Ring-opening reactions of cyclopropanes. Part 7.[1] Selenenylation and cyanoselenenylation of ethyl 2,2-dimethoxycyclopropanecarboxylates

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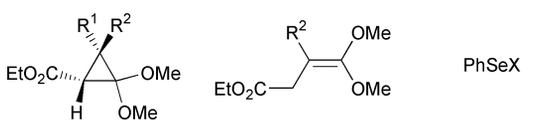
The uncatalyzed reaction of C3-substituted cyclopropanes **1b–d** with benzeneselenenyl chloride **3** leads to 1-ethyl 4-methyl 2-(phenylseleno)butanedioates **5b–d** while the unsubstituted **1a** gives the 3-phenylseleno derivative **6a**. Formation of **5b–d** occurs regio- and stereoselectively *via* electrophilic ring-opening of **1** while **6a** results from the selenenylation of the alkene **2a** formed *via* isomerization of **1a**. The presence of $TiCl_4$ influences the stereochemistry of the reaction with chloride **3** while it is essential for reaction of the less reactive PhSeCN **4**. With this electrophile the reactions lead to α,α-dimethoxycarbonitriles **13a–d** while only **1a** and **1b** give also the expected cyanoselenenyl derivatives **12a** and **12b**. Moreover, from **1b** compound *syn*- **5b** is obtained, and **1a** gives, *via* the alkene **2a**, esters **14a** and **6a**. A mechanistic interpretation suggests the intermediacy of well-stabilized dipolar species **9** which should be formed by coordination of the Lewis acid to the carbonyl oxygen of **1** and subsequent ring opening.

Introduction

Vicinally donor–acceptor-substituted cyclopropanes are versatile building blocks in organic synthesis.[2] In particular, due to the push–pull combination of the *gem*-dialkoxy and alkoxycarbonyl groups, alkyl 2,2-dialkoxycyclopropanecarboxylates, *e.g.* **1** (Fig. 1) undergo easy regioselective ring-opening at the



a; R^1=R^2=H
b; R^1=H R^2=Me
c; R^1=H R^2=Et
d; R^1=R^2=Me

Fig. 1

C1–C2 bond by various unsaturated electrophiles such as heterocumulenes,[3a] alkenes,[3b] alkynes,[3c] carbonyl compounds,[3d] diazenes[3e] or oxidants[4] leading to interesting compounds. In many cases, this electrophilic ring-opening competes with the isomerization to 1,1-dialkoxyalkenes, *e.g.* **2**, especially for C3-unsubstituted derivatives.[1,3a,5] Recently, we reported that cyclopropanes **1** react smoothly also with saturated electrophiles such as sulfenyl chlorides and afford 1-ethyl 4-methyl 2-sulfenylbutanedioates and/or their 3-sulfenyl analogues, the latter deriving from the addition of the reagents to the alkenes **2**.[1] Continuing our investigation into the ring-opening of cyclopropanes **1** in order to identify new methods for compounds of applicative or biological interest, we examined the reaction of **1a–d** with benzeneselenenyl chloride **3** and phenyl selenocyanate **4**. It also appeared interesting to compare the data for areneselenenylation with those previously reported for arenesulfenylation since the reactivity of selenenyl compounds is often compared with that of their sulfenyl analogues.[6–8]

Both benzeneselenenyl chloride **3** and phenyl selenocyanate **4** add to alkenes giving rise to interesting compounds.[9] However, while the halide **3** reacts easily, the presence of a Lewis acid catalyst is necessary in the reactions of cyanate **4**,[10] with the exception of strongly nucleophilic alkenes such as enamines[11] or ketene acetals.[12] While no examples of cyanoselenenylation in cyclopropane derivatives have been hitherto reported, the addition of benzeneselenenyl chloride **3**[8,13] or analogues[14] has been found to occur in cyclopropane rings that form part of highly strained molecular frameworks. Moreover, selenenylation by chloride **3** has been also described for various 2-(trimethylsiloxy)cyclopropanecarboxylates but it occurs easily only if promoted by $TiCl_4$.[7]

Results and discussion

The reaction of the cyclopropanes **1a–d** with the halide **3** was performed under strictly anhydrous conditions at room temperature using CCl_4 as solvent and an equimolecular amount of **3**. The reaction was complete within 15 min for **1a–c** and within 24 h for **1d** (disappearance of the red colour of **3**). As shown in Scheme 1 and Table 1, cyclopropanes **1b–d** led to 1-ethyl 4-methyl 2-(phenylseleno)butanedioates **5b–d**; in particular, cyclopropanes **1b**,**c** which are of *trans*-configuration gave *syn*-**5b**,**c** preferentially. The only reaction product obtained from **1a** was the 3-phenylseleno derivative **6a**, and control experiments showed that it is formed through selenenylation of the alkene **2a** deriving from the isomerization of **1a**. In addition to the products **5b–d** and **6a**, NMR analysis showed the presence of MeCl in all the reaction mixtures, but it could not be quantified owing to its high volatility.

The reaction of cyclopropanes **1a–d** with halide **3** was also performed in the presence of $TiCl_4$ at −78 °C. As shown in Table 1, the catalyst influenced the ratio of the *syn* and *anti* isomers **5b**,**c** and enhanced the yield of **5d** while it had no effect on the reaction of **1a**.

The products were separated and purified chromatographically and satisfactory analytical and spectroscopic data were

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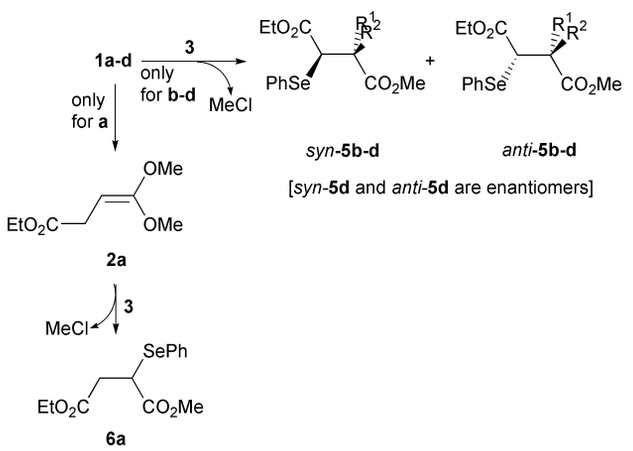
Table 1 Reactions of cyclopropanes **1a–d** with benzeneselenenyl chloride **3** in the absence[a] and in the presence[b] of $TiCl_4$

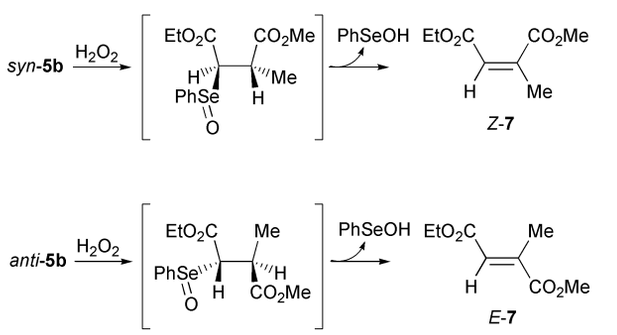
Cyclopropane	Reaction conditions	Product (Yield %)[c] **5** (*syn*/*anti*)	**6**
1a	**3**		65[d]
1a	**3**/$TiCl_4$		60
1b	**3**	60 (85/15)	
1b	**3**/$TiCl_4$	50 (50/50)	
1c	**3**	57 (80/20)	
1c	**3**/$TiCl_4$	55 (55/45)	
1d	**3**	15	
1d	**3**/$TiCl_4$	45	

[a] Equimolecular amounts of **1** and **3**; dry CCl_4; room temperature; 15 min (24 h for **1d**). [b] Equimolecular amounts of **1**, **3** and $TiCl_4$; dry CH_2Cl_2; −78 °C; 2 h. [c] Yield and isomeric ratio were evaluated by chromatography. [d] Compound **6a** can be obtained in 70% yield by treating **2a** under the same conditions used for **1a**.



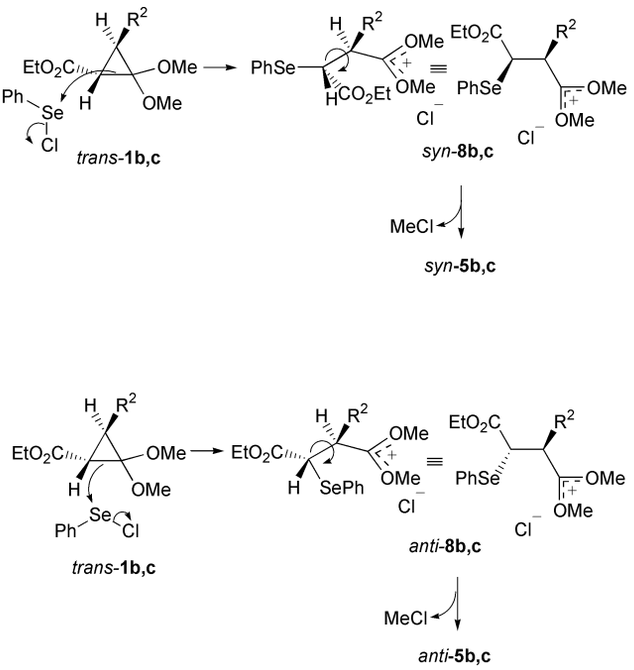
Scheme 1

obtained for all of them. Since the diastereomeric pairs **5b**,**c** exhibited the same value of the vicinal coupling constant for both isomers, configuration was assigned on the basis of a straightforward comparison of ^{1}H NMR spectral data with those of the corresponding thio analogues.[1] For the pair **5b** the *syn*-isomer shows the doublet due to 3-CH_3 (δ 1.43) at lower field than that for the *anti*-isomer (δ 1.27) while the signal for CO_2Me (δ 3.64) is at higher field than that of the *anti* (δ 3.73). For the pair **5c** the *syn*-isomer shows signals due to the chain methylene in the δ range 1.7–2.2 and the *anti*-counterpart in the δ range 1.5–1.8.[1] Configuration of pair **5b** was also confirmed chemically by stereoselective obtaining of the alkenes[15] (*Z*)-**7** or (*E*)-**7** from *syn*- or *anti*-**5b**, respectively, *via* the well-known oxidative selenoxide *syn*-elimination[16] (Scheme 2).



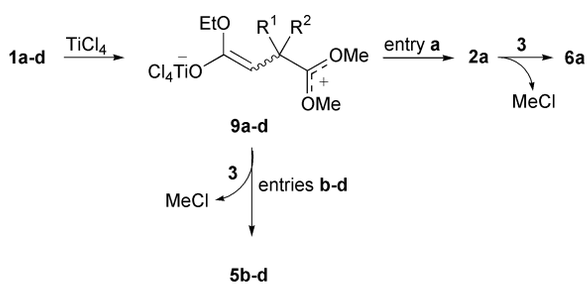
Scheme 2

The results given in Table 1 for **1b–d** may be explained in terms of the two classical competitive corner and edge attacks of an electrophile at a cyclopropane ring.[17] A representation of



Scheme 3

the two pathways is shown in Scheme 3 using *trans*-**1b**,**c** as substrates in order to evidence the configurations of the reaction products, too. The S_E2-type corner attack, which occurs with inversion of configuration at C1, should generate the well-stabilized ionic *syn* intermediates **8b**,**c** which, through an S_N2 type displacement, should lead to *syn*-**5b**,**c** and MeCl. Instead, the edge attack leads, with retention at the same carbon C1, to *anti*-**5b**,**c** and MeCl (Scheme 3). The high *syn* diastereoselectivity observed is due to the preferred corner attack as previously found in the sulfenylation.[1] In the presence of $TiCl_4$ we assume that, as reported,[3d,7] the Lewis acid promotes ring opening to the dipolar species **9** which may be attacked at both sides as shown by the obtaining of an almost equimolecular mixture of the *syn* and *anti*-isomers **5b**,**c** (Table 1, Scheme 4).



Scheme 4

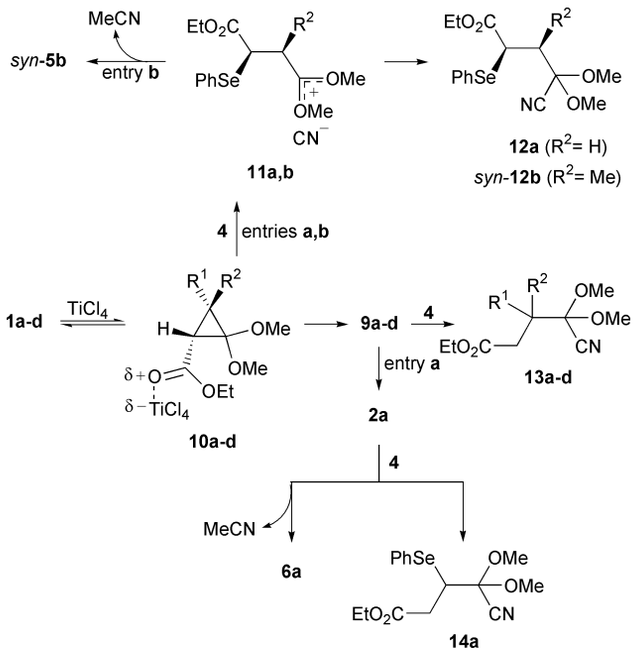
Unlike **1b–d**, the C3-unsubstituted **1a** never affords **5a** but only **6a**, which is the adduct to the alkene **2a**. This suggests that in the presence of $TiCl_4$ the intermediate **9a** once formed promptly isomerizes to **2a** before adding the electrophile **3**.[18] In the absence of $TiCl_4$ it is necessary to assume that the formation of **2a** is induced by selenenyl halide acting as Lewis acid catalyst since the uncatalyzed isomerization of **1a** occurs at prolonged times and high temperature.[5]

As expected, no reaction of **1a–d** took place with the less reactive PhSeCN **4** at both room temperature and at reflux in the absence of a catalyst, and only unchanged cyclopropane or its alteration product was observed (see Experimental section). When $TiCl_4$ was used, the best procedure was to add one equivalent of the acid to a precooled solution of equimolecular amounts of **1** and **4** at −78 °C. As shown in Scheme 5 and Table 2, all of the cyclopropanes **1a–d** gave the carbonitriles **13a–d** while only **1a** and **1b** led to 2-phenylseleno-4-cyanobutanoates

Table 2 Product distribution in the reactions of cyclopropanes **1a–d** with phenyl selenocyanate **4**[a]

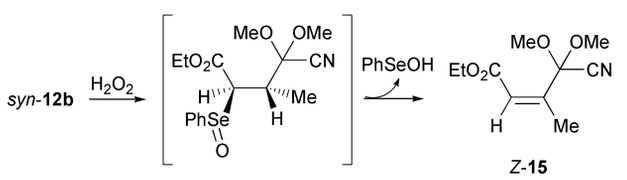
	Yields (%)[b]				
Cyclopropane	**5**	**6**	**12**	**13**	**14**
1a		10	20	20	6
1b	15[c]		22[c]	20	
1c				35	
1d				30	

[a] Equimolecular amounts of **1**, **4** and $TiCl_4$; dry CH_2Cl_2; −78 °C; 2 h. [b] Yield by chromatography. [c] *syn*-Isomer.



Scheme 5

12a and *syn*-**12b** which derive from the addition of the reagent **4** to the C1–C2 ring bond. Moreover, the cyclopropane **1b** also gave *syn*-**5b**, and **1a** led to **6a** and the 3-phenylseleno-4-cyanobutanoate **14a**, both of which are formed *via* the alkene **2a**, as confirmed by control experiments. All of the products were isolated and fully characterized. Stereochemistry of *syn*-**12b** was assigned by converting it, according to the above procedure, to the *Z*-alkene **15** (Scheme 6), whose configuration



Scheme 6

was determined on the basis of an NOESY experiment This showed NOE effects between Me and H as well as between OCH_2 and OMe.

Control experiments showed that: i) prolonged reaction times did not affect product distribution; ii) compounds **5b**, **6a**, **12a**,**b**, **13a–d**, **14a** were stable under the reaction conditions.

The peculiar results obtained by using selenocyanate **4** as electrophile can be explained by taking into account the experimental procedure used (the addition of $TiCl_4$ to the mixture of **1** and **4**), the lower reactivity of **4** than that of selenenyl chloride **3**, and the higher nucleophilicity of CN than the Cl moiety. Scheme 5 shows a reasonable mechanistic hypothesis. According to literature reports,[19] it is likely that the addition of $TiCl_4$ generates the primary complexes **10** which, at least in the cases of the more reactive[1] **1a**,**b**, are partly attacked by the selenocyanate through the preferred S_E2 mode and lead to the adducts **12a** and *syn*-**12b** *via* intermediates **11a**,**b**. Substitution at C3 should stabilize the positive charge of the intermediate **11b** so that an S_N2 type of displacement by cyanide can compete and give *syn*-**5b** and MeCN. For all cyclopropanes **1a–d** the primary complexes **10a–d** collapse to the dipolar species **9a–d** which lead to carbonitriles **13a–d** by the nucleophilic trapping of cyanide at the positive site and the subsequent hydrolytic work-up. As suggested above, the intermediate **9a** can partly isomerize to alkene **2a**, which adds the electrophile **4** leading to **14a** or, *via* an S_N2 nucleophilic displacement of the cyanide, to **6a** and MeCN.

Conclusions

This work confirms the role of donor–acceptor-substituted cyclopropanes **1** as building blocks for compounds of synthetic and applicative interest. They react with electrophilic selenenyl reagents such as **3** and **4** leading to selenobutanedioates or selenobutanoates *via* regioselective ring-opening at C1–C2 bond. Moreover, with selenocyanate **4** the functionalized α,α-dimethoxycarbonitriles **12–14** are formed in which the carbonyl group is protected as a ketal from nucleophilic attack and, hence, they would be especially suited to undergo selective nucleophilic reactions at the cyano carbon.

It is interesting to note that the results appear to indicate a higher reactivity, towards cyclopropanes **1**, of benzeneselenenyl chloride **3** than that of its thio analogue. Indeed, **3** is able to add without a catalyst even to disubstituted **1d**. For unsubstituted **1a**, however, isomerization is still faster than ring addition, as is also observed in the sulfenylation.[1]

Experimental

IR spectra were recorded on a Perkin-Elmer 1760/X-FT spectrophotometer using $CHCl_3$ as solvent. ^1H and ^{13}C NMR spectra were recorded with a Varian Gemini-300 spectrometer using $CDCl_3$ as solvent and Me_4Si as internal standard. *J*-Values are given in Hz. DEPT techniques were employed to determine the multiplicity in the ^{13}C NMR spectra. Elemental analyses were performed using a Carlo Erba EA 1108-Elemental analyzer. Low-resolution electron-impact mass spectra were obtained operating at 70 eV on a GCMS-QP5050A (Shimadzu). HPLC was performed on a Shimadzu LC-9A instrument equipped with an LCA-Shimadzu UV detector using a Merck Lichrosorb Si-60 (10 μm) column with 3 cm^3 min^{-1} flow rate of elution. CCl_4, and CH_2Cl_2 used in the reactions were anhydrous. Silica gel [0.063–0.20 mm (Macherey-Nagel)] and light petroleum (boiling range 40–60 °C) were used for column chromatography. TLC was performed on silica gel layers (Whatman PK6F). Cyclopropanes **1a**,[5] *trans*-**1b**,[5] *trans*-**1c**,[20] **1d**[5] and alkene **2a**[5] were prepared according to literature methods. Benzeneselenenyl chloride **3** was purchased from Fluka and used without purification while phenyl selenocyanate **4** was prepared from **3** and trimethylsilyl cyanate as reported.[21]

Selenenylation of cyclopropanes 1a–d

To a 0.2 mol dm^{-3} solution of **1** (1 mmol) in dry CCl_4 an equimolecular amount of benzeneselenenyl chloride **3** was added and the resulting mixture was kept under strictly anhydrous conditions[5,20] at room temperature until complete disappearance of the red colour of the selenenyl halide (15 min for **1a–c**, 24 h for **1d**). The completion of the reaction was confirmed by ^1H NMR analysis of a sample of the tetrachloride solution, recorded in $CDCl_3$, which also showed the presence of MeCl in all the reaction mixtures. The solvent was then removed under

reduced pressure and the residue chromatographed on silica gel. For the residues obtained starting from cyclopropanes **1a** and **1d** elution with light petroleum–Et_2O (9 : 1 v/v) gave the esters **6a** (204 mg, 65%) and **5d**, respectively. From cyclopropanes **1b**,**c** column chromatography as above led to a mixture of *syn*- and *anti*-**5b**,**c** which were separated by HPLC eluting with hexane–*tert*-butyl methyl ether (17 : 3 v/v). The new compound **6a** was identified by comparison with an authentic sample synthesized independently (see below).

1-Ethyl 4-methyl 3-methyl-2-(phenylseleno)butanedioate (*syn*-5b). Oil (164 mg, 50%); t_R = 9.9 min; ν_{max}/cm^{-1} 1729; δ_H 1.18 (3 H, t, *J* 7.0, OCH_2CH_3), 1.43 (3 H, d, *J* 7.0, 3-CH_3), 2.85 (1 H, m, *J* 10.3 and 7.0, 3-H), 3.64 (3 H, s, OCH_3), 3.71 (1 H, d, *J* 10.3, 2-H), 4.09 (2 H, m, *J* 7.0, OCH_2), 7.26–7.65 (5 H, m, C_6H_5); δ_C 13.9 (q), 16.3 (q), 40.9 (d), 46.4 (d), 51.9 (q), 61.0 (t), 128.8 (d), 129.1 (d), 129.6 (s), 135.8 (d), 172.2 (s), 174.9 (s); *m*/*z* (EI) 330 (M^+, ^{80}Se), 328 (M^+, ^{78}Se). Found: C, 51.1; H, 5.4. $C_{14}H_{18}O_4Se$ requires C, 51.07; H, 5.51%.

1-Ethyl 4-methyl 3-methyl-2-(phenylseleno)butanedioate (*anti*-5b). Oil (32 mg, 10%); t_R = 7.6 min; ν_{max}/cm^{-1} 1729; δ_H 1.19 (3 H, t, *J* 7.0, OCH_2CH_3), 1.27 (3 H, d, *J* 6.9, 3-CH_3), 3.01 (1 H, m, *J* 10.2 and 6.9, 3-H), 3.73 (3 H, s, OCH_3), 3.76 (1 H, d, *J* 10.2, 2-H), 4.10 (2 H, m, *J* 7.0, OCH_2), 7.25–7.65 (5 H, m, C_6H_5); δ_C 14.0 (q), 16.6 (q), 42.2 (d), 45.9 (d), 52.0 (q), 61.1 (t), 127.9 (s), 128.7 (d), 129.0 (d), 135.9 (d), 171.2 (s), 174.3 (s); *m*/*z* (EI) 330 (M^+, ^{80}Se), 328 (M^+, ^{78}Se). Found: C, 51.0; H, 5.5. $C_{14}H_{18}O_4Se$ requires C, 51.07; H, 5.51%.

1-Ethyl 4-methyl 3-ethyl-2-(phenylseleno)butanedioate (*syn*-5c). Oil (157 mg, 46%); t_R = 9.7 min; ν_{max}/cm^{-1} 1728; δ_H 0.88 (3 H, t, *J* 7.3, CH_2CH_3), 1.17 (3 H, t, *J* 7.3, OCH_2CH_3), 1.74–2.20 (2 H, m, CH_2), 2.75 (1 H, m, 3-H), 3.64 (3 H, s, OCH_3), 3.77 (1 H, d, *J* 11.2, 2-H), 4.08 (2 H, q, *J* 7.3, OCH_2), 7.25–7.64 (5 H, m, C_6H_5); δ_C 10.3 (q), 13.8 (q), 23.3 (t), 44.5 (d), 47.0 (d), 51.8 (q), 60.9 (t), 127.1 (s), 128.8 (d), 129.0 (d), 135.9 (d), 172.3 (s), 174.2 (s); *m*/*z* (EI) 344 (M^+, ^{80}Se), 342 (M^+, ^{78}Se). Found: C, 52.4; H, 5.9. $C_{15}H_{20}O_4Se$ requires C, 52.48; H, 5.87%.

1-Ethyl 4-methyl 3-ethyl-2-(phenylseleno)butanedioate (*anti*-5c). Oil (38 mg, 11%); t_R = 6.4 min; ν_{max}/cm^{-1} 1728; δ_H 0.90 (3 H, t, *J* 7.1, CH_2CH_3), 1.18 (3 H, t, *J* 7.0, OCH_2CH_3), 1.55–1.77 (2 H, m, CH_2), 2.88 (1 H, m, 3-H), 3.72 (d, *J* 11.2) and 3.74 (s) (together 4 H, 2-H and OCH_3), 4.10 (2 H, m, OCH_2), 7.25–7.65 (5 H, m, C_6H_5); δ_C 11.7 (q), 13.9 (q), 25.2 (t), 45.0 (d), 49.3 (d), 51.7 (q), 61.1 (t), 127.9 (s), 128.8 (d), 129.0 (d), 135.9 (d), 171.3 (s), 173.8 (s); *m*/*z* (EI) 344 (M^+, ^{80}Se), 342 (M^+, ^{78}Se). Found: C, 52.6; H, 5.8. $C_{15}H_{20}O_4Se$ requires C, 52.48; H, 5.87%.

1-Ethyl 4-methyl 3,3-dimethyl-2-(phenylseleno)butanedioate (5d). Oil (52 mg, 15%); ν_{max}/cm^{-1} 1723; δ_H 1.19 (3 H, t, *J* 7.1, OCH_2CH_3), 1.43 and 1.46 (6 H, 2 s, 2 × 3-Me), 3.65 (3 H, s, OCH_3), 3.82 (1 H, s, 2-H), 4.12 (2 H, m, OCH_2), 7.23–7.70 (5 H, m, C_6H_5); δ_C 13.9 (q), 23.7 (q), 23.9 (q), 45.0 (s), 52.0 (q), 53.8 (d), 60.8 (t), 128.1 (d), 129.1 (d), 130.1 (s), 134.7 (d), 172.2 (s), 176.0 (s); *m*/*z* (EI) 344 (M^+, ^{80}Se), 342 (M^+, ^{78}Se). Found: C, 52.5; H, 5.9. $C_{15}H_{20}O_4Se$ requires C, 52.48; H, 5.87%.

Selenenylation of alkene 2a with selenenyl chloride 3

A 0.2 mol dm^{-3} solution of alkene **2a** (1 mmol) in dry CCl_4 was treated with halide **3** as reported above for **1a**. Then, the solvent was removed and chromatography of the residue on silica gel and elution with light petroleum–Et_2O (9 : 1 v/v) gave *1-ethyl 4-methyl 3-(phenylseleno)butanedioate* **6a** (220 mg, 70%) as an oil; t_R = 15.7 min (hexane–*tert*-butyl methyl ether, 9 : 1); ν_{max}/cm^{-1} 1734; δ_H 1.21 (3 H, t, *J* 7.0, CH_3), 2.70 (1 H, dd, *J* 17.4 and 5.9) and 2.89 (1 H, dd, *J* 17.4 and 9.9) (together CH_2), 3.68 (3 H, s, OCH_3), 4.01 (1 H, m, 3-H), 4.04 (2 H, q, *J* 7.0, OCH_2), 7.23–7.65 (5 H, m, C_6H_5); δ_C 13.7 (q), 36.7 (t + d), 51.9 (q), 60.5 (t), 126.3 (s), 128.7 (two overlapping d), 135.9 (d), 170.5 (s), 172.1(s); *m*/*z* (EI) 316 (M^+, ^{80}Se), 314 (M^+, ^{78}Se). Found: C, 49.5; H, 5.2. $C_{13}H_{16}O_4Se$ requires C, 49.53; H, 5.12%.

Selenenylation in the presence of $TiCl_4$

To a 0.2 mol dm^{-3} solution of a cyclopropane **1** (1 mmol) in dry CH_2Cl_2, kept at −78 °C, was added an equimolecular amount of $TiCl_4$ under nitrogen and the mixture was stirred. After 30 min, to the red solution, maintained at −78 °C, was added one equivalent of PhSeCl **3** in CH_2Cl_2 (4 cm^3) and stirring was continued for 2 hours. After addition of THF–water (1 : 1; 1 cm^3), the mixture was warmed to room temperature and then extracted with CH_2Cl_2 (3 × 5 cm^3). The combined extracts were dried ($MgSO_4$) and, finally, evaporated. Chromatography of the residues carried out as above gave the ester **6a** starting from **1a** and the esters **5b**–**d** starting from **1b**–**d** with the yields reported in Table 1.

Cyanoselenenylation of cyclopropanes 1

To a 0.2 mol dm^{-3} solution of a cyclopropane **1** (1 mmol) in dry CH_2Cl_2, kept at −78 °C, were added an equimolecular amount of PhSeCN **4** in the same solvent (4 cm^3) and $TiCl_4$ (1 mmol) in succession under nitrogen and the resulting mixture was stirred for 2 hours. Then, tetrahydrofuran–water (1 : 1; 1 cm^3) was added and the mixture was warmed to room temperature and extracted with CH_2Cl_2 (3 × 5 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated. Silica gel chromatography of the residue of **1a** and elution with light petroleum–Et_2O (9 : 1 v/v) followed by HPLC (hexane–*tert*-butyl methyl ether, 9 : 1 v/v) gave **12a** (71 mg, 20%), **14a** (22 mg, 6%), **6a** (32 mg, 10%) and **13a** (40 mg, 20%), successively. Column chromatography (light petroleum–Et_2O, 9 : 1 v/v) of the mixture from **1b** followed by HPLC (hexane–*tert*-butyl methyl ether, 17 : 3 v/v) gave the ester **13b** (43 mg, 20%), *syn*-**5b** (49 mg, 15%) and *syn*-**12b** (81 mg, 22%), successively. For the residues starting from **1c** and **1d** column chromatography (light petroleum–Et_2O, 9 : 1 v/v) gave **13c** (80 mg, 35%) and **13d** (68 mg, 30%), respectively. Compound **14a** was identified by comparison with an authentic sample (see below).

Ethyl 4-cyano-4,4-dimethoxy-2-(phenylseleno)butanoate (12a). Oil; t_R = 13.5 min; ν_{max}/cm^{-1} 1730, 2237; δ_H 1.17 (3 H, t, *J* 7.3, CH_3), 2.30 (1 H, dd, *J* 14.3 and 2.7) and 2.77 (1 H, dd, *J* 14.3 and 10.7) (CH_2), 3.35 and 3.36 (6 H, 2 s, 2 × OCH_3), 3.85 (1 H, dd, *J* 10.7 and 2.7, 2-H), 4.08 (2 H, m, *J* 7.3, OCH_2), 7.25–7.74 (5 H, m, C_6H_5); δ_C 13.9 (q), 36.4 (d), 38.8 (t), 52.0 (q), 52.2 (q), 61.3 (t), 99.2 (s), 114.8 (s), 127.1 (s), 129.0 (d), 129.2 (d), 135.9 (d), 171.9 (s); *m*/*z* (EI) 357 (M^+, ^{80}Se), 355 (M^+, ^{78}Se). Found: C, 50.6; H, 5.4; N, 3.8. $C_{15}H_{19}NO_4Se$ requires C, 50.57; H, 5.38; N, 3.93%.

Ethyl 4-cyano-4,4-dimethoxy-3-methyl-2-(phenylseleno)-butanoate (*syn*-12b). Oil; t_R = 12.1 min; ν_{max}/cm^{-1} 1729, 2237; δ_H 1.09 (3 H, t, *J* 7.0, OCH_2CH_3), 1.34 (3 H, d, *J* 6.8, 3-CH_3), 2.83 (1 H, m, *J* 6.8 and 10.2, 3-H), 3.32 and 3.37 (6 H, 2 s, 2 × OCH_3), 3.80 (1 H, d, *J* 10.2, 2-H), 3.96 (2 H, m, *J* 12.4 and 7.0, OCH_2), 7.23–7.68 (5 H, m, C_6H_5); δ_C 13.8 (q), 14.4 (q), 39.4 (d), 46.4 (d), 50.9 (q), 52.7 (q), 60.7 (t), 103.4 (s), 114.1 (s), 128.0 (s), 128.5 (d), 129.0 (d), 135.5 (d), 172.3 (s); *m*/*z* (EI) 371 (M^+, ^{80}Se), 369 (M^+, ^{78}Se). Found: C, 52.0; H, 5.8; N, 3.9. $C_{16}H_{21}NO_4Se$ requires C, 51.89; H, 5.72; N, 3.78%.

Ethyl 4-cyano-4,4-dimethoxybutanoate (13a). Oil; t_R = 16.7 min; ν_{max}/cm^{-1} 1730, 2235; δ_H 1.27 (3 H, t, *J* 7.0, CH_3), 2.20–2.32 (2 H, m, CH_2), 2.48–2.60 (2 H, m, CH_2), 3.41 (6 H, s, 2 × OCH_3), 4.15 (2 H, q, *J* 7.0, OCH_2); δ_C 14.0 (q), 28.4 (t), 31.1 (t), 51.2 (q), 60.7 (t), 99.4 (s), 115.2 (s), 172.5 (s); *m*/*z* (EI) 201

(M^+). Found: C, 53.6; H, 7.5; N, 6.8. $C_9H_{15}NO_4$ requires C, 53.72; H, 7.51; N, 6.96%.

Ethyl 4-cyano-4,4-dimethoxy-3-methylbutanoate (13b). Oil; t_R = 9.0 min; ν_{max}/cm^{-1} 1729, 2237; δ_H 1.10 (3 H, d, *J* 7.0, 3-CH_3), 1.27 (3 H, t, *J* 7.3, OCH_2CH_3), 2.16–2.30 (1 H, m, *J* 16.6 and 10.2) and 2.55–2.71 (2 H, m) ($CHCH_2$), 3.38 and 3.41 (6 H, 2 s, 2 × OCH_3), 4.15 (2 H, q, *J* 7.3, OCH_2); δ_C 14.1 (q), 14.4 (q), 35.0 (d), 36.1 (t), 51.0 (q), 51.8 (q), 60.5 (t), 102.9 (s), 114.3 (s), 171.8 (s); *m*/*z* (EI) 215 (M^+). Found: C, 55.7; H, 7.9; N, 6.4. $C_{10}H_{17}NO_4$ requires C, 55.80; H, 7.96; N, 6.51%.

Ethyl 4-cyano-3-ethyl-4,4-dimethoxybutanoate (13c). Oil; ν_{max}/cm^{-1} 1729, 2244; δ_H 0.97 (3 H, t, *J* 7.1, CH_2CH_3), 1.27 (t, *J* 6.9), 1.30–1.45 (m) and 1.65–1.85 (m) (together 5 H, OCH_2CH_3 and CH_2CH_3), 2.26–2.60 (3 H, m, $CHCH_2$), 3.39 (6 H, s, 2 × OCH_3), 4.14 (2 H, q, *J* 6.9, OCH_2); δ_C 11.4 (q), 14.0 (q), 22.8 (t) 34.0 (t), 41.3 (d), 51.3 (q), 51.6 (q), 60.5 (t), 103.0 (s), 114.6 (s), 172.4 (s); *m*/*z* (EI) 229 (M^+). Found: C, 57.6; H, 8.4; N, 6.1. $C_{11}H_{19}NO_4$ requires C, 57.62; H, 8.35; N, 6.11%.

Ethyl 4-cyano-4,4-dimethoxy-3,3-dimethylbutanoate (13d). Oil; ν_{max}/cm^{-1} 1724, 2234; δ_H 1.23 (6 H, s, 2 × 3-CH_3), 1.29 (3 H, t, *J* 7.0, OCH_2CH_3), 2.46 (2 H, s, CH_2), 3.65 (6 H, s, 2 × OCH_3), 4.15 (2 H, q, *J* 7.0, OCH_2); δ_C 14.2 (q), 21.7 (two overlapping q), 40.4 (t), 43.8 (s), 56.2 (q), 60.2 (t), 106.4 (s), 113.3 (s), 171.5 (s); *m*/*z* (EI) 229 (M^+). Found: C, 57.7; H, 8.4; N, 6.1. $C_{11}H_{19}NO_4$ requires C, 57.62; H, 8.35; N, 6.11%.

When the reaction mixture was stirred for 6 h and worked as described, the results were very similar. When an equimolecular solution of **1** and **4** in CH_2Cl_2 was kept in the absence of $TiCl_4$ at room temperature under anhydrous conditions for 12 h, the ^{1}H NMR spectrum showed only the presence of the starting material **1** and no trace of the above products. At higher temperature, after 6 h, the results were similar except for the presence of polymeric material and for **1a** a little of the alkene **2a**, too.

Cyanoselenenylation of 2a

A 0.2 mol dm^{-3} solution of **2a** (1 mmol) in dry CH_2Cl_2 was treated with cyanate **4** as reported above for **1a**. Chromatography of the residue on silica gel (light petroleum–Et_2O, 9 : 1) followed by HPLC (hexane–*tert*-butyl methyl ether, 9 : 1 v/v) led to the esters **14a** (32 mg, 9%), **6a** (72 mg, 23%) and **13a** (36 mg, 18%), successively.

Ethyl 4-cyano-4,4-dimethoxy-3-(phenylseleno)butanoate (14a). Oil; t_R = 14.4 min; ν_{max}/cm^{-1} 2238, 1726; δ_H 1.22 (3 H, t, *J* 7.2, Me), 2.67 and 3.00 (2 H, 2 dd, *J* 13.7, 9.8, 4.2, CH_2), 3.36 and 3.42 (6 H, 2 s, 2 × OMe), 3.90 (1 H, dd, *J* 9.8 and 4.2, 3-H), 4.10 (2 H, q, *J* 7.2, OCH_2), 7.20–7.75 (5 H, m, C_6H_5); δ_C 14.0 (q), 35.9 (t), 44.0 (d), 52.7 (q), 52.9 (q), 61.0 (t), 103.1 (s), 114.2 (s), 127.5 (s), 128.5 (d), 129.1 (d), 135.8 (d), 170.8 (s); *m*/*z* (EI) 357 (M^+, ^{80}Se), 355 (M^+, ^{78}Se). Found: C, 50.7; H, 5.4; N, 3.9. $C_{15}H_{19}NO_4Se$ requires C, 50.57; H, 5.38; N, 3.93%.

When the reaction was carried out in the absence of the Lewis acid at −78 °C for 2 h and at room temperature for 24 h, after work-up only ethyl methyl butanedioate[5] was recovered, derived from hydrolysis of **2a**.†

1-Ethyl 4-methyl (*E*)- and (*Z*)-3-methylbutenedioates (7)

Oxidation was carried out as reported,[16] by adding three drops of 30% H_2O_2 to a solution of *syn*-**5b** (46 mg, 0.14 mmol) in THF (5 cm^3) kept at 0 °C. NMR analysis of the mixture after 30 min showed the presence of only *Z*-alkene **7**, which was isolated (16 mg, 65%) by TLC using light petroleum–Et_2O (8 : 2 v/v) as eluent and identified by comparing its ^{1}H NMR spectrum with that reported.[15]

The same procedure was carried out starting from *anti*-**5a** (46 mg, 0.14 mmol) and led to the alkene *E*-**7** (18 mg, 73%) which was identified by comparing its ^{1}H NMR spectrum with that reported.[15]

Ethyl (*Z*)-4-cyano-4,4-dimethoxy-3-methylbut-2-enoate (15)

The same oxidative procedure as for *syn*-**5b** was carried out starting from *syn*-**12b** (74 mg, 0.2 mmol) and led, after purification by TLC (light petroleum–Et_2O, 17 : 3 v/v), to the alkene *Z*-**15** (25 mg, 60%) as an oil; ν_{max}/cm^{-1} 2236, 1724, 1650; δ_H 1.31 (3 H, t, *J* 7.0, CH_3), 1.92 (3 H, d, *J* 1.7, 3-CH_3), 3.35 (6 H, s, 2 × OCH_3), 4.21 (2 H, q, *J* 7.0, OCH_2), 6.02 (1 H, q, *J* 1.7, 2-H); *m*/*z* (EI) 213 (M^+). Found: C, 56.4; H, 7.1; N, 6.3. $C_{10}H_{15}NO_4$ requires C, 56.32; H, 7.09; N, 6.57%.

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† The ketene ketals which have been reported to undergo uncatalyzed cyanoselenenylation are 1,1-diethoxyethene, which is well known to be highly reactive, and ketene alkyl silyl ketals.[12]