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Ring Opening of Methylenecyclopropane Moieties in the Palladium-Catalyzed Cross-Coupling of Methylenecyclopropyl Bromides with Metallated CH-Acidic Compounds

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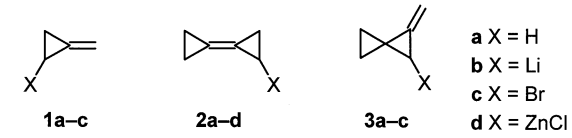
Palladium-catalyzed cross-coupling reactions of bromo(methylenecyclopropanes) **1c**, **2c** with the sodium enolate of dimethyl malonate **4a** and the chlorozinc enolates of the glycine equivalent (diphenylmethyleneamino)acetate **4c** and diethyl malonate **4d**, respectively, have been found to proceed with opening of the three-membered ring in each case, to give the corresponding dienyl-substituted CH-acidic compounds **5**−**7** in moderate to good yields. On the other hand, coupling of bicyclopropylidenylzinc chloride (**2d**) with diethyl bromomalonate (**4e**) and the electrophilic glycine equivalent ethyl 2-acetoxy-2-(diphenylmethyleneamino)acetate (**4f**) gave **7** and **6** in 27 and 29% yield, respectively.

Palladium-catalyzed nucleophilic substitution of allylic substrates with carbon nucleophiles, proceeding via π-allylpalladium intermediates, has become one of the most important C−C bond forming processes employed in modern organic synthesis[1]. The range of applicable allylic substrates covers a considerable structural variety, and even includes alkenylcyclopropyl derivatives[2]. The most commonly used carbon nucleophiles are malonate and other suitably stabilized ester enolates. The enolate of ethyl α-(diphenylmethyleneamino)acetate (O′Donnell′s glycine equivalent[3]) has frequently been employed in palladium-catalyzed allylic substitutions to prepare precursors of α-amino acids[4], including some containing a methylenecyclopropyl fragment[2b][2c]. Due to their wide-ranging biological activities, α- and β-amino acids containing a three-membered ring have attracted ever increasing interest over the last two decades[5]. In continuation of our investigations in this area[6] we have now tested the applicability of palladium-catalyzed allylic substitutions with the O′Donnell glycine equivalent in the preparation of amino acids containing a methylenecyclopropane fragment attached directly to the α-position[7].

The required starting materials, the allylic bromides 2-bromo-1-methylenecyclopropane (**1c**), bromobicyclopropylidene (**2c**), and 2-bromo-1-methylenespiropentane (**3c**) were prepared by deprotonation[8] of the corresponding hydrocarbons **1a**−**3a**[9] with butyllithium and subsequent reaction of the lithio derivatives **1b**−**3b** with 1,2-dibromoethane[8] (see Experimental Section).



4	a	b	c	d	e	f
X	CO_2Me	CO_2Et	CO_2Et	CO_2Et	CO_2Et	CO_2Et
Y	CO_2Me	$N{=}CPh_2$	$N{=}CPh_2$	CO_2Et	CO_2Et	$N{=}CPh_2$
M	Na	Li	ZnCl	ZnCl	Br	AcO

In order to find the appropriate conditions for the palladium-catalyzed substitution of **1c**−**3c** with stabilized enolates, 2-bromo-1-methylenecyclopropane (**1c**) was treated with dimethyl sodiomalonate (**4a**) in the presence of palladium bis(dibenzylideneacetonate) [$Pd(dba)_2$] and bis(diphenylphosphano)ethane (dppe), a commonly used catalyst system for such transformations[2][4]. This reaction proceeded smoothly at 60°C to give dimethyl (2′-buta-1′,3′-dienyl)malonate (**5**) as the only isolated product in 60% yield. Apparently, the substitution of bromine in **1c** had taken place only with complete ring opening of the three-membered ring. However, the lithiated glycine equivalent **4b** did not undergo this type of reaction with **2c** under such conditions. At room temperature, no reaction was observed, whereas upon heating the reaction mixture to 35°C, complete decomposition of the starting material **4b** was observed.

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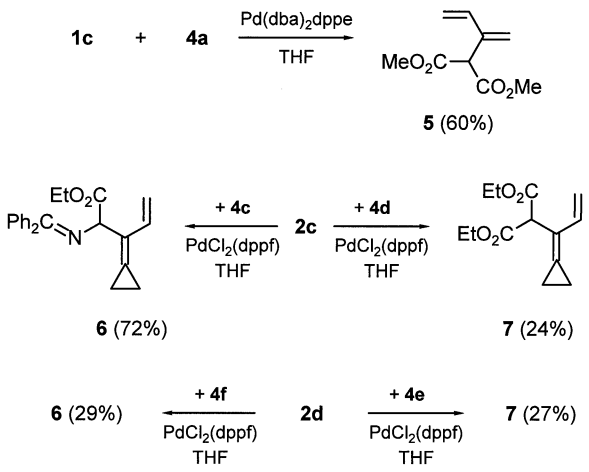
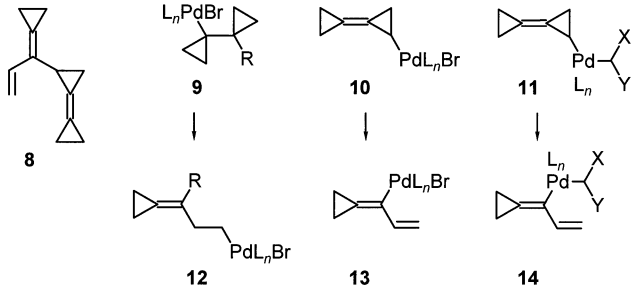
Scheme 1



Among the great number of palladium catalysts available, dichloro[1,1′-bis(diphenylphosphano)ferrocene]palladium(II) [$PdCl_2$(dppf)] has been reported to be by far the most active and selective in the coupling reactions of *n*-, *sec*-, and *tert*-alkylzinc and -magnesium halides, leading to high yields without any side reactions (β-elimination, etc.)[10]. Under the action of this catalyst, the coupling of 2-bromobicyclopropylidene (**2c**) with the chlorozinc derivative **4c** of the glycine equivalent (prepared from the lithio derivative **4b** by transmetallation with zinc chloride) proceeded even at room temperature, to give the dienyl-substituted glycine derivative **6** as the only isolated product in 72% yield. The structure of **6** is indicative of the same mode of cyclopropane ring opening as that seen in the reaction of **1c** with sodiomalonate to give **5**. Surprisingly, no reaction of the chlorozinc derivative **4c** with 2-bromo-1-methylenespiropentane (**3c**) could be observed under the same conditions, even after 56 h at room temperature.

In contrast, reaction of **2c** with the chlorozinc derivative of diethyl malonate **4d** in the presence of $PdCl_2$(dppf) gave the dienylmalonate **7**, but only in moderate yield (24%), along with some polymeric material. This result can be rationalized by assuming a rapid bromine exchange between the compounds **2c** and **4d**, leading to **2d** and diethyl bromomalonate **4e**. The subsequent palladium-catalyzed coupling of **2c** with **2d** would then presumably produce the triene **8**, which would be prone to polymerization. The ^{13}C-NMR spectrum of an unstable fraction with R_f = 0.73, isolated by column chromatography, showed signals consistent with the structure **8**. Thus, essentially the same product distribution was observed in the coupling of a twofold excess of the zinc derivative **2d** with diethyl bromomalonate **4e**, and compound **7** was isolated in 27% yield.

Formally, the structural transformations observed in these reactions are very similar to those reported for the coupling of bicyclopropylidene (**2a**) itself with haloarenes and alkenes under Heck conditions[11]. Mechanistically, however, there is a difference. Whereas in the Heck reaction of **2a**, ring opening occurs at the stage of the (cyclopropylmethyl)palladium intermediate **9**, in the reactions reported here, cyclopropylpalladium intermediates of the types **10** and/or **11** must be involved.

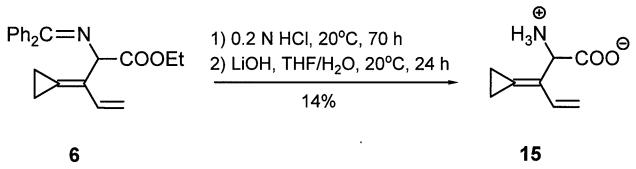


The conversion of **9** to **12** corresponds to the well-known (cyclopropylmethyl)metal to homoallylmetal[12a] rearrangement, while the conversion of **10** or **11** to **13** and **14**, respectively, is analogous to the cyclopropylmetal (or cyclopropyl carbanion) to allylmetal (or allyl anion) ring opening[12b].

To probe this mechanistic assumption, palladium-catalyzed coupling of O′Donnell′s electrophilic glycine equivalent, the acetate **4f**[13], with bicyclopropylidenylzinc chloride (**2d**) was examined. The chlorozinc derivative **2d** was generated by transmetallation of the lithio derivative **2b** with $ZnCl_2$. Indeed, only the cyclopropylideneallyl-substituted glycine derivative **6** was isolated from this reaction, albeit in only 29% yield. This result confirms that the ring opening can at least occur in a cyclopropylpalladium intermediate of type **11**.

Deprotection of compound **6** with 0.2 N hydrochloric acid followed by saponification (LiOH, THF/H_2O) yielded the amino acid **15**, which represents an interesting example of a highly unsaturated α-amino acid containing a methylenecyclopropane moiety (Scheme 2).

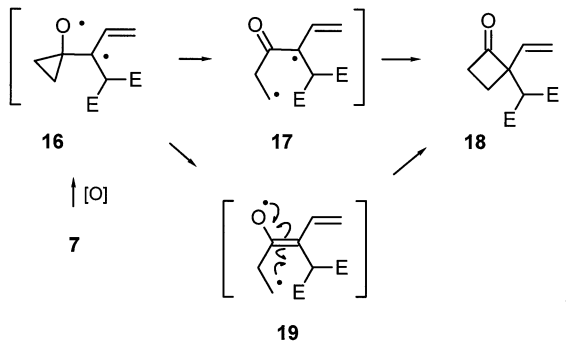
Scheme 2



The diene **7** was found to be rather unstable and polymerized even at −20°C, probably as a result of autooxidation. After a pure sample had been stored in a freezer for 6 months, only 4% of **7** could be recovered after repeated column chromatography, along with the cyclobutanone derivative **18** (9.2%). The ketone **18** can be formed from **7** via the intermediate diradicals **16**, **17**, or **19** (Scheme 3), with a cyclopropylmethyl to homoallyl radical rearrangement as a key step[14].

In conclusion, palladium-catalyzed reaction of 2-bromo-1-methylenecyclopropane (**1c**) and bromobicyclopropylidene (**2c**) with deprotonated CH-acidic compounds **4a**−**d** proceeds with an unexpected, yet readily rationalized ring opening of a three-membered ring, to produce dienyl-substituted derivatives **5**−**7**. Compound **15** represents a new potentially interesting amino acid incorporating a cyclopropylidenepropenyl substituent.

Scheme 3



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Experimental Section

^{1}H- and ^{13}C-NMR spectra: at 250 (^{1}H) and 62.9 MHz [^{13}C, additional DEPT (Distortionless Enhancement by Polarization Transfer)] on a Bruker AM 250 instrument in $CDCl_3$ solution, $CHCl_3$/$CDCl_3$ as internal reference. − FT-IR: Bruker IFS 66, measured as KBr pellets, or as oils between NaCl plates. − MS (EI) and MS (HR-EI): Finnigan MAT 95 spectrometer (70 eV). MS (HR-EI): pre-selected ion peak matching at $R >> 10\,000$ to be within ±2 ppm of the exact masses. − CI-MS: with NH_3. − TLC: Macherey-Nagel precoated sheets, 0.25 mm Sil G/UV$_{254}$. − Column chromatography: Merck silica gel, grade 60, 230−400 mesh.

Starting Materials: Anhydrous diethyl ether and THF were obtained by distillation from sodium benzophenone ketyl. Compounds **2a**[9a], **3a**[9c], **2c**[8], and **4f**[13] were prepared according to published procedures. All other chemicals were used as commercially available (Merck, BASF, Bayer, Hoechst, Degussa, and Hüls AG). Organic extracts were dried over $MgSO_4$. All reactions were performed under argon.

General Procedure (GP1) for the Preparation of Bromides **1c** *and* **3c**: *n*BuLi (10 mmol, 4.29 ml of a 2.33 M solution in hexane) was added to a solution of the hydrocarbon **1a**, **3a** (10 mmol) in anhydrous THF (20 ml) at −78°C. After stirring the solution at 0°C for 1 h, it was cooled to −78°C once more, whereupon 1,2-dibromoethane (1.08 ml, 12.5 mmol) was added. The mixture was allowed to warm to room temperature, then diluted with pentane (50 ml), and washed with water (10 × 50 ml) and satd. NaCl solution (100 ml). The organic layer was dried and slowly concentrated under normal (for **1c**) or reduced (for **3c**) pressure. The residue was bulb-to-bulb distilled (20°C, 0.1 Torr) to give **1c**, **3c** as colorless oils.

2-Bromomethylenecyclopropane (**1c**): From **1a** (0.82 ml, 0.70 g, 13 mmol), 0.94 g (54%) of **1c** was obtained according to GP1; b.p. 92°C. − ^{1}H NMR: δ = 0.78−1.45 (m, 2 H, Cpr), 3.45 (m, 1 H, CH), 5.65 (br. s, 1 H, =CH_2), 5.80 (br. s, 1 H, =CH_2). − ^{13}C NMR: δ = 12.77, 118.43 (CH_2), 35.32 (CH), 107.18 (C). − MS (EI), *m*/*z* (%): 134/132 (14/14) [M^+], 109/107 (43/41) [$M^+ - C_2H$], 53 (100) [$C_4H_5^+$]. − MS (HR-EI): 131.9574 (C4H5^{79}Br, calcd. 131.9575).

2-Bromo-1-methylenespiropentane (**3c**): From **3a** (0.761 g, 9.5 mmol), **3c** was obtained as a 59% solution in pentane (1.495 g, 59%) according to GP1. − ^{1}H NMR: δ = 1.25−1.35 (m, 2 H, Cpr), 1.36−1.42 (m, 1 H, Cpr), 1.50−1.58 (m, 1 H, Cpr), 3.82 (br. s, 1 H, CH), 5.31 (d, J = 1.5 Hz, 1 H, =CH_2), 5.65 (br. s, 1 H, =CH_2). − ^{13}C NMR: δ = 12.72, 14.40, 103.12 (CH_2), 23.40 (CH), 20.28, 136.29 (C). − MS (CI), *m*/*z* (%): 161/159 (25/44) [M^+ + H], 146/144 (11/16) [$M^+ - CH_2$], 133/131 (8/21) [$M^+ - C_2H_3$], 121 (100). − C_6H_7Br (159.0): calcd. C 45.32, H 4.44; found C 46.32, H 5.06.

Dimethyl (Buta-1,3-dien-2-yl)malonate (**5**): To a solution of bis(dibenzylideneacetone)palladium(0) [Pd(dba)$_2$] (53.4 mg, 92.9 μmol) and 1,2-bis(diphenylphosphano)ethane (dppe) (47.2 mg, 118 μmol) in THF (1 ml), which had been stirred for 5 min at room temp., was added 2-bromo-1-methylenecyclopropane (**1c**) (500 mg, 3.76 mmol). After 5−10 min, the solution turned green, and a solution of dimethyl sodiomalonate, freshly prepared from NaH (100 mg, 3.33 mmol, 80% in mineral oil) and dimethyl malonate (530 mg, 4.01 mmol) in THF (3 ml), was added dropwise. After stirring at 60°C for 24 h and allowing to cool, the solution was poured into diethyl ether (20 ml), and the resulting mixture was washed with 10% NH_4Cl solution (40 ml). The aqueous phase was extracted with diethyl ether (3 × 20 ml), the combined organic phases were dried, and then concentrated under reduced pressure. Column chromatography of the residue on silica gel (petroleum ether/Et_2O, 20:1) gave 415 mg (60%) of **5** as a colorless oil, which readily polymerized; R_f = 0.31. − ^{1}H NMR: δ = 3.33 (s, 1 H, CH), 3.79 (s, 6 H, 2 OCH_3), 5.13 (d, J = 11.0 Hz, 1 H, =CH_2), 5.20 (d, J = 17.5 Hz, 1 H, =CH_2), 5.27 (s, 1 H, =CH_2), 5.41 (s, 1 H, =CH_2), 6.39 (dd, J = 11.0, 17.5 Hz, 1 H, =CH). − ^{13}C NMR: δ = 52.31 (CH_3), 114.34, 120.18 (CH_2), 41.10, 137.07 (CH), 138.56, 166.91 (C). − MS (EI), *m*/*z* (%): 184 (15) [M^+], 153 (3) [$M^+ - CH_3O$], 125 (100) [$M^+ - CH_3CO_2$], 65 (37) [$M^+ - 2\,CH_3CO_2 - H$], 59 (55) [$CH_3CO_2^+$].

General Procedure (GP2) for the Palladium(0)-Catalyzed Substitution of the Allyl Bromide **2c**: To a stirred solution of lithium diisopropylamide (LDA), prepared from *n*BuLi (9 mmol, 3.86 ml of a 2.33 M solution in hexane) and diisopropylamine (1.33 ml, 9.5 mmol) in THF (50 ml), a solution of ethyl *N*-(diphenylmethylene)glycinate (2.406 g, 9 mmol) or diethyl malonate (1.442 g, 9 mmol) in THF (10 ml) was added dropwise at −75°C over a period of 1 h. After stirring for a further 1 h at this temperature, a solution of anhydrous $ZnCl_2 \cdot$THF complex[15] (2.085 g, 10 mmol) in THF (10 ml) was added to the suspension of lithio compound over a period of 15 min, with the temperature maintained at −75°C. The mixture was stirred for 0.5 h at 0°C and then for 1 h at 20°C, before being cannulated into a solution of bromobicyclopropylidene (**2c**) (1.590 g, 10 mmol) and $PdCl_2$(dppf) (365 mg, 5 mol%) in THF (40 ml) at 0°C. After stirring for 24 h at 20°C, the solution was poured into a cold, satd. NH_4Cl solution (40 ml), the resulting mixture was diluted with diethyl ether (20 ml), and the organic layer was separated. It was washed with satd. NH_4Cl solution, dried, and concentrated under reduced pressure, and the residue was purified by column chromatography on silica gel deactivated with ammonia.

Ethyl N-(Diphenylmethylene)(1-cyclopropylideneprop-2-enyl)glycinate (**6**): By reaction of **2c** (1.431 g, 9.0 mmol) and **4b** [prepared from ethyl *N*-(diphenylmethylene)glycinate (2.388 g, 9 mmol), *n*BuLi (9.4 mmol, 4.03 ml of a 2.33 M solution in hexane), diisopropylamine (1.33 ml, 9.5 mmol) and anhydrous $ZnCl_2 \cdot$THF (2.126 g, 10.2 mmol) in THF (50 ml)] according to GP2, 2.232 g (72%) of **6** was obtained after column chromatography (100 g of deactivated silica gel, 40 × 4 cm, hexane/EtOAc, 3:1); R_f = 0.49, m.p. 32−34°C (H_2O/MeOH). − ^{1}H NMR: δ = 0.84−1.05 (m, 2 H, Cpr), 1.03−1.35 (m, 2 H, Cpr), 1.22 (t, J = 7.1 Hz, 3 H, CH_3),

4.19 (q, J = 7.1 Hz, 2 H, OCH_2), 5.09 (s, 1 H, CH), 5.12 (d, J = 11.3 Hz, 1 H, $=CH_2$), 5.52 (d, J = 17.8 Hz, 1 H, $=CH_2$), 6.55 (dd, J = 11.3, 17.8 Hz, 1 H, =CH), 7.09−7.88 (m, 10 H, Ph-H). − ^{13}C NMR: δ = 14.17 (CH_3), 2.67, 3.02, 60.95, 114.0 (CH_2), 127.94, 128.30, 128.42, 128.87 (2 CH), 68.12, 128.54, 130.25, 134.70 (CH), 125.63, 128.11, 136.30, 139.50, 169.89, 171.60 (C). − MS (EI), *m/z* (%): 345 (18) [M^+], 272 (50) [$M^+ - CO_2C_2H_5$], 182 (70) [$NH_2CPh_2^+$], 165 (16) [$M^+ - NCPh_2$], 105 (100) [$C_7H_7N^+$], 77 (43) [$C_6H_5^+$], 51 (10) [$C_4H_3^+$]. − MS (HR-EI): 345.1728 ($C_{23}H_{23}NO_2$, calcd. 345.1729). − $C_{23}H_{23}NO_2$ (345.4): calcd. C 79.97, H 6.71; found C 80.02, H 6.47.

To a suspension of **2b**, prepared from **2a** (1.800 g, 22.5 mmol) and *n*BuLi (22.5 mmol, 9.67 ml of a 2.33 M solution in hexane) as described above, a solution of anhydrous $ZnCl_2 \cdot THF$ (5.620 g, 27 mmol) in THF (15 ml) was added at −78°C. After stirring at 20°C for 1 h, the solution was cannulated into a mixture of **4f** (4.880 g, 15 mmol) and $PdCl_2$(dppf) (548 mg, 5 mol%) in THF (100 ml). After stirring this mixture at 20°C for 24 h, the solution was worked-up according to GP2. Yield 1.488 g (29%) of **6** after column chromatography (200 g of deactivated silica gel, 40 × 5 cm, hexane/Et_2O, 7:3).

Diethyl (1-Cyclopropylideneprop-2-enyl)malonate (**7**): By reaction of **2c** (1.590 g, 10.0 mmol) and **4d** [prepared from *n*BuLi (10.5 mmol, 4.51 ml of a 2.33 M solution in hexane), diisopropylamine (1.47 ml, 10.5 mmol), diethyl malonate (1.52 ml, 10.0 mmol), and a solution of anhydrous $ZnCl_2 \cdot THF$ (2.50 g, 12 mmol) in THF (15 ml) as described above] according to GP2, **7** (0.563 g, 24%) was obtained after column chromatography on deactivated silica gel (hexane/diethyl ether, 5:2); R_f = 0.40. − IR (film): $\tilde{\nu}$ = 2982 cm^{-1}, 1734, 1446, 1368, 1311, 1247, 1153, 1035. − ^{1}H NMR: δ = 1.20−1.29 (m, 10 H, 2 Cpr, 2 CH_3), 4.14−4.25 (m, 4 H, 2 OCH_2), 4.49 (br. s, 1 H, CH), 5.04 (d, J = 12.8 Hz, 1 H, $=CH_2$), 5.10 (d, J = 19.2 Hz, 1 H, $=CH_2$), 6.59 (dd, J = 12.8, 19.2 Hz, 1 H, =CH). − ^{13}C NMR: δ = 13.96 (2 CH_3), 61.41 (2 CH_2), 2.27, 3.55, 111.62 (CH_2), 53.94, 136.29 (CH), 120.57, 129.84, 168.01 (C). − MS (EI), *m/z* (%): 238 (3) [M^+], 209 (7) [$M^+ - C_2H_5$], 165 (100) [$M^+ - CO_2C_2H_5$], 137 (5), 119 (17), 91 (27). − MS (HR-EI): 238.1205 ($C_{13}H_{18}O_4$, calcd. 238.1205). − $C_{13}H_{18}O_4$ (238.3): calcd. C 65.53, H 7.61; found C 65.27, H 7.81.

The solution of **2d**, prepared as described above from **2a** (1.593 g, 19.9 mmol), *n*BuLi (19.9 mmol, 8.54 ml of a 2.33 M solution in hexane) in THF (35 ml) and anhydrous $ZnCl_2 \cdot THF$ (4.585 g, 22 mmol) in THF (10 ml), was cannulated into a mixture of diethyl bromomalonate (**4e**) (2.391 g, 1.71 ml, 10 mmol) and $PdCl_2$(dppf) (366 mg, 5 mol%) in THF (50 ml). After stirring at 20°C for 24 h, the solution was worked-up according to GP2. Yield 0.641 g (27%) of **7** after column chromatography (150 g of deactivated silica gel, 40 × 4 cm, hexane/Et_2O, 5:2).

[3-(Cyclopropylidene)prop-1-en-3-yl]glycine (**15**): Compound **6** (2.304 g, 6.67 mmol) was stirred in 0.2 N HCl solution (200 ml) for 70 h at 20°C, completely protected from light. The reaction mixture was adjusted to pH 8 with conc. NH_4OH solution and then extracted with Et_2O. After concentration under reduced pressure, the ethereal extract was diluted with a 3:1 mixture of THF and H_2O (120 ml) and stirred with LiOH (156 mg, 6.5 mmol) for 24 h at 20°C. The reaction mixture was then concentrated under reduced pressure and brought to pH 2 with 0.2 N HCl solution. Subsequent concentration of the solution, filtration through Dowex-50 (3 × 20 cm column, eluent 0.9 N NH_4OH), followed by repeated concentration and recrystallization from acetone/H_2O gave 139 mg (14%) of **15**, m.p. 148−150°C (decomp.). − IR (KBr): $\tilde{\nu}$ = 2978 cm^{-1}, 1735, 1617, 1576, 1446, 1284, 1181, 1030, 911, 732, 696. − ^{1}H NMR (D_2O): δ = 1.05 (br. s, 4 H, Cpr), 4.47 (s, 1 H, CH), 5.00 (d, J = 11.0 Hz, 1 H, $=CH_2$), 5.15 (d, J = 18.4 Hz, 1 H, $=CH_2$), 6.36 (dd, J = 11.0, 18.4 Hz, 1 H, =CH). − ^{13}C NMR (D_2O): δ = 3.23, 4.09, 114.38 (CH_2), 55.40, 135.81 (CH), 122.69, 134.63, 174.56 (C). − MS (CI), *m/z* (%): 187 (100) [$M^+ + 2\ NH_3$]. − $C_8H_{11}NO_2$ (153.2): calcd. C 62.72, H 7.24; found C 62.58, H 7.11.

Diethyl (2-Vinylcyclobutan-1-one-2-yl)malonate (**18**): Compound **7** (500 mg, 2.1 mmol) was stored at −20°C for 6 months. Thereafter, repeated column chromatography on deactivated silica gel (50 g, column 25 × 3.2 cm, hexane/Et_2O, 5:2) gave **7** (21 mg, 4.2%) and **18** (49 mg, 9.2%); R_f = 0.32. − ^{1}H NMR: δ = 1.22 (t, J = 7.1 Hz, 3 H, CH_3), 1.24 (t, J = 7.1 Hz, 3 H, CH_3), 2.17 (dt, J = 12.1, 7.7 Hz, 1 H, CH_2), 2.57 (dt, J = 12.1, 9.0 Hz, 1 H, CH_2), 3.08 (dd, J = 7.7, 9.0 Hz, 2 H, CH_2), 4.16 (q, J = 7.1 Hz, 2 H, OCH_2), 4.17 (s, 1 H, CH), 4.18 (q, J = 7.1 Hz, 2 H, OCH_2), 5.23 (d, J = 10.3 Hz, 1 H, $=CH_2$), 5.29 (d, J = 16.7 Hz, 1 H, $=CH_2$), 5.81 (dd, J = 10.3, 16.7 Hz, 1 H, =CH). − ^{13}C NMR: δ = 13.86, 13.97 (CH_3), 19.95, 43.61, 61.43, 61.86, 116.72 (CH_2), 56.44, 134.68 (CH), 68.67, 166.80, 167.28, 207.51 (C). − MS (EI), *m/z* (%): 254 (4) [M^+], 180 (8) [$M^+ - H - CO_2C_2H_5$], 160 (8) [$M^+ - C_6H_6O$], 133 (61) [$M^+ - C_6H_7O - C_2H_2$], 115 (100) [$M^+ - C_6H_7O - C_2H_2 - H_2O$], 111 (5), 88 (32). − MS (HR-EI): 254.1154 ($C_{13}H_{18}O_5$, calcd. 254.1154). − $C_{13}H_{18}O_5$ (254.3): calcd. C 61.41, H 7.14; found C 61.72, H 7.35.

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