Synthesis of Cyclic Enol Ethers from Alkenyl-β-dicarbonyl Compounds

Helena M. C. Ferraz,* Myrian K. Sano, Marta R. S. Nunes, and Graziela G. Bianco

Instituto de Química, Universidade de São Paulo, CEP 05508-900, São Paulo-SP, Brazil

hmferraz@iq.usp.br

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In this work we describe the cyclofunctionalization of eleven differently substituted alkenyl-β-dicarbonyl compounds, employing three electrophilic reagents, namely, iodine, *p*-methoxyphenyltellurium trichloride, and phenylselenenyl bromide. The reactions occur through the enolic form of the substrates, to afford the corresponding iodo-, telluro-, or selenocyclic enol ethers. Substrates bearing trisubstituted double bonds failed in reacting with the selenium and tellurium reagents. In general, β-diketones reacted faster than β-keto esters with the three studied electrophiles.

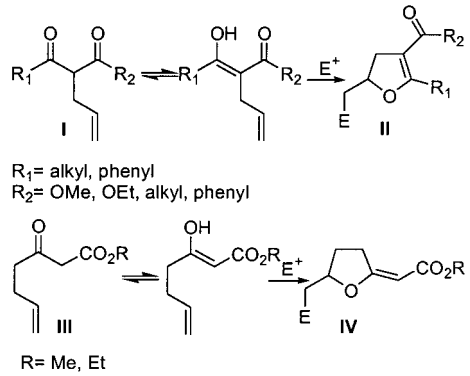
Introduction

Cyclic ethers constitute important building blocks in organic synthesis, being the core of several natural products, such as polyether antibiotics[1] and annonaceous acetogenins.[2]

The electrophilic cyclofunctionalization of unsaturated carboxylic acids and alcohols, leading to the corresponding lactones and cyclic ethers, has been exhaustively reported in the literature.[3−6] β-Keto esters and β-diketones bearing a double bond suitably positioned can also react with electrophiles, probably through their enolic forms,[7] to give the corresponding product of an O-cyclization, as shown in the general equations of Scheme 1.

Nevertheless, the use of alkenyl-β-dicarbonyl compounds as substrates for the electrophilic cyclization is less common than might be expected. Thus, Antonioletti et al.[8,9] reported the iodocyclization of a series of α-alkenylated substrates such as **I**, which led to the corresponding iodocyclic ethers **II** in very good yields. The selenocyclization of various substrates of general formulas **I** and **III** has already been studied by Ley et al.,[7,10,11] as well as by Tiecco et al.,[12,13] using different selenium electrophiles. In all the conditions studied, the selenocyclic ethers **II** and **IV** were obtained in reasonable to good yields. In a preliminary communication,[14] we reported the iodo- and tellurocyclization of some β-keto esters analogous to **I** or **III**, as will be discussed in the next section. The tellurocyclization of **I** (R_1 = Me, R_2 = OEt) has also been described by us.[15]

Scheme 1



The synthetic utility of the above-mentioned kind of products stimulated us to undertake the present work, to establish the scope and limitations of different electrophiles toward the cyclofunctionalization reaction. We chose β-dicarbonyl derivatives bearing allylic and homoallylic chains, with different patterns of substitution in the double bond, which would give diversely functionalized five- and six-membered ring enol ethers.

Results and Discussion

The alkenyl-β-keto esters were prepared from ethyl acetoacetate, by previously described methods. Thus, the γ-alkenylated substrates **1**, **8**, **9**, and **18** were obtained employing the procedure described by Huckin and Weiler,[16] while the α-alkenyl-β-keto esters **2**, **10**, and **17** were prepared as described by Ranu and Bhar.[17] These substrates were then submitted to the electrophilic cycliza-

(1) Boivin, T. L. B. *Tetrahedron* **1987**, *43*, 3309.
(2) Zeng, L.; Ye, Q.; Oberlies, N. H.; Shi, G.; Gu, Z. M.; He, K.; McLaughlin, J. L. *Nat. Prod. Rep.* **1996**, 275.
(3) Cardillo, G.; Orena, M. *Tetrahedron* **1990**, *46*, 3321.
(4) Harmange, J. C.; Figadère, B. *Tetrahedron: Asymmetry* **1993**, *4*, 1711.
(5) Petragnani, N.; Stefani, H. A.; Valduga, C. J. *Tetrahedron* **2001**, *57*, 1411.
(6) Gruttadauria, M.; Meo, P. L.; Noto, R. *Tetrahedron* **2001**, *57*, 1819.
(7) Jackson, W. P.; Ley, S. V.; Morton, J. A. *J. Chem. Soc., Chem. Commun.* **1980**, 1028.
(8) Antonioletti, R.; Bonadies, F.; Scettri, A. *Tetrahedron Lett.* **1988**, *29*, 4987.
(9) Antonioletti, R.; Cecchini, C.; Ciani, B.; Magnanti, S. *Tetrahedron Lett.* **1995**, *36*, 9019.
(10) Jackson, W. P.; Ley, S. V.; Whittle, A. J. *J. Chem. Soc., Chem. Commun.* **1980**, 1173.
(11) Brussani, G.; Ley, S. V.; Wright, J. L.; Williams, D. J. *J. Chem. Soc., Perkin Trans. 1* **1986**, 303.
(12) Tiecco, M.; Testaferri, L.; Tingoli, M.; Bartoli, D.; Balducci, R. *J. Org. Chem.* **1990**, *55*, 429.
(13) Tingoli, M.; Tiecco, M.; Testaferri, L.; Temperini, A. *Synth. Commun.* **1998**, *28*, 1769.
(14) Ferraz, H. M. C.; Sano, M. K.; Scalfo, A. C. *Synlett* **1999**, 567.
(15) Ferraz, H. M. C.; Comasseto, J. V.; Borba, E. B.; Brandt, C. A. *Quím. Nova* **1992**, *15*, 298.
(16) Huckin, S. N.; Weiler, L. *J. Am. Chem. Soc.* **1974**, *96*, 1082.
(17) Ranu, B. C.; Bhar, S. *J. Chem. Soc., Perkin Trans. 1* **1992**, 365.

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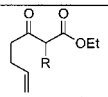
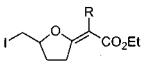
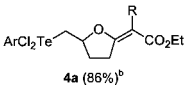
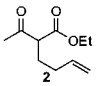
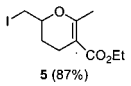
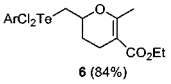
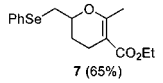
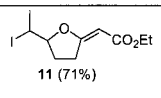
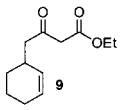
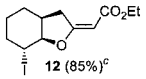
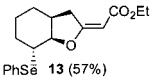
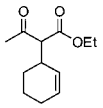
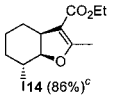
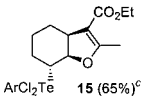
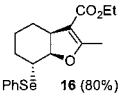
Table 1. Electrophilic Cyclization of β-Keto Esters Bearing a Monosubstituted Double Bond

Entry	Substrate	Reagents and Conditions	Product (yield)
1	 **1a** (R=H)	I_2/ Na_2CO_3/ CH_2Cl_2 r.t., 9h	 **3a** (84%)[b]
2	**1b** (R=Me)	I_2/ Na_2CO_3/ CH_2Cl_2 r.t., 7h	**3b** (81%)[b]
3	**1a** (R=H)	$ArTeCl_3$[a]/$CHCl_3$ reflux, 45 min	 **4a** (86%)[b]
4	**1b** (R=Me)	$ArTeCl_3$[a]/$CHCl_3$ reflux, 45 min	**4b** (82%)[b]
5	 **2**	I_2/ Na_2CO_3/ CH_2Cl_2 r.t., 12h	 **5** (87%)
6	**2**	$ArTeCl_3$[a]/$CHCl_3$ reflux, 8h	 **6** (84%)
7	**2**	PhSeBr/ THF r.t., 2h	 **7** (65%)

[a] Ar = *p*-MeOPh. [b] Previously communicated in ref 14.

Table 2. Electrophilic Cyclization of β-Keto Esters Bearing a Disubstituted Double Bond

Entry	Substrate	Reagents and Conditions	Product (yield)
1	 **8**	I_2/ Na_2CO_3/ CH_2Cl_2 r.t., 2h	 **11** (71%)
2	**8**	$ArTeCl_3$[a]/$CHCl_3$	Complex mixture[b]
3	**8**	PhSeBr/ THF	Complex mixture[b]
4	 **9**	I_2/ Na_2CO_3/ CH_2Cl_2 r.t., 4h	 **12** (85%)[c]
5	**9**	$ArTeCl_3$[a]/$CHCl_3$	Complex mixture[b,c]
6	**9**	PhSeBr/ THF r.t., 2h	 **13** (57%)
7	 **10**	I_2/ Na_2CO_3/ CH_2Cl_2 r.t., 6h	 **14** (86%)[c]
8	**10**	$ArTeCl_3$[a]/$CHCl_3$ reflux, 6h	 **15** (65%)[c]
9	**10**	PhSeBr/ THF r.t., 10h	 **16** (80%)

[a] Ar = *p*-MeOPh. [b] Different times (1−24 h) and temperatures (room temperature to reflux) were tried for these reactions. [c] Previously communicated in ref 14.

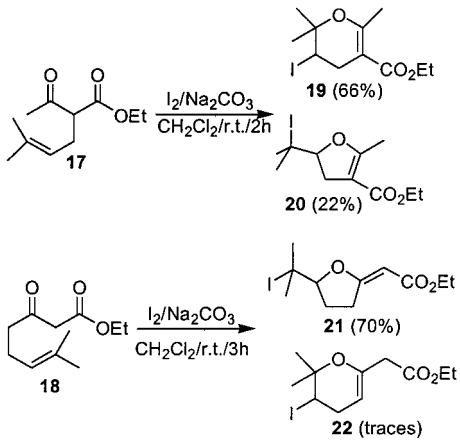
tion reactions, whose results are summarized in Tables 1 and 2 and in Scheme 2.

The iodocyclization of the alkenyl-β-keto esters was performed under kinetic conditions, to avoid a reversible process and, consequently, the formation of any C-cyclization product. The reactions occurred in a clean fashion, giving exclusively the expected product of a Markovnikov addition to the double bond (Table 1, entries 1, 2, and 5; Table 2, entries 1, 4, and 7). The only exceptions were the substrates **17** and **18** (Scheme 2), which bear trisubstituted double bonds.

The β-keto ester **17** gave an isomeric mixture of the six-membered and five-membered ring enol ethers **19** (Markovnikov product) and **20** (anti-Markovnikov product), which were isolated in 66% and 22% yields, respectively. On the other hand, the iodocyclization of **18** did not follow Markovnikov's rule, since the major product of the reaction was the five-membered ring ether **21**, accompanied by minor amounts of the endocyclic enol ether **22**.[18] Probably, this behavior is due more to steric than to electronic factors.

The next set of reactions was the selenocyclization, using phenylselenenyl bromide as the electrophilic reagent. The substrates **2**, **9**, and **10** (Table 1, entry 7; Table 2, entries 6 and 9) furnished the expected products **7**, **13**, and **16**, respectively, although the yields of these reactions were always lower than those of the corresponding iodocyclizations. The β-keto esters **8** and **17**

Scheme 2

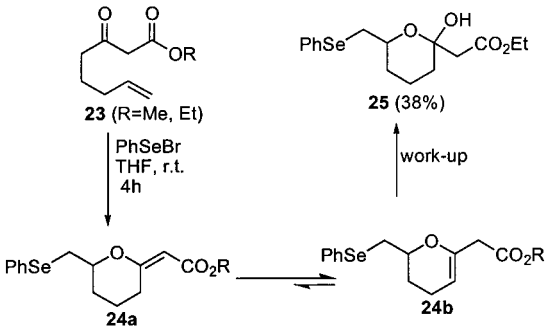


gave a complex mixture of products. The reaction of **18** with phenylselenenyl chloride has already been reported in the literature.[19] Using acetonitrile or dichloromethane as solvent, the authors obtained a mixture containing predominantly the product of addition to the double bond, while running the reaction in the presence of aluminum trichloride afforded the C-cyclization product in 84% yield. In view of these observations, as well as the negative results obtained with the substrates **8** and **17**,

(18) The cyclic ethers **19**−**22** are very unstable, decomposing on storage, but their structures could be clearly deduced by NMR spectroscopy; their tendency for losing iodine (or iodide) is so high that we could not obtain pure samples for elemental analysis. NMR data for product **22**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 (t, *J* = 7.1 Hz, 3H), 1.34 (s, 3H), 1.38 (s, 3H), 2.63−2.68 (m, 2H), 2.92 (m, 2H), 4.07 (q, *J* = 7.1 Hz, 2H), 4.06−4.17 (m, 1H), 4.41 (t, *J* = 3.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.9, 27.2, 32.8, 33.3, 40.2, 60.7, 76.6, 97.5, 146.3, 169.9.

(19) Alderdice, M.; Weiler, L. *Can. J. Chem.* **1981**, *59*, 2239.

Scheme 3



we did not submit the β-keto ester **18** to the selenocyclization reaction.

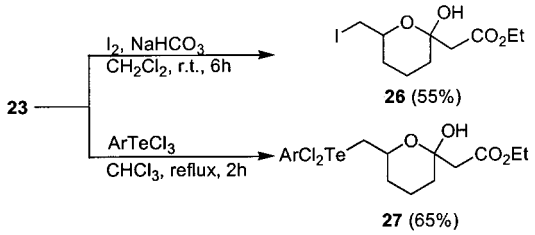
The reactions of tellurocyclization of the β-keto esters were performed using *p*-methoxyphenyltellurium trichloride. The substrates bearing di- and trisubstituted double bonds (with the exception of **10**, Table 2, entry 8) always furnished a complex mixture of products. It should be mentioned that almost all the tellurocyclizations of unsaturated carboxylic acids and alcohols described in the literature[20] were performed on substrates bearing monosubstituted double bonds. Accordingly, the β-keto esters **1a**, **1b**, and **2** (Table 1, entries 3, 4, and 6) gave good yields of the cyclic products.

The bicyclic products **12**−**16** (Table 2) exhibit *cis*-fused rings, assigned by NMR spectroscopy[14] and by analogy with related compounds.[21,22] The *cis* arrangement of the rings, as well as the *trans* relationship between the electrophile and the ring oxygen atom, is a direct consequence of the mechanism of the electrophile-promoted cyclization, which is believed to proceed via a *trans*-diaxial addition to the double bond.[23]

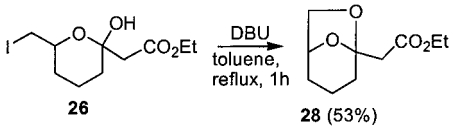
In addition to the substrates already discussed, the β-keto ester **23** (R = Et) was also submitted to the cyclization reactions. It is noteworthy that Ley and coworkers[24] were able to isolate a 9:1 mixture of the double bond isomers **24b** (R = Me) and **24a** (R = Me), by treating **23** (R = Me) with *N*-phenylselenophthalimide and a trace amount of $SnCl_4$. Nevertheless, under the conditions employed by us, the only characterizable product of selenocyclization of **23** (R = Et) was the hemiketal **25**, probably formed from **24b** (Scheme 3).

In a similar fashion, treatment of **23** (R = Et) with iodine and *p*-methoxyphenyltellurium trichloride led to the corresponding hemiketals **26** and **27**, respectively, in moderate yields (Scheme 4).[25] It must be noted that in all the other examples studied, we did not observe any similar hydration of the cyclic products. The incorporation of the hydroxyl group only in the products of cyclization of **23** can be understood considering that an enol ether such as **24b** is more prone to hydration than the earlier compounds, which are all substituted 3-alkoxy acrylates.

Scheme 4



Scheme 5



Finally, in a preliminary experiment, the reaction of **26** with DBU furnished the bicyclic ketal **28**, in a nonoptimized yield of 53% (Scheme 5).

To compare the behavior of alkenyl-β-keto esters and β-diketones toward electrophilic cyclization, the α-allyl-β-cyclohexanediones **30** and **31** were submitted to treatment with the three electrophilic reagents. The cyclization reactions occur smoothly, giving the tetrahydrobenzofuranones in very good yields, as summarized in Table 3.[26]

Conclusions

The results shown in this work extend the usefulness of the electrophile-mediated cyclization of alkenyl-substituted β-keto esters and ketones, especially when iodine is employed as the electrophile. With few exceptions, only the substrates bearing monosubstituted double bonds react cleanly with phenylselenenyl bromide and *p*-methoxyphenyltellurium trichloride. Nevertheless, the methodology herein presented provides access to cyclic ethers and tetrahydrobenzofuranones differently functionalized, in yields ranging from moderate to very good. Moreover, these products can be submitted to further elimination or reduction reactions, as described previously for the compounds **3a** and **4a**.[14] Studies toward these kinds of reactions are in progress in our laboratory.

Experimental Section

The β-keto esters and β-diketones were prepared by previously described methods.[16,17,27] Column chromatography was performed using 230−400 mesh silica gel. TLC analyses were performed with silica gel plates, using vanillin solution or iodine for visualization.

General Procedure for Iodocyclization. A mixture of I_2 (1.5 mmol), anhydrous Na_2CO_3 or $NaHCO_3$ (1.5 mmol), and the β-dicarbonyl compound (1 mmol) in dry CH_2Cl_2 (20 mL) was stirred at room temperature till the starting material disappeared (GC). Then AcOEt was added, the organic phase

(20) Petragnani, N.; Comasseto, J. V. *Synthesis* **1991**, 897.

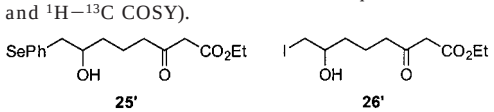
(21) Ferraz, H. M. C.; Pereira, F. L. C.; Leite, F. S.; Nunes, M. R. S.; Arrúa, M. E. P. *Tetrahedron* **1999**, *55*, 10915.

(22) Husebye, S.; Meyers, E. A.; Zingaro, R. A.; Comasseto, J. V.; Petragnani, N. *Acta Crystallogr.* **1987**, *C43*, 1147.

(23) Dowle, M. D.; Davies, D. I. *Chem. Soc. Rev.* **1979**, *8*, 171.

(24) Ley, S. V.; Lygo, B.; Molines, H. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2403.

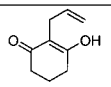
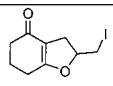
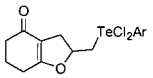
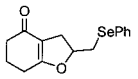
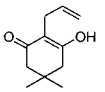
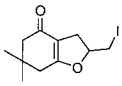
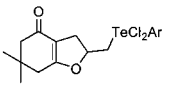
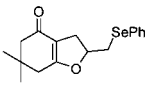
(25) The relative configuration of the hemiketals **25**−**27** could not be unequivocally assigned. An equilibrium involving hydration/dehydration was observed in $CDCl_3$ solution, during the compilation of the spectra. The products of hydrolysis of **25** and **26** were identified as the β-keto esters **25′** and **26′**, respectively. The telluro-containing product **27** is more stable, and allowed the acquisition of 2D spectra ($^1H-^1H$ and $^1H-^{13}C$ COSY).



(26) Preliminary results of this study were communicated at the 8th International Conference on the Chemistry of Selenium and Tellurium, Sao Paulo, Brazil, 2000.

(27) Barrios, H.; Rock, M. C.; Salmon, M.; Walls, F. *Bol. Inst. Quím. Univ. México* **1969**, *21*, 146.

Table 3. Electrophilic Cyclization of Alkenyl-β-diketones

Entry	Substrate	Reagents and Conditions	Product (yield)
1	 **30**	I_2/ $NaHCO_3$ /CH_2Cl_2 r.t., 3h	 **32** (85%)
2	**30**	$ArTeCl_3$[a]/ $CHCl_3$ reflux, 45min	 **33** (81%)
3	**30**	PhSeBr/ THF r.t., 15 min	 **34** (83%)
4	 **31**	I_2/ $NaHCO_3$ /CH_2Cl_2 r.t., 30 min	 **35** (69%)
5	**31**	$ArTeCl_3$[a]/ $CHCl_3$ reflux, 6h	 **36** (94%)[b]
6	**31**	PhSeBr/ THF r.t., 15 min	 **37** (80%)

[a] Ar = *p*-MeOPh. [b] Previously reported in ref 15.

was washed with sodium thiosulfate solution (0.1 N) and brine and dried over anhydrous $MgSO_4$, and the solvent was evaporated.

6-Iodomethyl-2-methyl-5,6-dihydro-4*H*-pyran-3-carboxylic Acid Ethyl Ester (5). The crude product was purified by column chromatography (hexane/ethyl acetate (9:1) as eluent), giving **5** (oil) in 87% yield: IR (film) ν_{max} 2975, 1704, 1626 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.27 (t, J = 7.1 Hz, 3H), 1.64−1.69 (m, 1H), 2.03−2.07 (m, 1H), 2.24 (s, 3H), 2.27−2.29 (m, 1H), 2.40−2.44 (m, 1H), 3.28 (dd, J = 6.0 and 10.4 Hz, 1H), 3.31 (dd, J = 5.7 and 10.4 Hz, 1H), 3.85−3.88 (m, 1H), 4.15 (q, J = 7.1 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 7.1, 14.4, 20.1, 20.8, 26.6, 59.7, 75.1, 101.4, 163.9, 168.2. Anal. Calcd for $C_{10}H_{15}O_3I$: C, 38.73; H, 4.87. Found: C, 38.75; H, 4.85.

[5-(1-Iodoethyl)dihydrofuran-2-ylidene]acetic Acid Ethyl Ester (11). The crude product was purified by column chromatography (hexane/ethyl acetate (9:1) as eluent), giving **11** (mp 66−67 °C) in 71% yield: IR (film) ν_{max} 2983, 1694, 1637, 1124 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.19 (t, J = 7.1 Hz, 3H), 1.80−1.90 (m, 1H), 1.87 (d, J = 6.4 Hz, 3H), 2.25−2.34 (m, 1H), 2.84−2.97 (m, 1H), 3.23−3.33 (m, 1H), 4.05 (q, J = 7.1 Hz, 2H), 4.10−4.17 (m, 2H), 5.22 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 24.2, 28.8, 29.3, 30.0, 59.0, 86.9, 89.9, 168.0, 175.4. Anal. Calcd for $C_{10}H_{15}O_3I$: C, 38.73; H, 4.87. Found: C, 38.57; H, 4.78.

5-Iodo-2,6,6-trimethyl-5,6-dihydro-4*H*-pyran-3-carboxylic Acid Ethyl Ester (19) and 5-(1-Iodo-1-methylethyl)-2-methyl-4,5-dihydrofuran-3-carboxylic Acid Ethyl Ester (20). The crude product was chromatographed on silica gel (hexane/ethyl acetate (9:1) as eluent), giving **19** (oil) in 66% yield and **20** (oil) in 22% yield. Data for **19**: IR (film) ν_{max} 1703, 1641 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.24 (t, J = 7.1 Hz, 3H), 1.37 (s, 3H), 1.44 (s, 3H), 2.16−2.17 (m, 3H), 2.80−2.90 (m, 1H), 2.97−3.05 (m, 1H), 4.11 (q, J = 7.2 Hz, 2H), 4.14−4.17 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3, 20.2, 23.3, 27.4, 31.1, 33.6, 59.7, 77.9, 100.0, 163.2, 167.0. Data for **20**: IR (film) ν_{max} 1693, 1649, 1223 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.24 (t, J = 7.1 Hz, 3H), 1.86 (s, 3H), 1.87 (s, 3H), 2.15 (t, J = 1.6 Hz, 3H), 2.70−2.78 (m, 1H), 2.90−3.00 (m, 1H), 4.02−4.12 (m, 1H), 4.13 (q, J = 7.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 14.4, 31.8, 33.1, 35.1, 50.2, 59.5, 89.6, 102.0, 165.7, 167.3.

[5-(1-Iodo-1-methylethyl)dihydrofuran-2-ylidene]acetic Acid Ethyl Ester (21). The crude product was chromatographed on silica gel (hexane/ethyl acetate (9:1) as eluent), giving **21** (unstable oil) in 70% yield: IR (film) ν_{max} 1696, 1654, 1144 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.26 (t, J = 7.4 Hz, 3H), 1.87−2.11 (m, 1H), 1.92 (s, 3H), 1.94 (s, 3H), 2.24−2.41 (m, 1H), 2.89−3.09 (m, 1H), 3.32−3.47 (m, 1H), 3.84 (t, J = 7.3 Hz, 1H), 4.12 (q, J = 7.4 Hz, 2H), 5.32 (t, J = 2.2 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.4, 28.3, 30.3, 32.7, 33.8, 49.1, 59.1, 89.8, 91.3, 168.3, 175.7.

(2-Hydroxy-6-iodomethyltetrahydropyran-2-yl)acetic Acid Ethyl Ester (26). The crude product was chromatographed on silica gel (hexane/ethyl acetate (9:1) as eluent), giving **26** (oil) in 55% yield: ^1H NMR (300 MHz, $CDCl_3$) δ 1.16−1.43 (m, 2H), 1.31 (t, J = 7.2 Hz, 3H), 1.57−2.02 (m, 4H), 2.55 and 2.64 (AB system, J = 15.0 Hz, 2H), 3.09 (dd, J = 10.0 and 6.9 Hz, 1H), 3.15 (dd, J = 10.0 and 5.1 Hz, 1H), 3.89−3.97 (m, 1H), 4.16−4.30 (m, 2H), 5.02 (d, J = 2.4 Hz, 1H); the other signals in the ^1H NMR spectrum correspond to the product **26′**, formed by hydrolysis of the hemiketal in $CDCl_3$ solution, during the compilation of the spectrum; ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.2, 14.2, 18.4, 30.6, 34.1, 45.1, 61.0, 69.7, 95.7, 172.1; the minor signals (14.1, 15.9, 19.5, 35.6, 42.5, 49.3, 61.4, 70.7, ca.167, ca. 202) correspond to the product **26′**; HRMS *m/z* calcd for $C_{10}H_{17}IO_4$ 328.01716, found 328.01533.

2-Iodomethyl-3,5,6,7-tetrahydro-2*H*-benzofuran-4-one (32). The crude product was purified by column chromatography (hexane/ethyl acetate (6:4) as eluent), giving **32** (mp 74−77 °C) in 85% yield: IR (film) ν_{max} 2950, 1633, 1617 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.05−2.10 (m, 2H), 2.35−2.40 (m, 2H), 2.43−2.48 (m, 2H), 2.60 (ddt, J = 14.8, 6.7, and 1.9 Hz, 1H), 2.99 (ddt, J = 14.8, 10.0, and 1.9 Hz, 1H), 3.3−3.4 (m, 2H), 4.80−4.89 (m, 1H); ^{13}C NMR δ 8.1, 21.6, 23.9, 32.6, 36.4, 83.5, 112.9, 176.7, 195.4. Anal. Calcd for $C_9H_{11}O_2I$: C, 38.87; H, 3.99. Found: C, 38.96; H, 4.29.

2-Iodomethyl-6,6-dimethyl-3,5,6,7-tetrahydro-2*H*-benzofuran-4-one (35). The crude product was purified by column chromatography (hexane/ethyl acetate (6:4) as eluent), giving **35** (oil) in 69% yield: IR (film) ν_{max} 2959, 1627 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.11 (s, 3H), 1.12 (s, 3H), 2.23 (s, 2H), 2.30 (br s, 2H), 2.60 (ddt, J = 14.8, 6.7, and 1.9 Hz, 1H), 2.99 (ddt, J = 14.8, 10.0, and 1.9 Hz, 1H), 3.35 (d, J = 5.3 Hz, 2H), 4.8−4.9 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 8.6, 28.5, 28.9, 32.4, 34.1, 37.7, 50.9, 83.4, 111.4, 175.5, 194.5. Anal. Calcd for $C_{11}H_{15}O_2I$: C, 43.16; H, 4.94. Found: C, 43.17; H, 4.96.

General Procedure for Tellurocyclization. A mixture of the β-dicarbonyl compound (2 mmol) and *p*-methoxyphenyltellurium trichloride (2.2 mmol) in 30 mL of recently distilled chloroform was heated under reflux for the time indicated in the tables or schemes. The solvent was evaporated and the residue filtered through silica gel, using chloroform as eluent.

6-(*p*-Methoxyphenyldichlorotelluro)methyl-2-methyl-5,6-dihydro-4*H*-pyran-3-carboxylic Acid Ethyl Ester (6). The crude product was purified by column chromatography (hexane/ethyl acetate (7:3) as eluent), giving **6** (mp 139−142 °C) in 83% yield: IR (film) ν_{max} 2943, 1708, 1630, 1257, 1091 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.29 (t, J = 7.4 Hz, 3H), 1.69−1.82 (m, 1H), 2.05−2.13 (m, 1H), 2.30 (s, 3H), 2.26−2.62 (m, 2H), 3.81−3.86 (m, 2H), 3.86 (s, 3H), 4.17 (q, J = 7.4 Hz, 2H), 4.67−4.80 (m, 1H), 7.03−7.10 (m, 2H), 8.03−8.11 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.3, 19.9, 21.1, 27.4, 55.5, 56.9, 59.8, 71.3, 102.2, 115.6, 120.0, 135.1, 162.3, 163.1, 167.9. Anal. Calcd for $C_{17}H_{22}O_4TeCl_2$: C, 41.77; H, 4.54. Found: C, 41.40; H, 4.28.

[2-Hydroxy-6-(*p*-methoxyphenyldichlorotelluro)-methyltetrahydropyran-2-yl]acetic Acid Ethyl Ester (27).

The crude product was purified by column chromatography (hexane/ethyl acetate (7:3) as eluent), giving **27** (mp 90−91 °C) in 65% yield: IR (film) ν_{max} 3421, 2943, 1743, 1700, 1260, 1038 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.19−2.07 (m, 6H), 1.28 (t, J = 7.1 Hz, 3H), 2.58 and 2.70 (AB system, J = 15.7 Hz, 2H), 3.59−3.82 (m, 2H), 3.76 (s, 3H), 4.13−4.29 (m, 2H), 4.69−4.79 (m, 1H), 5.09 (br s, 1H), 6.91−6.99 (m, 2H), 7.87−7.98 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.9, 18.3, 30.6, 33.4, 44.3, 55.3, 58.6, 61.1, 65.4, 96.3, 115.2, 120.7, 135.0, 161.7, 171.8. Anal. Calcd for $C_{17}H_{24}O_5TeCl_2$: C, 40.28; H, 4.77; Cl, 13.99. Found: C, 40.80; H, 4.74; Cl, 14.30.

2-(*p*-Methoxyphenyldichlorotelluro)methyl-3,5,6,7-tetrahydro-2*H*-benzofuran-4-one (33). The crude product was purified by column chromatography (hexane/ethyl acetate (7:3) as eluent), giving **33** (mp 160−162 °C) in 81% yield: IR (film) ν_{max} 2916, 1646 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.05−2.11 (m, 2H), 2.36−2.41 (m, 2H), 2.43−2.68 (m, 3H), 3.11−3.20 (m, 1H), 3.80−3.91 (m, 2H), 3.87 (s, 3H), 5.55−5.65 (m, 1H), 7.03−7.08 (m, 2H), 8.04−8.09 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 23.8, 32.8, 36.5, 55.6, 57.5, 79.5, 112.7, 115.8, 119.3, 135.1, 162.4, 176.2, 195.6. Anal. Calcd for $C_{16}H_{18}O_3TeCl_2$: C, 42.07; H, 3.97. Found: C, 41.77; H, 4.12.

General Procedure for Selenocyclization. A mixture of the β-keto ester (1 mmol) or β-diketone (2 mmol) and PhSeBr (2 mmol) in dry THF was stirred at room temperature till the starting material disappeared (GC). Then AcOEt was added, the organic phase was washed with brine and dried over anhydrous $MgSO_4$, and the solvent was evaporated.

2-Methyl-6-phenylselanylmethyl-5,6-dihydro-4*H*-pyran-3-carboxylic Acid Ethyl Ester (7). The crude product was purified by column chromatography (hexane/ethyl acetate (9:1) as eluent), giving **7** (oil) in 65% yield: IR (film) ν_{max} 2931, 1703, 1623 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.26 (t, J = 7.1 Hz, 3H), 1.60−1.66 (m, 1H), 2.00−2.06 (m, 1H), 2.18 (t, J = 0.9 Hz, 3H), 2.23−2.26 (m, 1H), 2.37−2.41 (m, 1H), 3.00 (dd, J = 12.7 and 6.7 Hz, 1H), 3.19 (dd, J = 12.7 and 6.0 Hz, 1H), 4.00−4.05 (m, 1H), 4.14 (q, J = 7.1 Hz, 2H), 7.24−7.27 (m, 3H), 7.52−7.54 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.4, 20.2, 21.1, 26.3, 31.7, 59.6, 75.8, 101.3, 127.2, 129.1, 130.0, 132.9, 164.2, 168.4. Anal. Calcd for $C_{16}H_{20}O_3Se$: C, 56.64; H, 5.94. Found: C, 56.36; H, 5.92.

(7-Phenylselanylhexahydrobenzofuran-2-ylidene)acetic Acid Ethyl Ester (13). The crude product was purified by column chromatography (hexane/ethyl acetate (9:1) as eluent), giving **13** (oil) in 57% yield: IR (film) ν_{max} 2934, 1701, 1643 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.22−2.05 (m, 6H), 1.25 (t, J = 7.2 Hz, 3H), 2.53−2.62 (m, 1H), 2.90−3.10 (m, 2H), 3.54 (br q, J = 4.9 Hz, 1H), 4.11 (q, J = 7.2 Hz, 2H), 4.38 (t, J = 4.9 Hz, 1H), 5.31 (t, J = 1.4 Hz, 1H), 7.26−7.30 (m, 3H), 7.54−7.57 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.4, 20.4, 26.1, 27.7, 34.0, 36.9, 42.3, 59.1, 84.3, 91.4, 127.8, 128.6, 129.1, 134.5, 168.4, 175.4; the other signals in the spectra were attributed to traces of the *Z* isomer of **13.** Anal. Calcd for $C_{18}H_{22}O_3Se$: C, 59.18; H, 6.07. Found: C, 58.84; H, 6.06.

2-Methyl-7-phenylselanyl-3a,4,5,6,7,7a-hexahydrobenzofuran-3-carboxylic Acid Ethyl Ester (16). The crude product was purified by column chromatography (hexane/ethyl acetate (9:1) as eluent), giving **16** (oil) in 80% yield: IR (film) ν_{max} 2935, 1698, 1638 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (t, J = 7.0 Hz, 3H), 1.22−1.40 (m, 1H), 1.46−1.55 (m, 2H), 1.78−1.87 (m, 1H), 1.94−2.05 (m, 2H), 2.15 (d, J = 1.0 Hz, 3H), 3.11−3.19 (m, 1H), 3.66 (dd, J = 10.5 and 4.5 Hz, 1H), 4.11−4.22 (m, 2H), 4.49 (dd, J = 7.5 and 4.5 Hz, 1H), 7.24−7.31 (m, 3H), 7.54−7.60 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.4, 14.5, 19.6, 27.1, 27.5, 39.2, 41.8, 59.4, 85.1, 109.6, 127.8, 128.9, 129.2, 134.7, 166.1, 168.2.

(2-Hydroxy-6-phenylselanylmethyltetrahydropyran-2-yl)acetic Acid Ethyl Ester (25). The crude product was chromatographed on silica gel (hexane/ethyl acetate (9:1) as eluent), giving **25** (oil) in 38% yield: IR (film) ν_{max} 3457, 2939, 1739, 1714 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19−1.44 (m, 2H), 1.30 (t, J = 7.1 Hz, 3H), 1.59−1.96 (m, 4H), 2.53 and 2.62 (AB system, J = 15.1 Hz, 2H), 2.90 (dd, J = 12.0 and 5.6 Hz, 1H), 3.02 (dd, J = 12.0 and 7.3 Hz, 1H), 4.10−4.18 (m, 1H), 4,20 (q, J = 7.1 Hz, 2H), 4.92 (d, J = 2.5 Hz, 1H), 7.19−7.28 (m, 3H), 7.46−7.54 (m, 2H); the other signals in the ^{1}H NMR spectrum correspond to the product **25′**, formed by hydrolysis of the hemiketal in $CDCl_3$ solution, during the compilation of the spectrum; ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 18.5, 30.6, 33.6, 34.2, 45.1, 60.9, 69.7, 95.4, 126.5, 128.9, 131.1, 132.3, 172.0; the minor signals (14.1, 19.7, 35.6, 37.0, 42.6, 49.2, 61.3, 69.5, 127.3, 129.2, 131.1, 133.0, ca. 167, ca. 203) correspond to the product **25′**.

2-Phenylselanylmethyl-3,5,6,7-tetrahydro-2*H*-benzofuran-4-one (34). The crude product was purified by column chromatography (hexane/ethyl acetate (8:2) as eluent), giving **34** (mp 69−70 °C) in 83% yield: IR (film) ν_{max} 2935, 1633, 1613 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.00 (q, J = 6.5 Hz, 2H), 2.32 (t, J = 6.5 Hz, 4H), 2.62 (ddt, J = 14.7, 10.0, and 1.6 Hz, 1H), 2.91−3.00 (m, 1H), 3.07 (dd, J = 12.7 and 5.8 Hz, 1H), 3.21 (dd, J = 12.7 and 5.9 Hz, 1H), 4.92−4.97 (m, 1H), 7.25−7.28 (m, 3H), 7.52−7.55 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.5, 23.7, 31.6, 32.5, 36.3, 84.2, 112.8, 127.3, 128.9, 129.1, 133.1, 176.7, 195.2. Anal. Calcd for $C_{15}H_{16}O_2Se$: C, 58.64,H, 5.25. Found: C, 58.15; H, 5.08.

6,6-Dimethyl-2-phenylselanylmethyl-3,5,6,7-tetrahydro-2*H*-benzofuran-4-one (37). The crude product was purified by column chromatography (hexane/ethyl acetate (8:2) as eluent), giving **37** (mp 47−48 °C) in 80% yield: IR (film) ν_{max} 2955, 1625 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.08 (s, 6H), 2.20 (br s, 4H), 2.64 (ddt, J = 14.7, 10.0, and 1.6 Hz, 1H), 2.93−3.02 (m, 1H), 3.08 (dd, J = 12.7 and 6.7 Hz, 1H), 3.21 (dd, J = 12.7 and 5.7 Hz, 1H), 4.93−5.02 (m, 1H), 7.26−7.28 (m, 3H), 7.52−7.55 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.6, 28.7, 31.6, 32.8, 34.0, 37.7, 50.9, 84.5, 111.4, 127.5, 129.1, 129.2, 133.3, 175.8, 194.7. Anal. Calcd for $C_{17}H_{20}O_2Se$: C, 60.90,H, 6.01. Found: C, 60.66; H, 5.89.

Preparation of (6,8-Dioxabicyclo[3.2.1]oct-5-yl)acetic Acid Ethyl Ester (28). To a stirred solution of **26** (1 mmol, 328 mg) in dry toluene (8 mL) was added DBU (1.2 mmol, 182 mg). The mixture was refluxed for 1 h and then filtered through a silica gel pad. The solvent was evaporated, and the crude product was purified by column chromatography (hexane/ethyl acetate (8:2) as eluent), giving 106 mg of **28**: yield 53%; IR (film) ν_{max} 2044, 1738, 1013 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (t, J = 7.1 Hz, 3H), 1.47−1.51 (m, 1H), 1.62−1.67 (m, 1H), 1.75−1.93 (m, 4H), 2.74 (s, 2H), 3.86−3.89 (m, 1H), 3.94 (dd, J = 6.6 and 0.6 Hz, 1H), 4.17 (q, J = 7.1 Hz, 2H), 4.56−4.58 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 16.8, 28.1, 33.9, 43.6, 60.6, 69.2, 75.2, 106.5, 169.1. The ^{1}H NMR data are in good agreement with those reported for the analogous methyl ester.[28]

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for compounds **5**, **13**, **19**, **20**, **22**, **25**−**28**, **33**−**35**, and **37**, IR spectra for **25**, **27**, and **28**, and MS spectra for **26** and **28**. This material is available free of charge via the Internet at http://pubs.acs.org.

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