Diethyl Cyclopropylidenemalonate: Facile Preparation, Generation in situ, and Various Transformations

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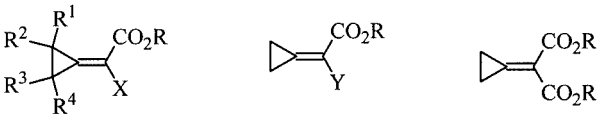
Reductive cyclopropanation of triethyl methanetricarboxylate (**4a**) with ethylmagnesium bromide in the presence of titanium tetraisopropoxide furnished diethyl 2-(1′-hydroxycyclopropyl)malonate (**5a**) in 50% yield. Dehydromesylation of the mesylate of cyclopropanol **5a**, generated in situ, by treatment with an excess of triethylamine gave diethyl cyclopropylidenemalonate **3**-Et as a highly reactive, unstable compound, which could be isolated as an oil in 39% yield, but more favorably could also be generated in situ from the mesylate or the acetate **11** (prepared from **5a** in 90% yield) and trapped without isolation with various N-, O-, S-, and C-nucleophiles. Thus, ammonia, dimethylamine, isopropylamine, diethylamine, dibenzylamine, morpholine, *N*-methylpiperazine, piperazine, aniline, *p*-cresol, 1-thionaphthol, and cyanide anion easily add to the double bond of the diester **3**-Et generated in situ at ambient temperature, forming 1′-substituted cyclopropylmalonates **10a–i** in 18–95% yields. The α,β-unsaturated diester **3**-Et also easily enters into 1,3-dipolar and Diels–Alder cycloadditions with nitrones, ethyl diazoacetate, azide anion, and dienes to give the corresponding cycloadducts in 12–83% yields.

Introduction

The cyclopropane ring can be regarded as a unique three-carbon functional group capable of undergoing transformations that are either more difficult or impossible with any of the more conventional functional groups. Simple cyclopropanes are nucleophilic, and the nucleophilicity of a cyclopropane ring, like that of a C=C double bond, can be altered by the choice of substituents: electron-donating substituents tend to increase the nucleophilicity, while electron-withdrawing substituents make the cyclopropane ring susceptible to nucleophilic attack.[1,2] Furthermore, because of its ring strain and electronic properties, the combination of the cyclopropane unit with multiple bonds and other functional groups establishes composite functional groups[3] that exhibit unique reactivities and so offer wide potential as building blocks for organic synthesis.[4] In this respect, the chemistry of substituted methylenecyclopropanes **1**−**3** is of particular interest, as the a priori high reactivity of their methylenecyclopropane units should be enhanced by the electron-withdrawing substituents. The two functionalities on the methylene group of compounds **1**−**3** make them oligo-functional and thereby give rise to very special chemical behavior.



1-R (X = Cl, Br) **2**-R (Y = OR[1], NHBoc) **3**-R

Synthetic methodologies based on the reactions of highly functionalized methylenecyclopropanes **1**-R[5] and **2**-R,[6] which can be regarded as homologues of correspondingly substituted allenecarboxylates, have been growing steadily over the past few years. However, very little has been published concerning the preparation and reactivity of dialkyl cyclopropylidenemalonates (**3**-R),[7] which ought to be alkylidenemalonates with particularly enhanced reactivity.[8] In this communication we describe not only the first preparation of diethyl cyclopropylidenemalonate (**3**-Et), but also and in particular its facile generation in situ with immediately ensuing addition reactions.

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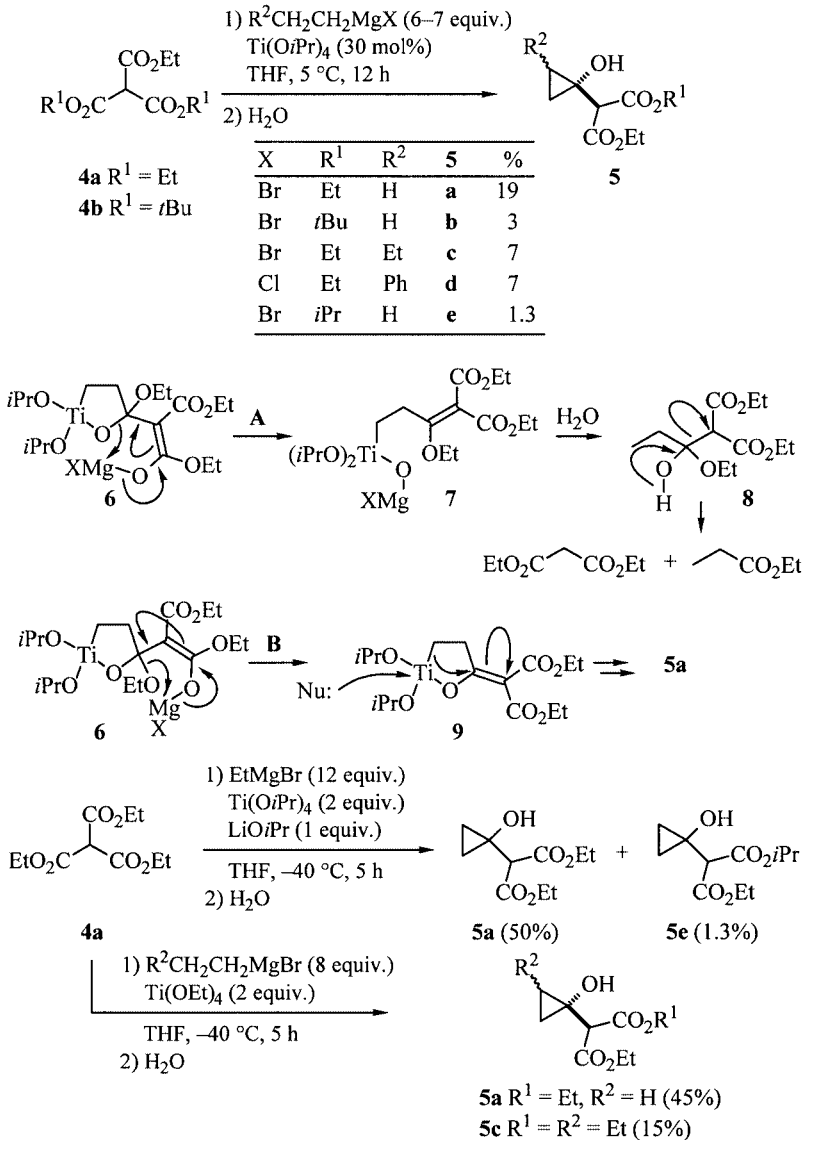
Results and Discussion

Among the conceivable routes to cyclopropylidenemalonates **3**-R, the most rational approach would be one starting from diethyl 2-(1-hydroxycyclopropyl)malonate (**5a**). Unfortunately, the common approach to such cyclopropanols, malonate anion-induced Favorskii-type rearrangement of α-haloketones according to Takeda et al.,[7b,9] cannot be used for the preparation of the parent cyclopropanol **5a** without any substituents on the three-membered ring.[7b] The alternative generation from (arylselenomethylene)malonate in three steps[7c] requires the application of expensive and hazardous reagents. We therefore examined the possibility of transforming one of the three alkoxycarbonyl groups in the known and readily available triethyl methanetricarboxylate (**4a**)[10] through the action of low-valent titanium reagents, formed in situ from titanium alkoxides and organomagnesium halides, into a cyclopropanol moiety (the so-called Kulinkovich reaction[11]).

However, none of the expected product was formed upon addition of 2−11 equivalents of ethylmagnesium bromide as a solution in THF to a solution of the ester **4a** (1 equiv.) and $Ti(OiPr)_4$ (1−3 equiv.) in THF at 5 °C; the main component in the obtained complex reaction mixtures was always diethyl malonate (*cf.* also ref.[12]). Upon variation of the relative amounts of the Grignard reagent and titanium tetraisopropoxide, however, the desired transformation (Scheme 1) turned out to proceed smoothly when substoichiometric amounts of $Ti(OiPr)_4$ (30 mol %) and a sevenfold excess of ethylmagnesium bromide were employed, albeit the yield of the cyclopropanol **5a** was only 27% according to GC analysis, and 19% after isolation. The use of di-*tert*-butyl ethyl methanetricarboxylate (**4b**) did not improve the yield at all and neither did it show the expected chemo-



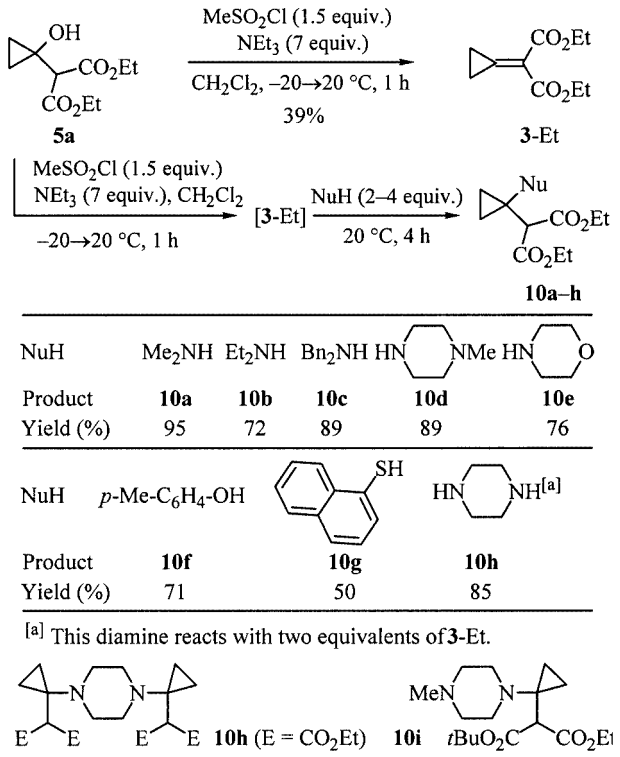
Scheme 1. Reductive cyclopropanation of triethyl methanetricarboxylate (**4a**) and di-*tert*-butyl ethyl methanetricarboxylate (**4b**) under various conditions and its mechanistic rationalization

selectivity for the ethoxycarbonyl group. In fact, the only cyclopropanol isolated after column chromatography was the *tert*-butyl ethyl malonate-substituted compound **5b**, in negligible yield (3%). Low yields of ring-substituted cyclopropanols **5c** and **5d** (7% in both cases) were also obtained by application of sixfold excesses of *n*-butylmagnesium bromide and phenethylmagnesium chloride, respectively (Scheme 1).

The first attempts to convert one ester group in the trialkyl methanetricarboxylates **4a** or **4b** to provide the corresponding cyclopropanols **5a**−**c** were thus only very moderately successful. Most probably, the initially formed oxatitanacyclopentane **6** with a dialkylmalonate enolate substituent can react by two different competitive pathways (Scheme 1). The first possibility (A) is a sigmatropic rearrangement with ring-opening of the oxatitanacyclopentane moiety to give a homoallyltitanium species **7**, which upon hydrolysis yields diethyl malonate, essentially by Michael addition of water followed by retro-Claisen condensation of the Michael adduct **8**. The second route (B) furnishes a new oxatitanacyclopentane intermediate **9**, which is able to undergo ring contraction to give the cyclopropanol **5a** after hydrolysis. On the assumption that the intermediate **9** might be more stable than the intermediate of type **6** − just like the intermediate formed from nitriles on treatment with organomagnesium halides and titanium tetraisopropoxide[13] − the possibility of facilitating the ring-contraction to a cyclopropoxide by addition of nucleophiles was tested.[14] Indeed, the yield of **5a** increased to 50% in the presence of 1 equiv. of lithium isopropoxide[14b] (Scheme 1) when the cyclopropanation of **4a** was performed with two equiv. of Ti(O*i*Pr)$_4$ at −40 °C, and **5a** was isolated, along with 1.3 % of the transesterified cyclopropanol **5e**. However, it was the temperature effect rather than the effect of lithium isopropoxide that was ultimately critical to the success of the reaction, as the cyclopropanation of **4a** with two equiv. of Ti(O*i*Pr)$_4$ at −40 °C, but without added LiO*i*Pr, furnished virtually the same yield of the product **5a**. This demonstrated that Ti(O*i*Pr)$_4$ and ROMgBr can serve as the external nucleophile enhancing the ring-contraction of the oxacyclopentane intermediate.

To avoid transesterification to **5e**, Ti(OEt)$_4$ was employed instead of Ti(O*i*Pr)$_4$, to give pure **5a** in 45% isolated yield. It is interesting that, even with the optimized method, *n*-butylmagnesium bromide (8 equiv.) in the presence of Ti(O*i*Pr)$_4$ (2 equiv.) gave **5c** in only 3% yield, and it had to be isolated from a complex reaction mixture; yet in the presence of Ti(OEt)$_4$ (2 equiv.) the cyclopropanol **5c** could be isolated in 15% yield.

The mesylate of cyclopropanol **5a**, generated in situ, furnished the highly reactive diethyl cyclopropylidenemalonate (**3**-Et) as an oil in 39% yield upon dehydromesylation with an excess of triethylamine (Scheme 2). The exceptional reactivity of **3**-Et is exemplified by its spontaneous addition of water to yield **5a**. On the other hand, however, **3**-Et does not polymerize as unsubstituted methylenemalonates or simple acrylates do. Even when **3**-Et was heated at 120 °C for 3 hours, it did not yield a dimer or a well defined oligomer (see ref.[5a]), but only a complex mixture of unidentified products.

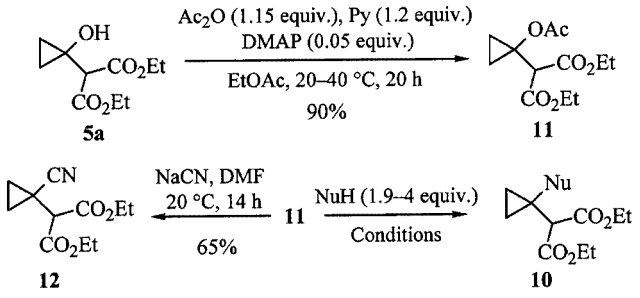


Scheme 2. Preparation of diethyl cyclopropylidenemalonate (**3**-Et) and Michael additions onto **3**-Et generated in situ

The cyclopropylidenemalonate **3**-Et should be a significantly better Michael acceptor than any other alkylidenemalonate,[15] its enhanced reactivity stemming from the fact that a substantial amount of strain would be released upon going from an *sp*- to an *sp*^{2}-hybridized carbon in the tetrasubstituted methylenecyclopropane C,C-double bond, just as in a Michael addition onto 2-substituted cyclopropylideneacetates.[5a,16] Not least due to this high reactivity, the adducts of nucleophiles to **3**-Et (**10a**−**i**) can be prepared in much better yields than **3**-Et itself. Without isolation of **3**-Et, but just by addition of the appropriate N-, O-, and S-nucleophiles (dimethylamine, diethylamine, dibenzylamine, morpholine, *N*-methylpiperazine, piperazine, *p*-cresol, 1-thionaphthol) to reaction mixtures containing **5a**, mesyl chloride, and triethylamine at ambient temperature, the 1′-substituted cyclopropylmalonates **10a**−**i** were formed in 50−95% yields (Scheme 2).[17] Piperazine, with its two nucleophilic nitrogen atoms, reacted with two molecules of **3**-Et to give the 1:2 adduct **10h**, while the addition of *N*-methylpiperazine to *tert*-butyl ethyl (1-hydroxy-1-cyclopropyl)malonate **5b** produced the Michael adduct **10i** in 51% yield.

Alternatively, the cyclopropylidenemalonate **3**-Et can be conveniently generated in situ from the acetate **11**, which is easily prepared from the alcohol **5a** by treatment with acetic anhydride in the presence of pyridine and dimethylaminopyridine (DMAP). In contrast to the corresponding mesyl-

ate, the acetate **11** is a reasonably stable compound that can be distilled and stored for a long time, but reacts in essentially the same way as the mesylate of **5a**. Since many nucleophilic reagents are basic enough to eliminate acetic acid from **11**, no addition of a tertiary amine is necessary. Thus, upon addition of morpholine to **11**, the adduct **10e** was obtained in 90% yield (Scheme 3) versus 76% from **5a** via the corresponding mesylate (Scheme 2). Isopropylamine, aniline, and ammonia all reacted with **11** in this way to give the corresponding Michael adducts **10j**, **10k**, and **10l** of **3**-Et in 98, 74, and 18% yields, respectively. Even the 1′-cyanocyclopropylmalonate **12** could be prepared in 65% yield from the acetate **11** upon treatment with sodium cyanide in dimethylformamide at ambient temperature (*cf.*[15d]).

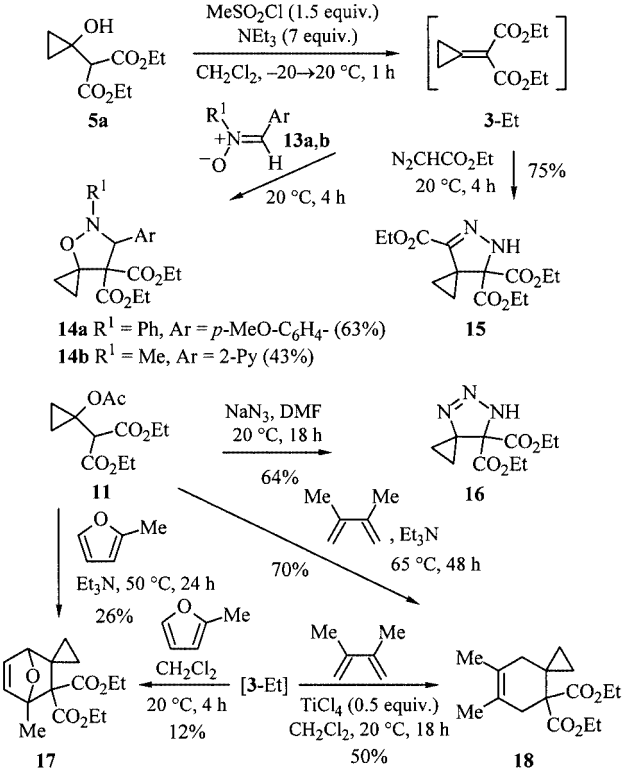


NuH	Me_2NH	HN O	$iPrNH_2$	$PhNH_2$	NH_3
T [°C]	20	50	50	60	20
t [min]	30	5	5	120	30
Product	**10a**	**10e**	**10j**	**10k**	**10l**
Yield (%)	78	90	98	74	18

Scheme 3. Preparation of diethyl 1′-acetoxycyclopropylmalonate (**11**) followed by generation of **3**-Et in situ and Michael additions

As should be expected in view of the high polarity of its double bond, diethyl cyclopropylidenemalonate **3**-Et is also a reasonably good dipolarophile. When prepared by treatment of the mesylate of **5a** (again generated in situ) with triethylamine, **3**-Et, without isolation, readily underwent cycloaddition to *N*-phenyl-(4-methoxyphenyl)nitrone (**13a**) and to *N*-methyl-(2-pyridyl)nitrone (**13b**) to give 5-spirocyclopropaneisoxazolidines **14a** and **14b** regioselectively in 63 and 43% yields, respectively (Scheme 4). Analogous regioselectivity had previously been observed for cycloadditions of nitrones to methyl 2-chloro-2-cyclopropylideneacetate (**1**-Me, R^1-R^4 = H, X = Cl)[18] or ethyl 2-cyclopropylideneacetate.[19] Furthermore, the cyclopropylidenemalonate **3**-Et also readily reacted with ethyl diazoacetate and sodium azide at room temperature to provide the corresponding cycloadducts **15** and **16** in 75 and 64% yields, respectively (Scheme 4).

Not only is **3**-Et a good dipolarophile, but it also smoothly undergoes [4+2] cycloadditions in spite of its tetrasubstituted and hence sterically encumbered double bond. The Diels–Alder reactivity of **3**-Et, however, appears to be less pronounced than that of methyl 2-chloro-2-cyclo-



Scheme 4. [3+2] and [4+2] cycloaddition reactions of diethyl cyclopropylidenemalonate (**3**-Et)

propylideneacetate **1**-Me (R^1-R^4 = H, X = Cl).[5a] Thus, 2-methylfuran did indeed undergo Diels–Alder reaction even at ambient temperature with **3**-Et prepared in situ from mesylate or acetate **11** to give the corresponding 7-oxabicyclo[2.2.1]heptene derivative **17**, but the isolated yields were only 12 and 26%, respectively (Scheme 4). For comparison, the chloroester **1**-Me (R^1-R^4 = H, X = Cl) and 2-methylfuran furnished the corresponding cycloadduct in 76% yield under the same conditions.[20] Better results were obtained for the Diels–Alder reaction of **3**-Et generated in situ from the mesylate of **5a** or the acetate **11**, respectively, with 2,3-dimethyl-1,3-butadiene under $TiCl_4$ catalysis or simply at elevated temperature, respectively, the corresponding cycloadduct **18** being isolated in 50 and 70% yields, respectively. Under similar conditions, however, the yield of the respective cycloadduct with **1**-Me (R^1-R^4 = H, X = Cl) was 79%.[20,21]

In conclusion, a convenient approach to the previously unknown diethyl cyclopropylidenemalonate (**3**-Et), its Michael adducts with various nucleophiles, and its cycloadducts with 1,3-dipolar reagents and 1,3-dienes has been elaborated. The cyclopropane ring not only enhances the reactivity of the starting material **3**-Et over that of simple alkylidenemalonates, but also adds to the versatility of its products, since the three-membered ring can be regarded as a functional group in its own right.[1,22] The potential to trap **3**-Et generated in situ directly with various reagents in high yields and to use a storable, stable precursor such as the acetate **11** promises possible future applications of

3-Et in combinatorial chemistry to build small molecule libraries.

Experimental Section

General: NMR: spectra were recorded on a Bruker AM 250 instrument (250 MHz for ^{1}H and 62.9 MHz for ^{13}C NMR). Multiplicities were determined by DEPT (Distortionless Enhancement by Polarization Transfer) measurements. Chemical shifts refer to δ_{TMS} = 0.00 according to the chemical shifts of residual $CHCl_3$ signals. IR: Bruker IFS 66 (FT-IR) spectrophotometer, measured as KBr pellets, oils between KBr plates. MS (EI, 70 eV): Finnigan MAT 95 spectrometer. M.p.: Büchi 510 capillary melting point apparatus, uncorrected values. TLC: Macherey−Nagel precoated sheets, 0.25 mm Sil G/UV$_{254}$. Column chromatography: Merck silica gel, grade 60, 230−400 mesh. Starting materials: triethyl methanetricarboxylate (**4a**),[10] 4-methoxyphenyl-*N*-phenylnitrone (**13a**),[23] and 2-pyridyl-*N*-methylnitrone (**13b**)[24] were prepared by previously published procedures. All operations in anhydrous solvents were performed under argon in flame-dried glassware. Diethyl ether and THF were dried by distillation from sodium benzophenone ketyl, pyridine, DMF, and triethylamine from calcium hydride, CH_2Cl_2 and petroleum ether from P_2O_5. All other chemicals were used as commercially available. Organic extracts were dried over $MgSO_4$.

Di-*tert*-butyl Ethyl Methanetricarboxylate (4b): A solution of ethyl chloroformate (5.4 g, 4.8 mL, 50 mmol) in diethyl ether (30 mL) was added with ice-bath cooling to a mixture of di-*tert*-butyl malonate (10.8 g, 11.2 mL, 50 mmol), potassium *tert*-butoxide (7.2 g, 64 mmol), *tert*-butyl alcohol (25 mL), and diethyl ether (50 mL). The reaction mixture was stirred at 5 °C for an additional 2 h and was then heated under reflux overnight. According to GC analysis, the reaction mixture contained di-*tert*-butyl malonate (27.5%), di-*tert*-butyl ethyl methanetricarboxylate (**4b**, 61%), and tri-*tert*-butyl methanetricarboxylate (11.4%). The mixture was poured into a mixture of ice (160 g) and conc. H_2SO_4 (10 mL), and the resulting mixture was extracted with Et_2O (2 × 50 mL). The combined ethereal extracts were washed with sat. aq. $NaHCO_3$ solution and brine (50 mL each) and dried. After concentration under reduced pressure and distillation of the residue, also under reduced pressure, **4b** (6.1 g, 43%) was obtained as a colorless oil, b.p. 83−85 °C (0.5 Torr). IR (film): $\tilde{\nu}$ = 2981 cm^{-1}, 2938, 1735, 1477, 1458, 1370, 1312, 1258, 1140, 1035, 998, 847. ^{1}H NMR ($CDCl_3$): δ = 1.28 (t, J = 7.0 Hz, 3 H, CH_3) 1.47 (s, 18 H, 6 CH_3), 4.20 (s, 1 H, CH), 4.23 (q, J = 7.0 Hz, 2 H, OCH_2).^{13}C NMR ($CDCl_3$): δ = 13.9 (CH_3), 27.8 (6 CH_3), 61.0 (CH), 61.9 (CH_2), 83.0 (2 C), 163.2 (2 C), 164.5 (C). MS (CI): *m*/*z* (%) = 306 (100) (M + NH_4^+). $C_{14}H_{24}O_6$ (288.36): calcd. C 58.32, H 8.39; found C 58.69, H 8.61.

Preparation of 2-(1-Hydroxycyclopropyl)malonates 5a−c. General Procedure 1 (GP1): A solution of the appropriate Grignard reagent (120−140 mmol) was added at 5 °C over 1 h to a vigorously stirred solution of ester **4** (20 mmol) and titanium tetraisopropoxide (1.71 g, 1.8 mL, 6 mmol) in anhydrous THF (250 mL). The mixture was stirred overnight, and the reaction was quenched with brine (10 mL). Magnesium sulfate (10 g), petroleum ether (50 mL), and diethyl ether (50 mL) were then added with stirring. The obtained slurry was filtered through a short pad of silica (25 g) and concentrated under reduced pressure. The product was isolated by chromatography on silica gel.

Diethyl 2-(1-Hydroxycyclopropyl)malonate (5a): Column chromatography (R_f = 0.29, 150 g of silica gel, 4 × 30 cm column, pentane/EtOAc, 5:1) followed by kugelrohr distillation (125 °C, 0.1 Torr) of the residue (3.7 g) obtained from ester **4a** (4.65 g, 20 mmol), Ti(O*i*Pr)$_4$ (1.71 g, 1.8 mL, 6 mmol), and EtMgBr [140 mmol, freshly prepared from Mg (3.36 g, 140 mmol) and ethyl bromide (15.3 g, 10.5 mL, 140 mmol) in THF (100 mL)] by GP1 gave cyclopropanol **5a** (823 mg, 19%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3519 cm^{-1}, 3093, 2983, 2941, 2908, 1734, 1465, 1371, 1305, 1244, 1176, 1155, 1038. ^{1}H NMR ($CDCl_3$): δ = 0.66 (dd, J = 5.0, 7.5 Hz, 2 H, Cpr), 0.92 (dd, J = 5.0, 7.5 Hz, 2 H, Cpr), 1.28 (t, J = 7.0 Hz, 6 H, 2 CH_3), 2.99 (s, 1 H, OH), 3.87 (s, 1 H, CH), 4.24 (q, J = 7.1 Hz, 4 H, 2 CH_2). ^{13}C NMR ($CDCl_3$): δ = 12.8 (2 CH_2), 14.0 (2 CH_3), 54.9 (C), 58.2 (CH), 61.6 (2 CH_2), 168.7 (2 C). MS (CI): *m*/*z* (%) = 216 (100) [M$^+$]. $C_{10}H_{16}O_5$ (216.24): calcd. C 55.55, H 7.46; found C 55.50, H 7.20.

***tert*-Butyl Ethyl 2-(1-Hydroxycyclopropyl)malonate (5b):** Column chromatography (R_f = 0.30, 150 g of silica gel, 4 × 30 cm column, petroleum ether/EtOAc, 5:1) of the residue (5.17 g) obtained from ester **4b** (5.77 g, 20 mmol), Ti(O*i*Pr)$_4$ (1.71 g, 1.8 mL, 6 mmol), and EtMgBr [140 mmol, freshly prepared from Mg (3.36 g, 140 mmol) and ethyl bromide (15.3 g, 10.5 mL, 140 mmol) in THF (100 mL)] by GP1 gave cyclopropanol **5b** (155 mg, 3%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3518 cm^{-1}, 3093, 2981, 2937, 1725, 1460, 1394, 1370, 1306, 1251, 1147, 1097, 1035, 967, 936, 852. ^{1}H NMR ($CDCl_3$): δ = 0.65 (dd, J = 5.4, 7.1 Hz, 2 H, Cpr), 0.91 (dd, J = 5.4, 7.1 Hz, 2 H, Cpr), 1.29 (t, J = 7.1 Hz, 3 H, CH_3) 1.49 (s, 9 H, 3 CH_3), 2.92 (s, 1 H, OH), 3.90 (s, 1 H, CH), 4.25 (q, J = 7.1 Hz, 2 H, CH_2O). ^{13}C NMR ($CDCl_3$): δ = 12.6 (CH_2), 12.8 (CH_2), 14.1 (CH_3), 27.9 (3 CH_3), 55.0 (C), 59.0 (CH), 61.5 (CH_2), 82.6 (C), 168.0 (C), 169.0 (C). MS (EI): *m*/*z* (%) = 229 (2), 188 (7), 170 (8), 159 (20), 144 (8), 132 (22), 115 (24), 101 (8), 87 (12), 57 (100). MS (CI): *m*/*z* (%) = 262 (100) (M + NH_4^+). $C_{12}H_{20}O_5$ (244.29): calcd. C 59.00, H 8.25; found C 59.34, H 7.98.

Diethyl 2-(2-Ethyl-2-hydroxycyclopropyl)malonate (5c): Column chromatography (R_f = 0.29, 150 g of silica gel, 4 × 30 cm column, petroleum ether/EtOAc, 5:1) of the residue (5.42 g) obtained from ester **4a** (4.65 g, 20 mmol), Ti(O*i*Pr)$_4$ (1.71 g, 1.8 mL, 6 mmol), and *n*BuMgBr [120 mmol, freshly prepared from Mg (2.88 g, 120 mmol) and *n*-butyl bromide (16.44 g, 12.9 mL, 120 mmol) in THF (100 mL)] by GP1 gave the cyclopropanol **5c** (322 mg, 7%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3525 cm^{-1}, 3078, 2963, 2936, 2875, 1736, 1730, 1466, 1395, 1370, 1323, 1294, 1225, 1152, 1097, 1041, 960, 866. ^{1}H NMR ($CDCl_3$): δ = 0.33 (t, J = 6.0 Hz, 1 H, Cpr), 0.85−1.04 (m, 6 H, Et + Cpr), 1.29 (t, J = 7.1 Hz, 6 H, 2 CH_3), 1.50−1.70 (m, 1 H, Cpr), 3.11 (s, 1 H, OH), 3.88 (s, 1 H, CH), 4.25 (q, J = 7.1 Hz, 4 H, CH_2O). ^{13}C NMR ($CDCl_3$): δ = 13.5 (CH_3), 14.0 (CH_3), 14.04 (CH_3), 18.5 (CH_2), 23.1 (CH_2), 27.5 (CH), 54.9 (CH), 58.8 (C), 61.7 (2 CH_2), 169.0 (C), 169.3 (C). MS (EI): *m*/*z* (%) = 244 (1) [M$^+$], 215 (4), 202 (24), 187 (19), 171 (14), 160 (100), 141 (14), 133 (28), 115 (32), 105 (8), 87 (30). MS (CI): *m*/*z* (%) = 262 (100) (M + NH_4^+). $C_{12}H_{20}O_5$ (244.29): calcd. C 59.00, H 8.25; found C 59.31, H 8.21.

Diethyl 2-(*cis*-1-Hydroxy-2-phenylcyclopropyl)malonate (5d): Column chromatography (R_f = 0.29, 150 g of silica gel, 4 × 30 cm column, petroleum ether/EtOAc, 5:1) of the residue (5.0 g) obtained from ester **4a** (4.65 g, 20 mmol), Ti(O*i*Pr)$_4$ (1.71 g, 1.8 mL, 6 mmol), and Ph(CH$_2$)$_2$MgCl [120 mmol, freshly prepared from Mg (2.88 g, 120 mmol) and 2-phenylethyl chloride (16.87 g, 12.45 mL, 120 mmol) in THF (100 mL)] by GP1 gave cyclopropanol **5d** (400 mg, 7%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3510 cm^{-1}, 3086, 3061, 3027, 2982, 2938, 2908, 1743, 1604, 1498, 1456, 1370, 1328, 1291, 1236, 1152, 1096, 1037, 962, 776, 701. ^{1}H NMR ($CDCl_3$): δ = 1.09 (t, J = 7.1 Hz, 3 H, CH_3), 1.29 (t, J = 7.1 Hz, 3 H, CH_3),

1.40 (dd, J = 7.5, 9.7 Hz, 1 H, Cpr), 1.46 (t, J = 7.5 Hz, 1 H, Cpr), 2.52 (dd, J = 7.7, 9.7 Hz, 1 H, Cpr), 2.75 (s, 1 H, OH), 4.05 (dq, J = 0.7, 7.1 Hz, 2 H, OCH_2), 4.24 (dq, J = 1.7, 7.1 Hz, 2 H, OCH_2), 4.35 (s, 1 H, CH), 7.10−7.40 (m, 5 H, Ph). ^{13}C NMR ($CDCl_3$): δ = 13.8 (CH_3), 14.0 (CH_3), 16.1 (CH_2), 30.4 (CH), 54.4 (CH), 60.6 (C), 61.4 (CH_2), 61.7 (CH_2), 126.5 (2 CH), 128.2 (2 CH), 128.3 (CH), 136.8 (C), 168.5 (C), 169.7 (C). MS (EI): m/z (%) = 292 (19) [M^+], 246 (8), 200 (9), 160 (62), 145 (8), 133 (31), 115 (24), 104 (100), 87 (27). HRMS (EI) calcd. for $C_{16}H_{20}O_5$ 292.21311 [M^+], found 292.21311. $C_{16}H_{20}O_5$ (292.33): calcd. C 65.74, H 6.90; found C 65.74, H 6.87.

Synthesis of Diethyl 2-(1-Hydroxycyclopropyl)malonate (5a) with Ti(O*i*Pr)$_4$ at Low Temperature: A solution of EtMgBr in THF [prepared from Mg (3.6 g, 150 mmol) and EtBr (12 mL, 17.5 g, 160 mmol) in 150 mL of the solvent] was added with stirring over 1.75 h to a precooled (−35 to −40 °C) mixture of ester **4a** (2.92 g, 12.6 mmol), Ti(O*i*Pr)$_4$ (7.10 g, 25 mmol), and THF (100 mL). The reaction mixture was stirred at the same temperature for an additional 2.5 h, and the reaction was quenched carefully by dropwise addition of aq. H_2SO_4 (10%, 100 mL), the temperature being maintained in the −40 to −30 °C range. This mixture was diluted with Et_2O (250 mL) and stirred, and the layers were separated. The aqueous layer, which may have contained suspended solid, was extracted with Et_2O (100 mL), and the combined organic solutions were washed successively with sat. aq. $NaHCO_3$ and NaCl solutions (100 mL each) and dried. After removal of the solvents, the residual oil was subjected to flash chromatography [60 g of silica gel, 6.5 × 4.5 cm column, hexane/ethyl acetate (10:1, 1.1 L and 5:1, 0.6 L)]. The first fraction (0.5 L of 10:1 eluent) was discarded, and the column was eluted further, with 75 mL fractions being collected. The compound with R_f = 0.3 (hexane/EtOAc, 5:1) was collected and kugelrohr-distilled at 110−115 °C (0.01 Torr) to provide pure title compound **5a** (1.36 g, 50%). $C_{10}H_{16}O_5$ (216.24): calcd. C 55.55, H 7.46; found C 55.46, H 7.39.

Application of the same procedure to the ester **4a** (5.83 g, 25 mmol) in the presence of LiO*i*Pr (1 equiv., 1.65 g, 25 mmol) provided the target cyclopropanol **5a** (2.672 g, 12.4 mmol, 50%), and after repeated column chromatography on silica gel (hexane/EtOAc, 7:1, then hexane/EtOAc, 4:1) of the side fraction from the first separation, **ethyl isopropyl (1-hydroxy-1-cyclopropyl)malonate (5e**, 74 mg, 1.3%) was isolated as a colorless oil. IR (film): $\tilde{\nu}$ = 3518 cm^{-1}, 3092, 2983, 2940, 1734, 1466, 1375, 1246, 1107, 1035, 938, 918, 869, 818, 763, 673, 606. ^1H NMR ($CDCl_3$): δ = 0.62−0.72 (m, 2 H, Cpr), 0.86−0.96 (m, 2 H, Cpr), 1.26 (d, J = 7.1 Hz, 6 H, 2 CH_3), 1.27 (t, J = 7.1 Hz, 3 H, CH_3), 2.96 (s, 1 H, CH), 3.88 (s, 1 H, OH), 4.25 (q, J = 7.1 Hz, 2 H, CH_2O), 5.13 (sept, J = 7.1 Hz, 1 H, CH). MS (CI): m/z (%) = 248.1 (100) [M + NH_4^+]. The analytical sample was obtained by kugelrohr distillation at 130−150 °C (0.01 Torr). $C_{11}H_{18}O_5$ (230.26): calcd. C 57.38, H 7.88; found C 57.07, H 8.07.

Synthesis of Diethyl 2-(1-Hydroxycyclopropyl)malonate (5a) with Ti(OEt)$_4$: Compound **5a** (1.212 g, 45% after flash chromatography) was prepared from the ester **4a** (2.92 g, 12.6 mmol), Ti(OEt)$_4$ (5.86 g, 25 mmol) in THF (100 mL), and EtMgBr [prepared from Mg (2.4 g, 100 mmol) and EtBr (8 mL, 11.7 g, 107 mmol) in THF (100 mL)], by application of the procedure described above.

Synthesis of Diethyl 2-(2-Ethyl-1-hydroxycyclopropyl)malonate (5c) with Ti(OEt)$_4$: Compound **5c** (0.451 g, 15% after additional chromatographic purification) was prepared from the ester **4a** (2.92 g, 12.6 mmol), Ti(OEt)$_4$ (5.86 g, 25 mmol) in THF (100 mL), and *n*BuMgBr [prepared from Mg (2.4 g, 100 mmol) and BuBr (12 mL, 15.3 g, 112 mmol) in THF (100 mL)] by application of the procedure described above.

Diethyl Cyclopropylidenemalonate (3-Et): A solution of methanesulfonyl chloride (263 mg, 178 μL, 2.3 mmol) in dichloromethane (10 mL) was added dropwise to a precooled (−20 °C) solution of ester **5a** (324 mg, 1.5 mmol) and triethylamine (1.062 g, 1.46 mL, 10.5 mmol) in anhydrous CH_2Cl_2 (20 mL). The reaction mixture was stirred at −20 °C for 5 min and at ambient temperature for an additional 1 h. The solvent was then evaporated, and the residue was triturated with anhydrous petroleum ether (10 mL) and filtered off. Evaporation of the solvent under reduced pressure, followed by kugelrohr distillation of the residue at 100−110 °C (0.1 Torr), afforded diester **3**-Et (115 mg, 39%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3059 cm^{-1}, 2983, 2939, 2908, 2876, 1758, 1723, 1466, 1448, 1391, 1369, 1301, 1251, 1175, 1147, 1117, 1086, 1022, 965, 864, 793, 769. ^1H NMR ($CDCl_3$): δ = 1.31 (t, J = 7.1 Hz, 6 H, 2 CH_3), 1.53 (s, 4 H, 2 CH_2 Cpr), 4.27 (q, J = 7.1 Hz, 4 H, 2 OCH_2). ^{13}C NMR ($CDCl_3$): δ = 5.0 (2 CH_2), 14.2 (2 CH_3), 61.0 (2 CH_2), 118.1 (C), 152.0 (C), 164.0 (2 C). MS (CI): m/z (%) = 216 (100) [M + NH_4^+]. $C_{10}H_{14}O_4$ (198.22): calcd. C 60.59, H 7.12; found C 60.81, H 6.94.

Addition and Cycloaddition Reactions of Diethyl Cyclopropylidenemalonate 3-Et Obtained from the Mesylate of 5a. General Procedure 2 (GP2): A solution of methanesulfonyl chloride (263 mg, 178 μL, 2.3 mmol) in dichloromethane (10 mL) was added dropwise to a precooled (−20 °C) solution of ester **5a** (324 mg, 1.5 mmol) and triethylamine (1.062 g, 1.46 mL, 10.5 mmol) in anhydrous CH_2Cl_2 (20 mL). The reaction mixture was stirred at −20 °C for 5 min and at ambient temperature for an additional 1 h. An excess of the appropriate nucleophilic reagent (2−4 mmol) was then added, and the reaction mixture was stirred at ambient temperature for an additional 4 h, if not otherwise specified. The solvent was evaporated, and the residue was triturated with anhydrous petroleum ether (10 mL), filtered, and concentrated under reduced pressure. The product was isolated by column chromatography or by kugelrohr distillation.

Diethyl 2-(1-Dimethylaminocyclopropyl)malonate (10a): Kugelrohr distillation at 100 °C (0.5 Torr) of the residue obtained from ester **5a** (136 mg, 0.63 mmol), triethylamine (436 mg, 4.3 mmol), methanesulfonyl chloride (120 mg, 1.1 mmol), and dimethylamine (108 mg, 2.4 mmol) after treatment as described in GP2 afforded adduct **10a** (145 mg, 95%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3096 cm^{-1}, 2982, 2940, 2821, 2779, 1759, 1734, 1653, 1457, 1368, 1223, 1151, 1097, 1037, 864, 668. ^1H NMR ($CDCl_3$): δ = 0.72−0.79 (m, 4 H, Cpr), 1.24 (t, J = 7.1 Hz, 6 H, 2 CH_3), 2.28 (s, 6 H, 2 CH_3), 3.85 (s, 1 H, CH), 4.14 (q, J = 7.1 Hz, 4 H, 2 OCH_2). ^{13}C NMR ($CDCl_3$): δ = 13.7 (2 CH_2), 14.0 (2 CH_3), 41.0 (2 CH_3), 44.3 (C), 48.91 (CH), 61.2 (2 CH_2), 168.36 (2 C). MS (CI): m/z (%) = 244 (100) [M + H^+]. $C_{12}H_{21}NO_4$ (243.31): calcd. C 59.24, H 8.70; found C 59.01, H 8.64.

Diethyl 2-(1-Diethylaminocyclopropyl)malonate (10b): Kugelrohr distillation at 110−115 °C (0.5 Torr) of the residue obtained from ester **5a** (216 mg, 1.0 mmol), triethylamine (708 mg, 7.0 mmol), methanesulfonyl chloride (184 mg, 1.6 mmol), and diethylamine (292 mg, 4.0 mmol) after treatment as described in GP2 afforded adduct **10b** (196 mg, 72%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3097 cm^{-1}, 2979, 2937, 2811, 1761, 1734, 1457, 1368, 1317, 1232, 1176, 1145, 1096, 1039, 861, 786. ^1H NMR ($CDCl_3$): δ = 0.74−0.83 (m, 4 H, Cpr), 1.02 (t, J = 7.2 Hz, 6 H, 2 CH_3), 1.25 (t, J = 7.1 Hz, 6 H, 2 CH_3), 2.59 (q, J = 7.2 Hz, 4 H, 2 CH_2), 3.91 (s, 1 H, CH), 4.14 (q, J = 7.1 Hz, 4 H, 2 CH_2O). ^{13}C NMR ($CDCl_3$): δ = 13.4 (2 CH_2), 14.0 (2 CH_3), 14.7 (2 CH_3), 43.2 (C), 46.2 (2 CH_2), 50.8

(CH), 61.1 (2 CH_2), 168.5 (2 C). MS (EI): *m/z* (%) = 271 (14) [M^+], 242 (8), 198 (100), 170 (4), 126 (14), 112 (22). MS (CI): *m/z* (%) = 272 (100) [M + H^+]. HRMS (EI) calcd. for $C_{14}H_{25}NO_4$ [M^+] 271.1783, found 271.1783. Hydrochloride **10b**·HCl: m.p. 92−93 °C. $C_{14}H_{26}ClNO_4$ (307.82): calcd. C 54.63, H 8.51, N 4.55; found C 54.35, H 8.24, N 4.29.

Diethyl 2-(1-Dibenzylaminocyclopropyl)malonate (10c): Column chromatography (R_f = 0.53, 60 g of silica gel, 2.8 × 20 cm column, hexane/EtOAc, 5:1) of the residue obtained from ester **5a** (216 mg, 1.0 mmol), triethylamine (708 mg, 7.0 mmol), methanesulfonyl chloride (184 mg, 1.6 mmol), and dibenzylamine (530 mg, 2.7 mmol) after treatment as described in GP2 afforded adduct **10c** (353 mg, 89%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3086 cm^{-1}, 3063, 3029, 2981, 2938, 2904, 2806, 1757, 1732, 1495, 1451, 1367, 1319, 1264, 1226, 1173, 1096, 1033, 748, 699. ^1H NMR ($CDCl_3$): δ = 0.68−0.75 (m, 2 H, Cpr), 0.79−0.85 (m, 2 H, Cpr), 1.35 (t, *J* = 7.1 Hz, 6 H, 2 CH_3), 3.81 (s, 4 H, 2 CH_2), 4.25 (q, *J* = 7.1 Hz, 4 H, 2 OCH_2), 4.28 (s, 1 H, CH), 7.23−7.31 (m, 10 H, 2 Ph). ^{13}C NMR ($CDCl_3$): δ = 13.8 (2 CH_2), 14.0 (2 CH_3), 43.3 (C), 51.1 (CH), 56.2 (2 CH_2), 61.3 (2 CH_2), 126.7 (4 CH), 127.9 (4 CH), 129.0 (2 CH), 139.7 (2 C), 168.3 (2 C). MS (EI): *m/z* (%) = 395 (0.8) [M^+], 304 (100), 236 (11), 186 (10), 144 (6), 91 (58). $C_{24}H_{29}NO_4$ (395.50): calcd. C 72.89, H 7.39, N 3.54; found C 73.11, H 7.03, N 3.46.

Diethyl 2-[1-(4-Methylpiperazino)cyclopropyl]malonate (10d): Kugelrohr distillation at 150−160 °C (0.1 Torr) of the residue obtained from ester **5a** (216 mg, 1.0 mmol), triethylamine (708 mg, 7.0 mmol), methanesulfonyl chloride (184 mg, 1.5 mmol), and *N*-methylpiperazine (400 mg, 4.0 mmol) after treatment as described in GP2 afforded adduct **10d** (266 mg, 89%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3094 cm^{-1}, 2980, 2939, 2839, 2793, 2749, 1758, 1734, 1453, 1369, 1341, 1314, 1288, 1229, 1176, 1145, 1095, 1038, 1014, 863, 818. ^1H NMR ($CDCl_3$): δ = 0.71−0.75 (m, 4 H, Cpr), 1.22 (t, *J* = 7.1 Hz, 6 H, 2 CH_3), 2.22 (s, 3 H, NCH_3), 2.32 (m, 4 H, 2 CH_2), 2.60 (m, 4 H, 2 CH_2), 3.87 (s, 1 H, CH), 4.12 (q, *J* = 7.1 Hz, 4 H, 2 OCH_2). ^{13}C NMR ($CDCl_3$): δ = 12.9 (2 CH_2), 14.0 (2 CH_3), 43.5 (C), 46.0 (CH_3), 48.9 (2 CH_2), 50.1 (CH), 55.5 (2 CH_2), 61.2 (2 CH_2), 168.3 (2 C). MS (EI): *m/z* (%) = 298 (26) [M^+], 241 (16), 225 (40), 179 (38), 139 (35), 82 (10), 70 (100). HRMS (EI) calcd. for $C_{15}H_{26}N_2O_4$ [M^+] 298.1892, found 298.1892. Dihydrochloride hydrate **10d**·2HCl·H_2O: m.p. 100−102 °C. ^1H NMR ($CDCl_3$): δ = 1.08−1.15 (m, 2 H, Cpr), 1.26 (t, *J* = 7.1 Hz, 6 H, 2 CH_3), 1.83−1.88 (m, 2 H, Cpr), 2.88 (d, *J* = 4.3 Hz, 3 H, CH_3N), 3.52 (d, *J* = 10.2 Hz, 4 H, 2 CH_2N), 4.10−4.30 (m, 5 H, 2 CH_2N + CH), 4.21 (q, *J* = 7.1 Hz, 4 H, 2 OCH_2). ^{13}C NMR ($CDCl_3$): δ = 12.3 (2 CH_2), 13.9 (2 CH_3), 42.9 (CH_3), 46.0 (C), 46.2 (2 CH_2), 49.2 (CH), 49.7 (2 CH_2), 62.7 (2 CH_2), 165.8 (2 C). $C_{15}H_{26}N_2O_4$·2HCl·H_2O (389.32): calcd. 46.28, H 7.77; found C 46.74, H 7.90.

Diethyl 2-(1-Morpholinocyclopropyl)malonate (10e): Column chromatography (R_f = 0.22, 60 g of silica gel, 2.8 × 20 cm column, hexane/EtOAc, 5:1) of the residue obtained from ester **5a** (301 mg, 1.4 mmol), triethylamine (708 mg, 7.0 mmol), methanesulfonyl chloride (184 mg, 1.6 mmol), and morpholine (348 mg, 4.0 mmol) after treatment as described in GP2 afforded adduct **10e** (304 mg, 76%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3095 cm^{-1}, 2978, 2856, 2815, 1757, 1734, 1450, 1369, 1313, 1296, 1268, 1240, 1175, 1145, 1117, 1035, 991, 856. ^1H NMR ($CDCl_3$): δ = 0.74 (s, 4 H, Cpr), 1.23 (t, *J* = 7.1 Hz, 6 H, 2 CH_3), 2.55 (t, *J* = 4.6 Hz, 4 H, 2 CH_2N), 3.56 (t, *J* = 4.6 Hz, 4 H, 2 CH_2O), 3.81 (s, 1 H, CH), 4.13 (q, *J* = 7.1 Hz, 4 H, 2 OCH_2). ^{13}C NMR ($CDCl_3$): δ = 12.7 (2 CH_2), 14.0 (2 CH_3), 43.8 (C), 49.5 (2 CH_2N), 50.7 (CH), 61.2 (2 CH_2), 67.3 (2 CH_2), 168.2 (2 C). MS (EI): *m/z* (%) = 285 (14) [M^+], 212 (100), 194 (6), 179 (14), 167 (53), 166 (56), 149 (18), 126 (28). MS (CI): *m/z* (%) = 285 (100) [M^+]. $C_{14}H_{23}NO_5$ (285.35): calcd. C 58.93, H 8.12; found C 58.60, H 8.22. Hydrochloride **10e**·HCl: m.p. 140−141 °C. $C_{14}H_{24}ClNO_5$ (321.81): calcd. C 52.25, H 7.52; found C 52.56, H.7.61.

Diethyl 2-[1-(4-Methylphenoxy)cyclopropyl]malonate (10f): Kugelrohr distillation at 175−190 °C (0.01 Torr) of the residue obtained from ester **5a** (355 mg, 1.6 mmol), triethylamine (1.16 g, 11.5 mmol), methanesulfonyl chloride (300 mg, 2.6 mmol), and *p*-cresol (700 mg, 6.5 mmol) after treatment as described in GP2, with the difference that the excess *p*-cresol was removed by washing with aq. 5% NaOH solution, afforded adduct **10f** (359 mg, 71%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3095 cm^{-1}, 2983, 2938, 2873, 1761, 1734, 1612, 1586, 1507, 1462, 1447, 1369, 1323, 1246, 1224, 1177, 1111, 1096, 1036, 965, 861, 817. ^1H NMR ($CDCl_3$): δ = 1.13 (s, 4 H, Cpr), 1.28 (t, *J* = 7.2 Hz, 6 H, 2 CH_3), 2.31 (s, 3 H, CH_3), 4.22 (q, *J* = 7.2 Hz, 4 H, 2 CH_2O), 4.26 (s, 1 H, CH), 6.93 (d, *J* = 8.7 Hz, 2 H, Ar-H), 7.11 (d, *J* = 8.7 Hz, 2 H, Ar-H). ^{13}C NMR ($CDCl_3$): δ = 11.5 (2 CH_2), 14.0 (2 CH_3), 20.4 (CH_3), 53.1 (CH), 57.7 (C), 61.6 (2 CH_2), 116.0 (2 CH), 129.9 (2 CH), 130.7 (C), 153.8 (C), 166.8 (2 C). MS (EI): *m/z* (%) = 306 (31) [M^+], 233 (25), 198 (10), 187 (35), 166 (49), 159 (22), 137 (100), 118 (26), 108 (97), 105 (22), 91 (20), 81 (30). MS (CI): *m/z* (%) = 324 (100) [M + NH_4^+]. $C_{17}H_{22}O_5$ (306.36): calcd. C 66.65, H 7.24; found C 66.86, H 7.06.

Diethyl 2-[1-(1-Thionaphthyl)cyclopropyl]malonate (10g): Column chromatography (R_f = 0.45, 60 g of silica gel, 2.8 × 20 cm column, hexane/EtOAc, 5:1) of the residue obtained from ester **5a** (327 mg, 1.5 mmol), triethylamine (1.41 g, 14.0 mmol), methanesulfonyl chloride (276 mg, 2.4 mmol), and 1-thionaphthol (961 mg, 6.0 mmol) after treatment as described in GP2, with the difference that the excess 1-thionaphthol was removed by washing with aq. 5% NaOH solution, afforded adduct **10g** (276 mg, 50%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3055 cm^{-1}, 2981, 2938, 2904, 1757, 1734, 1590, 1565, 1503, 1446, 1384, 1368, 1312, 1224, 1150, 1095, 1035, 974, 859, 793, 772. ^1H NMR ($CDCl_3$): δ = 1.25 (t, *J* = 7.0 Hz, 6 H, 2 CH_3), 1.27−1.38 (m, 4 H, Cpr), 4.02 (s, 1 H, CH), 4.18 (q, *J* = 7.0 Hz, 4 H, CH_2O), 7.46−7.55 (m, 3 H, Ar-H), 7.73 (d, *J* = 2.8 Hz, 2 H, Ar-H), 7.85 (dd, *J* = 3.4, 5.8 Hz, 1 H, Ar-H), 8.20 (dd, *J* = 3.4, 6.2 Hz, 1 H, Ar-H). ^{13}C NMR ($CDCl_3$): δ = 14.0 (2 CH_3), 14.5 (2 CH_2), 23.5 (C), 56.3 (CH), 61.655 (2 CH_2), 124.2 (CH), 125.69 (CH), 125.72 (CH), 126.1 (CH), 126.3 (CH), 126.6 (CH), 128.4 (CH), 132.1 (C), 133.0 (C), 133.8 (C), 167.2 (2 C). MS (EI): *m/z* (%) = 358 (100) [M^+], 313 (12), 285 (19), 239 (31), 211 (38), 198 (62), 178 (12), 165 (49), 141 (30), 115 (46). MS (CI): *m/z* (%) = 376 (100) [M + NH_4^+]. $C_{20}H_{22}O_4S$ (358.46): calcd. C 67.02, H 6.19; found C 66.92, H 5.99.

1,4-Bis{1-[bis(ethoxycarbonyl)methyl]cyclopropyl}piperazine (10h): Column chromatography (R_f = 0.25, 60 g of silica gel, 2.8 × 20 cm column, hexane/EtOAc, 5:1) of the residue obtained from ester **5a** (216 mg, 1.0 mmol), triethylamine (708 mg, 7.0 mmol), methanesulfonyl chloride (184 mg, 1.6 mmol), and piperazine (44 mg, 0.5 mmol) after treatment as described in GP2 afforded adduct **10h** (206 mg, 85%) as a colorless solid, m.p. 62−63 °C. IR (KBr): $\tilde{\nu}$ = 3075 cm^{-1}, 2989, 2957, 2912, 2847, 2825, 1755, 1729, 1481, 1450, 1372, 1337, 1320, 1298, 1249, 1176, 1145, 1115, 1099, 1039, 998, 879, 819. ^1H NMR ($CDCl_3$): δ = 0.71−0.74 (m, 8 H, Cpr), 1.24 (t, *J* = 7.1 Hz, 12 H, 4 CH_3), 2.49 (s, 8 H, 4 CH_2N), 3.83 (s, 2 H, 2 CH), 4.13 (q, *J* = 7.1 Hz, 8 H, 4 CH_2O). ^{13}C NMR ($CDCl_3$): δ = 13.1 (4 CH_2), 14.0 (4 CH_3), 43.6 (2 C), 49.5 (4 CH_2), 50.2 (2 CH), 61.2 (4 CH_2), 168.3 (4 C). MS (CI): *m/z* (%) = 483 (100) [M

+ H^+]. $C_{24}H_{38}N_2O_8$ (482.58): calcd. C 59.73, H 7.94; found C 59.82, H 7.69.

***tert*-Butyl Ethyl 2-[1-(4-Methylpiperazino)cyclopropyl]malonate (10i):** Column chromatography (R_f = 0.20, 60 g of silica gel, 2.8 × 20 cm column, hexane/EtOAc, 5:1) of the residue obtained from ester **5b** (315 mg, 1.3 mmol), triethylamine (708 mg, 7.0 mmol), methanesulfonyl chloride (221 mg, 1.9 mmol), and *N*-methylpiperazine (517 mg, 5.2 mmol) after treatment as described in GP2 afforded adduct **10i** (218 mg, 51%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3095 cm^{-1}, 2977, 2938, 2879, 2839, 2793, 2749, 1757, 1734, 1456, 1369, 1315, 1288, 1246, 1176, 1140, 1096, 1035, 1014, 852, 833. ^1H NMR ($CDCl_3$): δ = 0.65−0.81 (m, 4 H, Cpr), 1.22 (t, J = 7.1 Hz, 3 H, CH_3), 1.40 (s, 9 H, 3 CH_3), 2.22 (s, 3 H, CH_3N), 2.20−2.30 (m, 4 H, 2 CH_2N), 2.50−2.60 (m, 4 H, 2 CH_2N), 3.78 (s, 1 H, CH), 4.11 (q, J = 7.1 Hz, 2 H, CH_2O). ^{13}C NMR ($CDCl_3$): δ = 12.9 (2 CH_2), 14.0 (CH_3), 27.8 (3 CH_3), 43.2 (C), 46.0 (CH_3), 48.8 (2 CH_2), 50.8 (CH), 55.4 (2 CH_2), 61.0 (CH_2), 81.57 (C), 167.3 (C), 168.5 (C). MS (CI): m/z (%) = 327 (100) [M + H^+]. $C_{17}H_{30}N_2O_4$ (326.441): calcd. C 62.55, H 9.26; found C 62.41, H.8.97.

Diethyl 6-(4-Methoxyphenyl)-5-phenyl-4-oxa-5-azaspiro[2.4]heptane-7,7-dicarboxylate (14a): Column chromatography (R_f = 0.19, 60 g of silica gel, 2.8 × 20 cm column, hexane/EtOAc, 10:1) of the residue obtained from ester **5a** (330 mg, 1.5 mmol), triethylamine (1.06 g, 10.5 mmol), methanesulfonyl chloride (276 mg, 2.41 mmol), and 4-methoxyphenyl-*N*-phenylnitrone (**13a**, 690 mg, 3.0 mmol) after treatment as described in GP2 afforded cycloadduct **14a** (412 mg, 63%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3061 cm^{-1}, 2980, 2937, 2905, 2832, 1734, 1599, 1512, 1489, 1464, 1367, 1252, 1097, 1033, 836, 755. ^1H NMR ($CDCl_3$): δ = 0.69−0.79 (m, 1 H, Cpr), 0.89 (t, J = 7.1 Hz, 3 H, CH_3), 0.93−1.11 (m, 1 H, Cpr), 1.23 (t, J = 7.1 Hz, 3 H, CH_3), 1.27−1.52 (m, 2 H, Cpr), 3.58 (dq, J = 7.1, 10.7 Hz, 1 H, CH_2O), 3.82 (s, 3 H, CH_3O), 3.85 (dq, J = 10.7, J = 7.1 Hz, 1 H, CH_2O), 4.15−4.27 (m, 2 H, CH_2O), 5.72 (s, 1 H, CH), 6.87−6.93 (m, 5 H, Ph), 7.20 (d, J = 8.6 Hz, 2 H, Ar-H), 7.57 (d, J = 8.6 Hz 2 H, Ar-H). ^{13}C NMR ($CDCl_3$): δ = 7.8 (CH_2), 10.1 (CH_2), 13.5 (CH_3), 13.9 (CH_3), 55.3 (CH_3), 61.3 (CH_2), 62.1 (CH_2), 66.7 (C), 70.6 (C), 74.5 (CH), 113.6 (2 CH), 114.4 (2 CH), 121.4 (2 CH), 128.6 (2 CH), 129.3 (CH), 130.0 (C), 151.3 (C), 159.5 (C), 166.5 (C), 167.2 (C). MS (EI): m/z (%) = 425 (19) [M^+] 278 (25), 238 (64), 211 (100), 168 (14), 132 (13), 77 (34). $C_{24}H_{27}NO_6$ (425.49): calcd. C 67.75, H 6.40; found C 68.01, H 6.23.

Diethyl 5-Methyl-6-(2-pyridyl)-4-oxa-5-azaspiro[2.4]heptane-7,7-dicarboxylate (14b): Column chromatography (R_f = 0.18, 60 g of silica gel, 2.8 × 20 cm column, hexane/EtOAc, 5:1) of the residue obtained from ester **5a** (327 mg, 1.5 mmol), triethylamine (1.06 g, 10.5 mmol), methanesulfonyl chloride (276 mg, 2.41 mmol), and 2-pyridyl-*N*-methylnitrone (**13b**, 418 mg, 3.0 mmol) after treatment as described in GP2 afforded cycloadduct **14b** (215 mg, 43%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3054 cm^{-1}, 2983, 2937, 2902, 2875, 1737, 1590, 1571, 1474, 1436, 1367, 1259, 1223, 1195, 1095, 1048, 1022, 881, 765, 751. ^1H NMR ($CDCl_3$): δ = 0.78 (t, J = 7.2 Hz, 3 H, CH_3), 0.94−1.08 (m, 2 H, Cpr), 1.12−1.26 (m, 1 H, Cpr), 1.24 (t, J = 7.1 Hz, 3 H, CH_3), 1.48 (ddd, J = 5.5, 7.0, 11.0 Hz, 1 H, Cpr), 2.86 (s, 3 H, CH_3N), 3.48 (dq, J = 7.2, 10.7 Hz, 1 H, CH_2O), 3.71 (dq, J = 7.2, 10.7 Hz, 1 H, CH_2O), 4.21 (dq, J = 7.1, 10.6 Hz, 1 H, CH_2O), 4.28 (dq, J = 7.1, 10.6 Hz, 1 H, CH_2O), 5.17 (s, 1 H, CHN), 7.17 (ddd, J = 1.4, 4.8, 7.3 Hz, 1 H, Py-H), 7.58 (ddd, J = 1.0, 1.4, 7.3 Hz, 1 H, Py-H), 7.65 (td, J = 1.8, 7.3 Hz, 1 H, Py-H), 8.54 (ddd, J = 4.8, J = 1.0, 1.8 Hz, 1 H, Py-H). ^{13}C NMR ($CDCl_3$): δ = 9.2 (CH_2), 10.0 (CH_2), 13.3 (CH_3), 13.9 (CH_3), 44.8 (CH_3), 60.9 (CH_2), 62.1 (CH_2), 66.6 (C), 69.9 (C), 79.2 (CH), 107.7 (C), 122.7 (CH), 123.3 (CH), 136.4 (CH), 148.7 (CH), 166.5 (C), 168.1 (C). MS (EI): m/z (%) = 334 (8) [M^+], 289 (10), 261, (10), 250 (26), 231 (49), 204 (54), 187 (34), 160 (41), 136 (29), 121 (100), 115 (40), 99 (27), 79 (46). $C_{17}H_{22}N_2O_5$ (334.38): calcd. C 61.06, H 6.63; found C 61.34, H 6.95.

Triethyl 5,6-Diazaspiro[2.4]hept-6-ene-4,4,7-tricarboxylate (15): Column chromatography (R_f = 0.13, 60 g of silica gel, 2.8 × 20 cm column, hexane/EtOAc, 10:1) of the residue obtained from ester **5a** (324 mg, 1.5 mmol), triethylamine (1.4 g, 13.8 mmol), methanesulfonyl chloride (276 mg, 2.41 mmol), and ethyl diazoacetate (400 mg, 3.5 mmol) after treatment as described in GP2 afforded cycloadduct **15** (353 mg, 75%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3456 cm^{-1}, 3341, 3095, 2984, 2941, 2900, 2875, 1750, 1559, 1467, 1447, 1419, 1370, 1240, 1175, 1092, 1059, 1020, 958, 860, 770. ^1H NMR ($CDCl_3$): δ = 1.28 (t, J = 7.1 Hz, 6 H, 2 CH_3), 1.32 (t, J = 7.1 Hz, 3 H, CH_3), 1.33−1.40 (m, 3 H, Cpr), 1.59−1.64 (m, 1 H, Cpr), 4.25 (q, J = 7.1 Hz, 4 H, 2 CH_2O), 4.19−4.37 (m, 2 H, CH_2O), 6.85 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$): δ = 10.6 (2 CH_2), 14.0 (2 CH_3), 14.1 (CH_3), 32.6 (C), 61.2 (CH_2), 62.5 (2 CH_2O), 76.0 (C), 144.8 (C), 160.5 (C), 166.9 (2 C). MS (EI): m/z (%) = 243 (2), 227 (32), 193 (5), 181 (38), 160 (6), 153 (16), 141 (36), 125 (22), 119 (70), 101 (11), 91 (100). MS (CI): m/z (%) = 300 (100).

Diethyl Spiro{cyclopropa-1,3′-(1′-methyl-7′-oxabicyclo[2.2.1]hept-5-ene-2,2-dicarboxylate)} (17): A) Column chromatography (R_f = 0.30, 60 g of silica gel, 2.8 × 20 cm column, hexane/EtOAc, 5:1) of the residue obtained from ester **5a** (327 mg, 1.5 mmol), triethylamine (1.06 g, 10.5 mmol), methanesulfonyl chloride (276 mg, 2.41 mmol), and 2-methylfuran (1.83 g, 22.3 mmol) after treatment as described in GP2 afforded cycloadduct **17** (51 mg, 12%) as a colorless oil.

B) A mixture of the acetate **11** (258 mg, 1.0 mmol), 2-methylfuran (0.5 g, 6.3 mmol), and triethylamine (0.5 mL) was stirred at 50 °C for 24 h and, after cooling, concentrated under reduced pressure. Column chromatography of the residue (40 g of silica gel, 2.8 × 11 cm column, hexane/EtOAc, 5:1) afforded cycloadduct **17** (72 mg, 26%). ^1H NMR ($CDCl_3$): δ = 1.00−1.14 (m, 4 H, Cpr), 1.26 (t, J = 7.2 Hz, 6 H, 2 CH_3), 2.22 (s, 3 H, CH_3), 3.53 (s, 1 H, CH), 4.20 (q, J = 7.2 Hz, 4 H, 2 CH_2O), 5.83 (d, J = 3.0 Hz, 1 H, = CH), 5.97 (d, J = 3.0 Hz, 1 H, =CH). ^{13}C NMR ($CDCl_3$): δ = 12.6 (2 CH_2), 13.5 (CH_3), 14.0 (2 CH_3), 18.6 (C), 56.8 (CH), 61.3 (2 CH_2), 106.0 (CH), 106.5 (CH), 112.5 (C), 150.2 (C), 167.9 (2 C). MS (EI): m/z (%) = 280 (42) [M^+], 235 (12), 207 (100), 189 (11), 179 (39), 161 (22), 134 (10), 121 (29), 91 (7). HRMS (EI) calcd. for $C_{15}H_{20}O_5$ [M^+] 280.1311; found 280.1311. $C_{15}H_{20}O_5$ (280.32): calcd. C 64.27, H 7.19; found C 64.00, H 6.95.

Diethyl 6,7-Dimethylspiro[2.5]oct-6-ene-4,4-dicarboxylate (18): A) 2,3-Dimethylbuta-1,3-diene (1.45 g, 2 mL, 17.6 mmol) and titanium tetrachloride (151 mg, 0.76 mmol) were added to a solution of diethyl cyclopropylidenemalonate (**3**-Et) prepared from ester **5a** (324 mg, 1.5 mmol), triethylamine (1.06 g, 10.5 mmol), and methanesulfonyl chloride (276 mg, 2.41 mmol) in anhydrous dichloromethane (20 mL) as described in GP2. The reaction mixture was stirred at ambient temperature for an additional 18 h. The usual workup as described in GP2 followed by chromatographic separation (R_f = 0.37, 60 g of silica gel, 2.8 × 20 cm column, hexane/EtOAc, 5:1) afforded cycloadduct **18** (209 mg, 50%) as a colorless oil.

B) A mixture of the acetate **11** (258 mg, 1.0 mmol), triethylamine (0.5 mL), and 2,3-dimethylbuta-1,3-diene (0.5 mL) was stirred at 65 °C for 48 h. The excess of the reagents was removed under reduced pressure (5 Torr), and the residue was purified by column chromatography (R_f = 0.37, 60 g of silica gel, 2.8 × 20 cm column, hexane/

EtOAc, 5:1) followed by kugelrohr distillation to give the cycloadduct **18** (195 mg, 70%). IR (film): $\tilde{\nu}$ = 3082 cm^{-1}, 2982, 2912, 2835, 1732, 1464, 1445, 1366, 1300, 1267, 1236, 1181, 1118, 1096, 1032, 863. ^1H NMR ($CDCl_3$): δ = 0.36 (t, J = 5.5 Hz, 2 H, Cpr), 0.72 (t, J = 5.5 Hz, 2 H, Cpr), 1.23 (t, J = 7.1 Hz, 6 H, 2 CH_3), 1.55 (s, 3 H, CH_3), 1.65 (s, 3 H, CH_3), 2.00 (s, 2 H, CH_2), 2.67 (s, 2 H, CH_2), 4.15 (q, J = 7.1 Hz, 4 H, CH_2O). ^{13}C NMR ($CDCl_3$): δ = 10.7 (2 CH_2), 14.0 (2 CH_3), 18.3 (CH_3), 19.0 (CH_3), 19.8 (C), 37.7 (CH_2), 42.3 (CH_2), 58.1 (C), 61.0 (2 CH_2), 123.0 (C), 125.2 (C), 170.4 (2 C). MS (EI): m/z (%) = 280 (0.8) [M^+], 207 (100), 191 (12), 179 (26), 161 (34), 133 (100), 119 (39), 107 (82), 91 (59), 77 (22). MS (CI): m/z (%) = 298 (100) [M + NH_4^+]. $C_{16}H_{24}O_4$ (280.37): calcd. C 68.54, H 8.63; found C 68.81, H 8.94.

Diethyl (1-Acetoxycyclopropyl)malonate (11): DMAP (70 mg) was added to a mixture of alcohol **5a** (2.83 g, 13.1 mmol), pyridine (1.25 g, 1.28 mL, 15.8 mmol), Ac_2O (1.51 g, 1.4 mL, 15.0 mmol), and EtOAc (20 mL). The mixture was heated at ca. 40 °C for 0.25 h and then stirred at ambient temperature overnight. It was then diluted with EtOAc (70 mL) and poured into 5% aq. $KHSO_4$ solution (150 mL), and after vigorous shaking the layers were separated. The aqueous layer was extracted with EtOAc (100 mL), and the combined organic phases were washed with brine (100 mL) and dried. The solvent was evaporated at room temperature at 5 Torr to give the title compound (3.05 g, 90%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3094 cm^{-1}, 2984, 2939, 2907, 2875, 1765, 1728, 1370, 1230, 1175, 1043, 861. ^1H NMR ($CDCl_3$): δ = 0.92−1.04 (m, 2 H, Cpr), 1.05−1.17 (m, 2 H, Cpr), 1.23 (t, J = 7.1 Hz, 6 H, 2 CH_3), 1.97 (s, 3 H, CH_3CO), 3.97 (s, 1 H, CH), 4.17 (q, J = 7.1 Hz, 4 H, 2 CH_2O). ^{13}C NMR ($CDCl_3$): δ = 11.0 (2 CH_2), 14.0 (2 CH_3), 21.2 (CH_3), 54.4 (CH), 57.0 (C), 61.5 (2 CH_2), 166.6 (2 C), 170.8 (C). MS (CI): m/z (%) = 534 (2) [2 M + NH_4^+], 276 (100) [M + NH_4^+]. An analytical sample was obtained by kugelrohr distillation at 130−135 °C (0.01 Torr). $C_{12}H_{18}O_6$ (258.27): calcd. C 55.81, H 7.02; found C 55.50, H 6.82.

Diethyl (1-Dimethylaminocyclopropyl)malonate (10a) from Acetate 11: A solution of acetate **11** (1.435 g, 5.56 mmol) in THF (6 mL) was added dropwise over 3 min to a 40% aq. dimethylamine solution (25 mL). The mixture was stirred for an additional 30 min and poured into a mixture of diethyl ether (200 mL), brine (100 mL), and water (200 mL). The organic phase was washed with water and brine (100 mL each) and dried, and the solvent was removed under reduced pressure. Kugelrohr distillation of the residue at 125−140 °C (0.5 Torr) furnished dimethylaminocyclopropylmalonate **10a** (1.04 g, 78%) as a colorless oil, its spectroscopic data were identical to those obtained as described in GP2 (see above).

Addition and Cycloaddition Reactions of Cyclopropylidenemalonate 3-Et Produced from Acetate 11. General Procedure 3 (GP3): A mixture of the acetate **11** (1.0 mmol) and the appropriate nucleophile (1.9−4.0 mmol) was stirred under conditions as indicated in Scheme 3. The mixture was then diluted with hexane (20 mL) and filtered through a pad of celite, and the solvent was removed under reduced pressure. The product was isolated by kugelrohr distillation or column chromatography.

Diethyl 2-(1-Morpholinocyclopropyl)malonate (10e): Column chromatography (R_f = 0.22, 10 g of silica gel, 2 × 7 cm column, hexane/EtOAc, 5:1) of the residue obtained from acetate **11** (35 mg, 0.136 mmol) and morpholine (50 mg, 0.05 mL, 0.574 mmol) after treatment as described in GP3 furnished malonate **10e** (35 mg, 90%), its spectroscopic data were identical to those obtained after treatment as described in GP2 (see above).

Diethyl 2-(1-Isopropylaminocyclopropyl)malonate (10j): Kugelrohr distillation at 125−135 °C (0.01 Torr) of the residue obtained from acetate **11** (86 mg, 0.333 mmol) and isopropylamine (69 mg, 0.1 mL, 1.2 mmol) after treatment as described in GP3 furnished malonate **10j** (84 mg, 98%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3341 cm^{-1}, 3097, 2983, 2964, 2936, 2873, 1756, 1725, 1472, 1446, 1367, 1310, 1240, 1179, 1145, 1096, 1042, 1031, 864, 738. ^1H NMR ($CDCl_3$): δ = 0.60−0.75 (m, 4 H, Cpr), 1.00 (d, J = 6.1 Hz, 6 H, 2 CH_3), 1.26 (t, J = 7.1 Hz, 6 H, CH_3), 2.23 (s, 1 H, NH), 2.99 (sept. J = 6.1 Hz, 1 H, CH), 3.68 (s, 1 H, CH), 4.21 (q, J = 7.1 Hz, 4 H, 2 CH_2O). ^{13}C NMR ($CDCl_3$): δ = 12.6 (2 CH_2), 14.0 (2 CH_3), 23.5 (2 CH_3), 35.7 (C), 44.9 (CH), 54.6 (CH), 61.1 (2 CH_2), 168.4 (2 C). MS (EI): m/z (%) = 257 (12) [M^+], 214.2 (8), 184.2 (48), 138.1 (100), 98.1 (44), 56.1 (34). $C_{13}H_{23}NO_4$ (257.33): calcd. C 60.68, H 9.01; found C 60.98, H 8.92.

Diethyl 2-(1-Phenylaminocyclopropyl)malonate (10k): Kugelrohr distillation at 160−175 °C (0.01 Torr) of the residue obtained from acetate **11** (258 mg, 1.0 mmol), aniline (177 mg, 1.9 mmol), and Et_3N (210 mg, 0.3 mL, 2.1 mmol) after treatment as described in GP3 furnished malonate **10k** (215 mg, 74%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3400 cm^{-1}, 3089, 3051, 2982, 2941, 2908, 1728, 1603, 1503, 1369, 1316, 1247, 1177, 1096, 1037, 751, 697, 510. ^1H NMR ($CDCl_3$): δ = 0.98 (s, 4 H, Cpr), 1.21 (t, J = 7.1 Hz, 6 H, 2 CH_3), 3.75 (s, 1 H, CH), 4.12 (q, J = 7.1 Hz, 4 H, 2 CH_2O), 4.83 (s, 1 H, NH), 6.63−6.76 (m, 3 H, Ph-H), 7.10−7.20 (m, 2 H, Ph-H). ^{13}C NMR ($CDCl_3$): δ = 13.4 (2 CH_2), 13.9 (2 CH_3), 33.2 (C), 54.8 (CH), 61.4 (2 CH_2), 113.5 (2 CH), 117.9 (CH), 129.2 (2 CH), 146.0 (C), 168.1 (2 C). MS (EI): m/z (%) = 291 (44) [M^+], 218.1 (20), 172.0 (88), 144.0 (42), 132.1 (100), 77.0 (24). $C_{16}H_{21}NO_4$ (291.35): calcd. C 65.96, H 7.27; found C 65.76, N 7.58.

Diethyl (1-Aminocyclopropyl)malonate (10l): Column chromatography (R_f = 0.35, 10 g of silica gel, 2 × 7 cm column, hexane/EtOAc, 1:1) followed by kugelrohr distillation at 125−150 °C (0.5 Torr) of the residue obtained from acetate **11** (0.52 g, 2.0 mmol) in THF (5 mL) and aq. 25% NH_3 (20 mL) after treatment as described in GP3 furnished aminomalonate **10l** (77 mg, 18%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3389 cm^{-1}, 3091, 2983, 2939, 2908, 1744, 1730, 1598, 1448, 1370, 1315, 1267, 1176, 1152, 1096, 1037, 861. ^1H NMR ($CDCl_3$): δ = 0.49−0.60 (m, 2 H, Cpr), 0.64−0.73 (m, 2 H, Cpr), 1.22 (t, J = 7.1 Hz, 6 H, 2 CH_3), 2.25 (s, 2 H, NH), 2.80 (s, 1 H, CH), 4.17 (q, J = 7.1 Hz, 4 H, 2 CH_2O). ^{13}C NMR ($CDCl_3$): δ = 14.0 (2 CH_3), 14.1 (2 CH_2), 33.7 (C), 59.5 (CH), 61.2 (2 CH_2), 168.4 (2 C). MS (EI): m/z (%) = 215 (26) [M^+], 142.2 (34), 114.1 (16), 96.1 (100), 69.1 (28), 56.1 (76), 49.1 (22). 3 × $C_{10}H_{17}NO_4$ × H_2O (663.77): calcd. C 54.29, H 8.05; found C 54.20, H 7.52.

Diethyl (1-Cyanocyclopropyl)malonate (12): A mixture of the acetate **11** (258 mg, 1.0 mmol), KCN (130 mg, 2.0 mmol), and anhydrous DMF (5 mL) was stirred at ambient temperature for 14 h. The solvent was then removed under reduced pressure (5 Torr) at 70 °C, and the residue was purified by column chromatography (R_f = 0.34, 10 g of silica gel, 2 × 7 cm column, hexane/EtOAc, 4:1) to give the title compound **12** (146 mg, 65%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3105 cm^{-1}, 2986, 2941, 2243, 1735, 1447, 1371, 1260, 1180, 1097, 1038, 861, 737. ^1H NMR ($CDCl_3$): δ = 1.03−1.08 (m, 2 H, Cpr), 1.38−1.43 (m, 2 H, Cpr), 1.28 (t, J = 7.1 Hz, 6 H, 2 CH_3), 2.86 (s, 1 H, CH), 4.27 (q, J = 7.1 Hz, 4 H, 2 CH_2O). ^{13}C NMR ($CDCl_3$): δ = 9.6 (C), 14.0 (2 CH_2), 14.1 (2 CH_3), 56.2 (CH), 62.3 (2 CH_2), 121.0 (CN), 166.2 (2 C). MS (CI): m/z (%) = 468 (2) [2M + NH_4^+], 243 (100) [M + NH_4^+]. An analytical sample was obtained by kugelrohr distillation at 140−150 °C (0.01 Torr). $C_{11}H_{15}NO_4$ (225.25): calcd. C 58.66, H 6.71; found C 58.42, H 7.02.

Diethyl 4,5,6-Triazaspiro[2,4]hept-4-ene-7,7-dicarboxylate (16): Column chromatography (R_f = 0.30, 10 g of silica gel, 2 × 7 cm col-

umn, hexane/EtOAc, 5:1) of the residue obtained from **11** (258 mg, 1.0 mmol) and NaN_3 (130 mg, 2.0 mmol) in anhydrous DMF (2 mL) under the conditions of the previous preparation (18 h stirring) afforded compound **16** (155 mg, 64%) as a colorless oil, together with some recovered starting material **11** (36 mg, 14%). IR (film): $\tilde{\nu}$ = 3372 cm^{-1}, 3018, 2983, 2939, 2906, 2874, 2480, 2096, 1771, 1714, 1519, 1473, 1445, 1368, 1209, 1037, 955, 862, 769. ^1H NMR ($CDCl_3$): δ = 1.26 (t, J = 7.1 Hz, 6 H, 2 CH_3), 1.53 (s, 4 H, Cpr), 4.22 (q, J = 7.1 Hz, 4 H, 2 CH_2O), 8.43 (s, 1 H, NH). ^{13}C NMR ($CDCl_3$): δ = 11.3 (2 CH_2), 14.0 (2 CH_3), 62.6 (2 CH_2), 65.5 (C), 67.9 (C), 167.0 (2 C). MS (CI): *m/z* (%) = 214 (100) [M − N_2 + H^+]. An analytical sample was obtained by kugelrohr distillation at 140−150 °C (0.01 Torr). $C_{10}H_{15}N_3O_4$ (241.25): calcd. C 49.79, H 6.27; found C 49.93, H 6.53.

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