhC*H*); ^{13}C NMR ($CDCl_3$) δ=13.80, 14.14, 26.18, 50.46, 60.87, 61.19, 128.43, 128.61, 128.69, 129.03, 134.97, 141.44, 167.35 (C=O), 168.73 (C=O); IR (neat) 3059 (Ph), 2983, 2938, 2906, 1732 (C=O), 1716 (C=O), 1635 (C=C), 1577 (Ph), 1446, 1369, 1234 (C–O), 1097, 1038, 860, 771, 700 cm^{-1}. Found: C, 65.43; H, 6.99%. Calcd for $C_{19}H_{24}O_6$: C, 65.50; H, 6.94%.

Irradiation of the proton at δ=3.20 (CH_2) showed 11% NOE to that at δ=7.32—7.34 (one of *o*-Ph) and 12% NOE to the one at δ=3.79 ($CH(CO_2Et)_2$), which established the (*E*)-stereochemistry of the double bond.

Diethyl (3-Hexynyl)(methyl)malonate (28). ^{1}H NMR ($CDCl_3$) δ=1.09 (t, J=7.2 Hz, 3H, CH_3CH_2C≡C), 1.24 (t J=6.9 Hz, 6H, $CO_2CH_2CH_3$), 1.41 (s, 3H, Me), 2.07—2.16 (m, 6H, CH_2C≡CCH_2CH_2), 4.17 (q, J=6.9 Hz, 4H, CO_2CH_2); ^{13}C NMR ($CDCl_3$) δ=12.24, 13.88, 14.02, 14.23, 19.63, 35.00, 53.17, 61.19, 78.26 (C≡C), 82.08 (C≡C), 172.03 (C=O); IR (neat) 2979, 2939, 1732 (C=O), 1464, 1379, 1265, 1234 (C–O), 1188, 1109, 1026, 862 cm^{-1}. Found: C, 66.09; H, 8.57%. Calcd for $C_{14}H_{22}O_4$: C, 66.12; H, 8.72%.

2-(Ethoxycarbonyl)-2-methyl-5-[(*E*)-propylidene]cyclopentanone (30). ^{1}H NMR ($CDCl_3$) δ=1.08 (t, J=7.5 Hz, 3H, CH_2CH_3), 1.23 (t, J=7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.35 (s, 3H, Me), 1.72—1.81 (m, 1H, one of C=CCH_2CH_2), 2.19 (quintet, J=7.5 Hz, 2H, CH_2CH_3), 2.44—2.65 (m, 3H, one of C=CCH_2CH_2, C=CCH_2), 4.15 (q, J=7.2 Hz, 2H, CO_2CH_2), 6.64 (tt, J=2.7, 7.5 Hz, 1H, C*H*=C); ^{13}C NMR ($CDCl_3$) δ=12.54, 13.86, 19.70, 23.02, 23.62, 32.62, 56.55, 61.16, 135.56 (C=C), 140.59 (C=C), 172.49 (OC=O), 203.39 (C=O); IR (neat) 2976, 2937, 2875, 1739 (OC=O), 1649 (C=C), 1610 (C=O), 1457, 1375, 1263, 1213, 1176, 1095, 1024, 877 cm^{-1}. Found: C, 68.21; H, 8.76%. Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63%.

The stereochemistry of the double bond was deduced by the following derivatization to the alcohol and ^{1}H NMR analysis.

2-(Ethoxycarbonyl)-2-methyl-5-[(*E*)-propylidene]cyclopentanol. 2-Ethoxycarbonyl-2-methyl-5-[(*E*)-propylidene]cyclopentanone (9 mg, 0.0429 mmol) and anhydrous cerium(III) chloride (10.6 mg, 0.0429 mmol) were dissolved in THF/methanol (2:1, 0.65 ml). Sodium borohydride (3.2 mg, 0.086 mmol) was added slowly with stirring at room temperature. After 5 min, the reaction mixture was quenched with 1 M HCl (0.220 ml) and extracted with CH_2Cl_2 (2×2 ml). The organic phase was washed with water (1.0 ml), dried over $MgSO_4$, and evaporated to give the title compound (9 mg, 100% yield) as an 86:14 mixture of steroisomers. Spectrum data for major isomer: ^{1}H NMR ($CDCl_3$) δ=0.98 (t, J=7.5 Hz, 3H, CH_3CH_2), 1.09 (s, 3H, Me), 1.26 (t, J=7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.74 (ddd, J=3.3, 8.3, 12.8 Hz, 1H, one of CH_2CCO_2), 1.91—2.06 (m, 3H, one of CH_2CCO_2, CH_3CH_2), 2.27—2.34 (m, 2H, C=CCH_2), 4.16 (q, J=7.2 Hz, 2H, CO_2CH_2), 4.63 (br s, 1H, C*H*(OH)), 5.50 (m, 1H, C*H*=C); IR (neat) 3489 (OH), 2962, 1726 (C=O), 1460, 1367, 1259 (C–O), 1180, 1084, 1026, 866 cm^{-1}.

Irradiation of the proton at δ=4.63 (C*H*(OH)) showed 3% NOE to that at δ=5.50 (C*H*=C), which confirmed the (*E*)-olefin.

Triethyl 4-Heptyne-1,1,1-tricarboxylate (31). To a suspension of NaH (0.259 g, 55% in oil, 5.93 mmol) in benzene (2.4 ml) and DMF (2.4 ml) was added triethyl methanetricarboxylate (1.31 g, 5.65 mmol) dropwise at 0 °C. The reaction mixture was warmed up to room temperature and stirred for 1 h. 1-Iodo-3-hexyne (1.00 g, 6.21 mmol) was added and the resulting solution was stirred at 90 °C for 12 h. After the addition of H_2O (10 ml) and extraction with benzene, the organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel, hexane–ether) to afford the title compound (0.963 g, 55% yield); ^{1}H NMR ($CDCl_3$) δ=1.09 (t, J=8.4 Hz, 3H, Me), 1.27 (t, J=7.1 Hz, 9H, $CO_2CH_2CH_3$), 2.13 (q, J=7.6 Hz, 2H, CH_3CH_2C≡C), 2.36 (m, 4H, C≡CCH_2CH_2), 4.24 (q, J=7.1 Hz, 6H, CO_2CH_2); ^{13}C NMR ($CDCl_3$) δ=12.11, 13.64, 13.90, 14.68, 32.64, 61.94, 64.78, 77.90 (C≡C), 82.01 (C≡C), 166.64 (C=O); IR (neat) 2981, 2938, 1739 (C=O), 1446, 1390, 1267, 1216 (C–C), 1191, 1080, 1022, 862, 771 cm^{-1}. Found: C, 61.18; H, 7.69%. Calcd for $C_{16}H_{24}O_6$: 61.52; H, 7.74%.

Diethyl [3-(Ethoxycarbonyl)-3-(*E*)-hexenyl]malonate (34). ^{1}H NMR ($CDCl_3$) δ=1.05 (t, J=7.6 Hz, 3H, Me), 1.27 (t, J=7.1 Hz, 6H, $CO_2CH_2CH_3$), 1.29 (t, J=7.1 Hz, 3H, C=C$CO_2CH_2CH_3$), 1.95—2.03 (m, 2H, C=CCH_2CH_2), 2.19 (quintet, J=7.6 Hz, 2H, CH_3CH_2C=C), 2.32—2.37 (m, 2H, C=CCH_2), 3.32 (t, J=7.4 Hz, 1H, $CH(CO_2Et)_2$), 4.15—4.28 (m, 6H, CO_2CH_2), 6.78 (t, J=7.6 Hz, 1H, C*H*=C); ^{13}C NMR ($CDCl_3$) δ=13.15, 13.78, 13.92, 21.68, 24.32, 28.03, 51.53, 60.29, 61.18, 130.31 (C=C), 145.21 (C=C), 167.38 (C=O), 169.14 (C=O); IR (neat) 2979, 2937, 2875, 1734 (C=O), 1720 (C=O), 1645 (C=C), 1464, 1369, 1246 (C–O), 1176, 1095, 1034, 863 cm^{-1}. Found: C, 61.15; H, 8.33%. Calcd for $C_{16}H_{26}O_6$: C, 61.13; H, 8.34%.

2-[3,3-Bis(ethoxycarbonyl)propyl]-3-ethyl-4-phenyl-2-buten-4-olide (36). ^{1}H NMR ($CDCl_3$) δ=1.00 (t, J=7.6 Hz, 3H, Me), 1.278 (t, J=7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.283 (t, J=7.1 Hz, 3H, $CO_2CH_2CH_3$), 2.04 (symmetric m, 1H, one of C=CCH_2CH_2), 2.14—2.19 (m, 2H, C=CCH_2CH_2), 2.37—2.46 (m, 3H, one of C=CCH_2CH_2, C=CCH_2Me), 3.38 (t, J=7.3 Hz, 1H, $CH(CO_2Et)_2$), 4.18—4.26 (m, 4H, CO_2CH_2), 5.72 (s, 1H, PhC*H*), 7.18—7.24 (m, 2H, Ph), 7.37—7.39 (m, 3H, Ph); ^{13}C NMR ($CDCl_3$) δ=12.30, 13.94, 19.75, 21.30, 27.11, 51.40, 61.53, 83.75, 125.48, 127.08, 128.31, 129.09, 129.47, 134.79, 165.92 (C=O), 169.22 (C=O); IR (neat) 3036 (Ph), 2976, 2940, 1736 (C=O), 1458, 1369, 1300, 1261 (C–O), 1230, 1180, 1158, 1115, 1096, 1024, 860, 757, 702 cm^{-1}. Found: C, 67.33; H, 7.48%. Calcd for $C_{21}H_{26}O_6$: C, 67.36; H, 7.00%.

Triethyl 6-(Trimethylsilyl)-5-hexyne-1,1,1-tricarboxylate (37). ^{1}H NMR ($CDCl_3$) δ=0.14 (s, 9H, Si*Me*$_3$), 1.28 (t, J=7.1 Hz, 9H, $CO_2CH_2CH_3$), 1.68—1.78 (m, 2H, C≡CCH_2CH_2), 2.16—2.22 (m, 2H, $CH_2C(CO_2Et)_3$), 2.25 (t, J=7.2 Hz, 2H, C≡CCH_2), 4.26 (q, J=7.1 Hz, 6H, CO_2CH_2); ^{13}C NMR ($CDCl_3$) δ=0.14 ($SiMe_3$), 13.70, 19.97, 23.99, 32.33, 61.91, 65.28, 84.88 (C≡C),

106.38 (C≡C), 166.98 (C=O); IR (neat) 2981, 2904, 2173, 1739 (C=O), 1446, 1367, 1252, 914, 845, 760, 640 cm^{-1}. Found: C, 58.53; H, 8.19%. Calcd for $C_{18}H_{30}O_6Si$: C, 58.35; H, 8.16%.

Diethyl [4-(Ethoxycarbonyl)-5-(trimethylsilyl)-4-(*E*)-pentenyl]malonate (38). ^1H NMR ($CDCl_3$) $\delta = 0.16$ (s, 9H, $SiMe_3$), 1.26 (t, $J = 7.1$ Hz, 6H, $CO_2CH_2CH_3$), 1.27 (t, $J = 7.1$ Hz, 3H, $C{=}CCO_2CH_3$), 1.46 (m, 2H, $C{=}C(CH_2)_2CH_2$), 1.93 (m, 2H, $C{=}CCH_2CH_2$), 2.40 (symmetric m, 2H, $C{=}CCH_2$), 3.32 (t, $J = 7.6$ Hz, 1H, $CH(CO_2Et)_2$), 4.18 (q, $J = 7.1$ Hz, 6H, CO_2CH_2), 6.83 (s, 1H, $CH{=}C$); ^{13}C NMR ($CDCl_3$) $\delta = -0.46$ ($SiMe_3$), 13.96, 14.12, 27.68, 28.73, 31.65, 51.87, 60.62, 61.17, 141.25 (C=C), 146.99 (C=C), 166.93 (C=O), 169.18 (C=O); IR (neat) 2956, 1736 (C=O), 1720 (C=O), 1603 (C=C), 1460, 1369, 1223 (C–O), 1151, 1099, 1028, 839, 766 cm^{-1}. Found: C, 58.24; H, 8.66%. Calcd for $C_{18}H_{32}O_6Si$: C, 58.03; H, 8.66%.

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