A Convenient Synthesis of Alkenyl-Substituted Glycidonitriles and Glycidates

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Abstract: α-Chloronitriles or α-chloroesters reacted with α,β-unsaturated carbonyl compounds in the presence of powdered sodium hydroxide, in ethereal solvents, giving alkenyl-substituted glycidonitriles or esters. The straightforward process affords nitriles in particularly high yields.

Key words: aldehydes, ketones, carbanions, condensation, epoxides

Nitriles and esters of glycidic acids (glycidonitriles and glycidates) are useful substrates for the preparation of a variety of important products, such as carbonyl compounds,[1,2] carboxylic acids,[3] fluorine-substituted carboxylic acids,[4–6] cyanodioxolanes,[7] aziridine carboxylic esters[8] and cyanodienes.[9] Chemical transformations of alkenyl-substituted glycidonitriles and glycidates, however, have only rarely been investigated. According to a few reports concerning such processes, the alkenyl function is preserved in the product (e.g. during homologation of α,β-unsaturated ketones to aldehydes,[10,11] in the preparation of a retinoic acid derivative[12] and base-mediated oxirane ring opening[13]) or, together with the oxirane ring, is involved in the formation of the final products (e.g. thermal conversion of epoxyhexenynes into 3,4-annulated 2-vinylfurans[14]). In our opinion, the synthetic utility of the title compounds in organic synthesis is still unrecognized.

Alkenyl-substituted glycidonitriles or glycidic esters are usually prepared by the reaction of either α-halogeno nitriles or α-halogeno esters with α,β-unsaturated carbonyl compounds. Such reactions are usually carried out in the presence of potassium *tert*-butoxide,[10,11,13–15] sodium hydride,[15] sodium hexamethyldisilazanide (NaHMDS)[15] or sodium ethoxide[16] in *tert*-butanol, HMPT, THF, diethyl ether or their mixtures, sometimes with the addition of benzene (Darzens-type condensation[17]). Typical phase-transfer catalysis (PTC) conditions[18–21] [50% aq sodium hydroxide and catalytic benzyltriethylammonium chloride (TEBAC) in acetonitrile] have been applied for the preparation of cyanoepoxyhexenynes via the condensation of chloroacetonitrile or 2-bromo-2-phenylacetonitrile with tetramethylsilane (TMS)-protected enynals.[13,14] In one case, the reaction of chloroacetonitrile with a dienone was carried out with powdered sodium hydroxide and a catalytic amount of DMF in toluene,[12] though these conditions proved unfeasible for the reaction with 1-acetylocyclohexene.[11] On the other hand, neither ethyl chloro- nor bromo-acetate underwent the reaction with either acrolein or methyl vinyl ketone under PTC conditions.[22]

Depending upon the structure of the halonitrile or haloester used, their carbanions can attack α,β-unsaturated carbonyl compounds either at the carbon–carbon double bond, leading to the formation of the corresponding cyclopropanes (1,4-addition), or at the carbonyl carbon, giving alkenylo-oxiranes (1,2-addition). Chloroacetonitrile[11–15] and chloroacetates[10,15,16] have been shown to react through 1,2-addition, while (α-chloro)phenylacetates react via 1,4-addition.[15,16] On the other hand, a survey of the literature reveals a discrepancy between the reported reactivities of (α-halo)phenylacetonitriles. Thus, α-bromo derivatives have been shown to behave in a manner similar to chloroacetonitrile, affording the 1,2-addition products,[13,14] while the corresponding α-chloro compounds reacted by 1,4-addition, forming substituted cyclopropanes.[15]

Taking into account this literature data, we considered that establishing a general, simple method with which to prepare alkenyl-substituted glycidonitriles and glycidates would be of value. To this end, we investigated the Darzens condensation of chloronitriles **1**, **2** and chloroesters **3**, **4** with a series of α,β-unsaturated aldehydes **5**–**8** and ketones **9**–**12** under PTC conditions.[23]

Stirring chloroacetonitrile (**1**) with aldehyde **8**, 50% aqueous sodium hydroxide, and catalytic TEBAC in benzene (20–30 °C for 4 h), however, resulted in only 57% conversion of **8** to the expected product **16** (determined by GC). When powdered sodium hydroxide and the same catalyst in THF were used, only an intractable mixture was formed. According to literature, Darzens condensation of halonitriles with carbonyl compounds can be realized with solid alkali-metal hydroxides, in aprotic dipolar solvents,[24] even in a catalytic amounts.[12] However, because these solvents are rather expensive and difficult to recover after work-up procedures, we decided to carry out the reaction of nitrile **1** with aldehyde **8** in the presence of powdered sodium hydroxide in THF, without any catalyst.

Though the reaction mixture charred a little under these conditions, the product **16** was isolated in 91% yield (Table 1, entry 4). Encouraged by this result, we conducted the same reaction with a range of α,β-unsaturated aldehydes **5**–**7** and ketones **9**–**12** with chloroacetonitrile (**1**); in the majority cases the expected products were obtained in high yields (Scheme 1, Table 1, entries 1–8).

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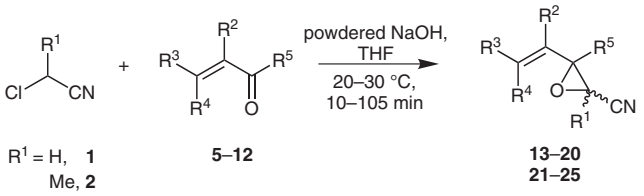
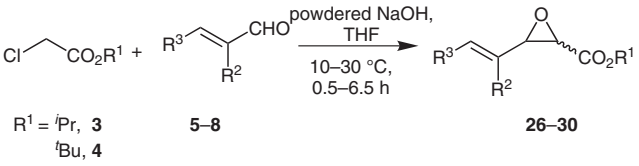


Scheme 1

Equally satisfactory results were obtained from the reaction of α-chloropropionitrile (**2**) with aldehydes **7**, **8** and ketone **10** (Table 1, entries 9, 10 and 11, respectively); however, the expected products **24** and **25** from the open chain and cyclic ketones, **11** and **12** respectively, were only formed in rather low yields and were accompanied by significant amounts of intractable materials (Table 1, entries 12 and 13). Except for the reaction of nitrile **2** with ketone **10** (Table 1, entry 11), the conversion was completed in less than one hour, and the products were usually isolated by vacuum distillation. Again, typical PTC conditions proved inefficient in the reaction of **2** with aldehyde **8**, with ~44% of starting material remaining after eight hours (determined by GC) .

When the reaction of nitrile **1** with aldehyde **8** was carried out using commercially available granules of sodium hydroxide, the glycidonitrile **16** was obtained in 78% yield, though the conversion required significantly longer to go to completion (~45 min). Importantly, after the sodium hydroxide had been removed by filtration, at least 90% of THF solvent used in the reaction of **1** with **8** could be recovered by distillation (**16** was obtained in 84% yield).

Chloroacetates **3** and **4** also reacted with α,β-unsaturated aldehydes **5–8** under the conditions described above, affording alkenylglycidates **26–30** in 30–73% yield (Scheme 2, Table 2).



Scheme 2

The progress of these reactions were followed by GC, and it is important to note that upon complete consumption of the carbonyl component, the reaction should be worked up, since otherwise, the glycidonitriles or glycidic ester products tended to degrade.

Table 1 Alkenyl-Substituted Glycidonitriles **13–25**

Entry		R^1		R^2	R^3	R^4	R^5	Time (min)	Product, yield[a] (%)	Oxirane ring stereochemical ratio (by GC)
1	**1**	H	**5**[b]	H	Me	H	H	10	**13**, 57	1.9 (*E*/*Z*)
2			**6**[b]	*n*-Bu	H	H	H	45	**14**, 83	2.4 (*E*/*Z*)
3			**7**[b]	H	Ph	H	H	10	**15**, 69	1.7 (*E*/*Z*)
4			**8**[b]	Me	Ph	H	H	15	**16**,[c] 91	1.6 (*E*/*Z*)
5			**9**[b]	H	H	H	Me	30	**17**, 36	1.8 (*E*/*Z*)[d]
6			**10**[b]	H	Me	Me	Me	45	**18**, 75	1.6 (*E*/*Z*)[d]
7			**11**[b]	H	Ph	H	Me	40	**19**, 80	1.8 (*E*/*Z*)
8			**12**[e]	H	H	$(CH_2)_3$		45	**20**, 79	1.5[f]
9	**2**	Me	**7**[e]	H	Ph	H	H	48	**21**, 62	1.3 (*E*/*Z*)[d]
10			**8**[e]	Me	Ph	H	H	40	**22**, 88	1.7 (*E*/*Z*)[d]
11			**10**[b]	H	Me	Me	Me	105	**23**, 76	3.4[f]
12			**11**[e]	H	Ph	H	Me	20	**24**,[g] 28	1.0
13			**12**[e]	H	H	$(CH_2)_3$		47	**25**, 36	1.8[f]

[a] Isolated by vacuum distillation.
[b] Conducted in 100 mL of THF.
[c] In DME, yield = 86%.
[d] Determined by ^{1}H and NOESY NMR (500 MHz).
[e] Conducted in 50 mL of THF.
[f] Ratio of major to minor diastereoisomers.
[g] Isolated by column chromatography.

Table 2 Alkenyl-Substituted Glycidates **26–30**

Entry		R^1		R^2	R^3	Time[a] (min)	Product, yield[b] (%)	Oxirane ring stereochemical ratio (by ^{1}H NMR)
1	**3**	*i*-Pr	**8**	Me	Ph	390[c]	**26**, 32	*E*
2	**4**	*t*-Bu	**5**	H	Me	37	**27**, 30	6.0 (*E*/*Z*)
3			**6**	*n*-Bu	H	48	**28**, 69	10.3 (*E*/*Z*)
4			**7**	H	Ph	30	**29**, 40	4.5 (*E*/*Z*)
5			**8**	Me	Ph	150	**30**,[d] 73	*E*

[a] Reaction conducted at 20–30 °C.
[b] Isolated by vacuum distillation.
[c] Reaction conducted at 10–15 °C.
[d] Isolated by crystallization from MeOH.

In summary, we have established a simple, fairly general method for the synthesis of substituted alkenylglycidonitriles and alkenylglycidates from readily available α-chloronitriles, α-chloroesters, α,β-unsaturated aldehydes and ketones. This method is particularly recommended for the synthesis of alkenyl-substituted glycidonitriles.

Melting points (determined in a capillary tube apparatus) and boiling points are uncorrected. ^{1}H and ^{13}C NMR spectra were measured in $CDCl_3$ on a Varian Mercury 400 or Varian Gemini 200 spectrometer (400 MHz or 200 MHz for ^{1}H and 100 MHz or 50 MHz for ^{13}C). ^{1}H and ^{1}H NOESY spectra were measured in $CDCl_3$ on a Brucker 500 spectrometer at 500 MHz. Chemical shifts (δ) are given in ppm relative to TMS and coupling constants (*J*) are given in Hz. Gas chromatography (GC) analyses were carried out with an Agilent 6850 chromatograph, equipped with HP50+ (30 m) capillary column. Elemental analyses were performed with a Perkin–Elmer CHNO/S Series II 2400 microanalyser. HR-MS analyses were performed with an AMD-604 spectrograph. Column chromatography was carried out using MERCK Aluminum oxide 90 active basic (70–230 mesh) with hexane as eluent. Chloroacetonitrile (**1**), isopropyl chloroacetate (**3**), carbonyl compounds **5–12** and all solvents were commercially available, while 2-chloropropionitrile (**2**)[1] and *tert*-butyl chloroacetate (**4**)[25] were synthesized according to literature procedures.

Synthesis of Compounds 13–25; General Procedure

Powdered NaOH (6.00 g, 0.15 mol) and THF (100 mL or 50 mL, Table 1) were stirred with a magnetic stirrer while a mixture of α-chloronitrile **1** or **2** (0.055 mol) and carbonyl compound **5–12** (0.05 mol) was added dropwise at 20–30 °C over 20 min. The mixture was stirred at the same temperature until GC analyses indicated the total consumption of the starting carbonyl compound (Table 1). The reaction mixture was then poured into a mixture of ice–water (~100 g) and CH_2Cl_2 (100 mL), the organic phase was taken and the aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were washed with brine (100 mL), dried over $MgSO_4$ and concentrated. The products **13–25** were isolated either by vacuum distillation or by column chromatography (Table 1).

3-(1-Propenyl)oxirane-2-carbonitrile (13)

Yield: 3.12 g (57%); colorless oil; bp 87–89 °C (20 Torr); mixture of diastereoisomers.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.77 (dd, *J* = 6.8, 1.6 Hz, 3 H, CH_3 *E*), 1.83 (dd, *J* = 6.8, 1.6 Hz, 3 H, CH_3 *Z*), 3.30 (d, *J* = 2.0 Hz, 1 H, C2-H *E*), 3.58–3.63 (m, 2 H, C2-H + C3-H *Z*), 3.72 (dd, *J* = 8.0, 2.0 Hz, 1 H, C3-H *E*), 5.10 (ddq, *J* = 15.6, 8.0, 1.6 Hz, 1 H, CH_3CH=C*H E*), 5.39 (ddq, *J* = 15.6, 8.0, 1.6 Hz, 1 H, CH_3CH=C*H Z*), 6.08–6.22 (m, 1 H, CH_3C*H*=CH *E* + *Z*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.9, 18.0, 42.7, 43.1, 57.0, 58.6, 115.6, 116.2, 123.0, 124.1, 136.2, 137.2.

HRMS (EI): *m*/*z* [M^+] calcd for C_6H_7NO: 109.0528; found 109.0524.

3-(1-Methylenepentyl)oxirane-2-carbonitrile (14)

Yield: 6.07 g (83%); colorless oil; bp 93–96 °C (10 Torr); mixture of diastereoisomers.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 7.2 Hz, 3 H, CH_3 *E*), 0.93 (t, *J* = 7.2 Hz, 3 H, CH_3 *Z*), 1.27–1.57 (m, 4 H, CH_2 *E* + *Z*), 1.87–2.01 (m, 2 H, CH_2C=C *E*), 2.15–2.20 (m, 2 H, CH_2C=C *Z*), 3.28 (d, *J* = 2.0 Hz, 1 H, C2-H *E*), 3.58 (d, *J* = 3.6 Hz, 1 H, C2-H *Z*), 3.60 (d, *J* = 3.6 Hz, 1 H, C3-H *Z*), 3.74 (d, *J* = 2.0 Hz, 1 H, C3-H *E*), 5.10 (q, *J* = 1.2 Hz, 1 H, C=CH_2 *E*), 5.16–5.18 (m, 1 H, C=CH_2 *Z*), 5.21–5.22 (m, 1 H, C=CH_2 *Z*), 5.22–5.26 (m, 1 H, C=CH_2 *E*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8 (*E* + *Z*), 22.2, 22.3, 29.8, 29.9, 30.3, 32.7, 41.9, 43.9, 57.8, 59.7, 113.5, 115.1, 115.3, 116.3, 139.9, 141.5.

Anal. Calcd for $C_9H_{13}NO$: C, 71.49; H, 8.67; N, 9.26. Found: C, 71.73; H, 8.65; N, 9.32.

3-Styryloxirane-2-carbonitrile (15)

Yield: 5.88 g (69%); yellowish oil; bp 113–118 °C (0.2 Torr); mixture of diastereoisomers.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.43 (d, *J* = 2.0 Hz, 1 H, C2-H *E*), 3.71 (d, *J* = 4.0 Hz, 1 H, C2-H *Z*), 3.83 (ddd, *J* = 8.0, 4.0, 0.4 Hz, 1 H, C3-H *Z*), 3.94 (ddd, *J* = 8.0, 2.0, 0.8 Hz, 1 H, C3-H *E*), 5.78 (dd, *J* = 16.0, 8.0 Hz, 1 H, PhCH=C*H E*), 6.07 (dd, *J* = 16.0, 8.0 Hz, 1 H, PhCH=C*H Z*), 6.92 (d, *J* = 16.0 Hz, 1 H, PhC*H*=CH *E*), 7.00 (d, *J* = 16.0 Hz, 1 H, PhC*H*=CH *Z*), 7.31–7.47 (m, 5 H, Ar-H *E* + *Z*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 43.2, 43.5, 57.4, 58.8, 115.5, 116.0, 120.2, 121.3, 126.7, 126.8, 126.9, 128.7, 128.8, 128.9, 129.0, 134.8, 134.9, 138.1, 139.2.

Anal. Calcd for $C_{11}H_9NO$: C, 77.17; H, 5.30; N, 8.18. Found: C, 76.95; H, 5.48; N, 8.21.

3-(1-Methylstyryl)oxirane-2-carbonitrile (16)

Yield: 8.38 g (91%); colorless oil; bp 108 °C (0.2 Torr); mixture of diastereoisomers.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.74 (d, *J* = 1.6 Hz, 3 H, CH_3 *E*), 2.02 (d, *J* = 1.6 Hz, 3 H, CH_3 *Z*), 3.47 (d, *J* = 2.0 Hz, 1 H, C2-H *E*), 3.64 (d, 1 H, *J* = 4.0 Hz, C2-H *Z*), 3.76 (dd, *J* = 4.0, 0.4 Hz, 1 H, C3-H *Z*), 3.92 (dd, *J* = 2.0, 0.8 Hz, 1 H, C3-H *E*), 6.75 (s, 1 H, PhC*H*=CCH_3 *Z*), 6.77 (s, 1 H, PhC*H*=CCH_3 *E*), 7.26–7.42 (m, 5 H, Ar-H *E* + *Z*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.5, 14.3, 40.9, 43.1, 59.8, 62.1, 115.3, 116.4, 127.2, 127.4, 128.1, 128.2, 128.4, 128.8, 128.9, 129.2, 129.4, 132.2, 135.7, 135.8.

HRMS (EI): *m*/*z* [M^+] calcd for $C_{12}H_{11}NO$: 185.0841; found 185.0843.

3-Methyl-3-vinyloxirane-2-carbonitrile (17)
Yield: 1.95 g (36%); colorless oil; bp 47–51 °C (10 Torr); mixture of diastereoisomers.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.53 (s, 3 H, CH_3 *Z*), 1.67 (s, 3 H, CH_3 *E*), 3.33 (s, 1 H, C2-H *E*), 3.44 (s, 1 H, C2-H *Z*), 5.37 (dd, *J* = 10.8, 0.8 Hz, 1 H, CH_2=CH *E*), 5.47 (dd, *J* = 17.2, 0.8 Hz, 1 H, CH_2=CH *E*), 5.52 (dd, *J* = 10.8, 0.8 Hz, 1 H, CH_2=CH *Z*), 5.57 (dd, *J* = 17.2, 0.8 Hz, 1 H, CH_2=CH *Z*), 5.61 (dd, *J* = 17.2, 10.8 Hz, 3 H, CH_2=C*H E*), 5.84 (dd, *J* = 17.2, 10.8 Hz, 3 H, CH_2=C*H Z*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.1, 19.0, 48.7, 49.0, 61.4, 61.7, 115.6 (*E* + *Z*), 119.9, 121.2, 133.4, 135.2.

Anal. Calcd for C_6H_7NO: C, 66.04; H, 6.47; N, 12.84. Found: C, 65.37; H, 6.49; N, 12.81.

3-Methyl-3-(2-methyl-1-propenyl)oxirane-2-carbonitrile (18)
Yield: 5.14 g (75%); colorless oil; bp 90–92 °C (20 Torr); mixture of diastereoisomers.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.46 (s, 3 H, CH_3 *Z*), 1.60 (s, 3 H, CH_3 *E*), 1.69 [d, *J* = 1.2 Hz, 3 H, CH=C(CH_3)$_2$ *E*], 1.73 [d, *J* = 1.6 Hz, 3 H, CH=C(CH_3)$_2$ *E*], 1.78 [d, *J* = 1.6 Hz, 3 H, CH=C(CH_3)$_2$ *Z*], 1.80 [d, *J* = 1.2 Hz, 3 H, CH=C(CH_3)$_2$ *Z*], 3.30 (s, 1 H, C2-H *E*), 3.34 (s, 1 H, C2-H *Z*), 5.30–5.34 [m, 1 H, C*H*=C(CH_3)$_2$ *E*], 5.38–5.41 [m, 1 H, C*H*=C(CH_3)$_2$ *Z*].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.1, 19.4, 20.4, 22.3, 25.2, 25.4, 48.0, 48.1, 61.3, 61.8, 116.1, 116.2, 119.2, 121.0, 139.0, 140.7.

HRMS (EI): *m*/*z* [M^+] calcd for $C_8H_{11}NO$: 137.0841; found: 137.0837.

3-Methyl-3-styryloxirane-2-carbonitrile (19)
Yield: 7.36 g (80%); yellowish oil; bp 119–125 °C (0.4 Torr); mixture of diastereoisomers.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.65 (s, 3 H, CH_3 *Z*), 1.80 (s, 3 H, CH_3 *E*), 3.43 (s, 1 H, C2-H *E*), 3.52 (s, 1 H, C2-H *Z*), 5.95 (d, *J* = 16.0 Hz, 1 H, PhCH=C*H E*), 6.17 (d, *J* = 16.0 Hz, 1 H, PhCH=C*H Z*), 6.75 (d, *J* = 16.0 Hz, 1 H, PhC*H*=CH *E*), 6.86 (d, *J* = 16.0 Hz, 1 H, PhC*H*=CH *Z*), 7.28–7.46 (m, 5 H, Ar-H *E* + *Z*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.8, 19.7, 49.2, 49.5, 61.7, 62.0, 115.6, 115.7, 124.1, 125.8, 126.6, 126.8, 128.6, 128.7, 134.2, 135.1, 135.2, 135.8.

Anal. Calcd for $C_{12}H_{11}NO$: C, 77.81; H, 5.99; N, 7.56. Found: C, 77.69; H, 6.21; N, 7.56.

1-Oxaspiro[2.5]oct-4-ene-2-carbonitrile (20)
Yield: 5.32 g (79%); colorless oil; bp 110–114 °C (15 Torr); mixture of diastereoisomers.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.62–2.32 (m, 6 H, CH_2), 3.41 (s, 1 H, C2-H major), 3.44 (s, 1 H, C2-H minor), 5.06–5.16 (m, 1 H, CC*H*=CH major), 5.43–5.53 (m, 1 H, CC*H*=CH minor), 6.20–6.42 (m, 1 H, CCH=C*H*).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 20.7, 20.8, 24.6, 24.7, 28.4, 30.3, 48.8 (*E* + *Z*), 61.5, 61.6, 115.8, 116.0, 123.0, 124.6, 139.5, 140.0.

Anal. Calcd for C_8H_9NO: C, 71.09; H, 6.71; N, 10.36. Found: C, 70.24; H, 6.59; N, 10.17.

2-Methyl-3-styryloxirane-2-carbonitrile (21)
Yield: 5.72 g (62%); yellowish oil; bp 123–127 °C (0.5 Torr); mixture of diastereoisomers.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.66 (s, 3 H, CH_3 *E*), 1.73 (s, 3 H, CH_3 *Z*), 3.59 (d, *J* = 8.0 Hz, 1 H, C3-H *Z*), 4.00 (d, *J* = 7.2 Hz, 1 H, C3-H *E*), 5.92 (dd, *J* = 16.0, 7.2 Hz, 1 H, PhCH=C*H E*), 6.08 (dd, *J* = 15.6, 8.0 Hz, 1 H, PhCH=C*H Z*), 6.88 (d, *J* = 16.0 Hz, 1 H, PhC*H*=CH *E*), 6.95 (d, *J* = 15.6 Hz, 1 H, PhC*H*=CH *Z*), 7.29–7.48 (m, 5 H, Ar-H *E* + *Z*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.1, 20.4, 50.0, 51.8, 62.6, 63.9, 117.5, 118.8, 119.0, 121.1, 126.7, 126.8, 128.7, 128.8, 128.9, 135.1, 138.6, 138.7.

HRMS (EI): *m*/*z* [M^+] calcd for $C_{12}H_{11}NO$: 185.0841; found 185.0844.

2-Methyl-3-(1-methylstyryl)oxirane-2-carbonitrile (22)
Yield: 8.80 g (88%); colorless oil; bp 114–118 °C (0.5 Torr); mixture of diastereoisomers.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.56 (s, 3 H, CH_3 *E*), 1.76 (s, 3 H, CH_3 *Z*), 1.97–2.00 (m, 3 H, PhCH=CCH_3 *E*), 2.01–2.03 (m, 3 H, PhCH=CCH_3 *Z*), 3.52 (s, 1 H, C3-H *Z*), 3.92 (s, 1 H, C3-H *E*), 6.48 (s, 1 H, PhC*H*=CCH_3 *E*), 6.71 (s, 1 H, PhC*H*=CCH_3 *Z*), 7.24–7.42 (m, 5 H, Ar-H *E* + *Z*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.6, 14.7, 15.5, 20.8, 49.4, 51.7, 64.8, 66.3, 117.3, 119.2, 127.1, 127.3, 127.4, 128.2, 128.3, 128.8, 128.9, 129.0, 135.8, 136.1.

Anal. Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.24; H, 6.59; N, 7.06.

2,3-Dimethyl-3-(2-methyl-1-propenyl)oxirane-2-carbonitrile (23)
Yield: 5.72 g (76%); colorless oil; bp 88–92 °C (20 Torr); mixture of diastereoisomers.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (s, 3 H, CH_3 minor), 1.51 (s, 3 H, CH_3 major), 1.61 (s, 3 H, CH_3 major), 1.65 (s, 3 H, CH_3 minor), 1.70 [d, *J* = 1.2 Hz, 3 H, CH=C(CH_3)$_2$ major], 1.73 [d, *J* = 1.6 Hz, 3 H, CH=C(CH_3)$_2$ major], 1.74–1.76 [m, 6 H, CH=C(CH_3)$_2$ minor], 5.16–5.19 [m, 1 H, C*H*=C(CH_3)$_2$ major], 5.41–5.44 [m, 1 H, C*H*=C(CH_3)$_2$ minor].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.4, 18.2, 18.4, 19.3, 19.4, 21.7, 25.1, 25.2, 54.1, 54.4, 64.5, 65.0, 118.7, 118.8, 119.3, 121.7, 139.1, 139.2.

HRMS (EI): *m*/*z* [M^+] calcd for $C_9H_{13}NO$: 151.0997; found: 151.0991.

2,3-Dimethyl-3-styryloxirane-2-carbonitrile (24)
Yield: 2.82 g (28%); yellowish oil; mixture of diastereoisomers.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.60 (s, 3 H, CH_3), 1.61 (s, 3 H, CH_3), 1.74 (s, 3 H, CH_3), 1.80 (s, 3 H, CH_3), 6.11 (d, *J* = 16.0 Hz, 1 H, PhCH=C*H*), 6.24 (d, *J* = 16.0 Hz, 1 H, PhCH=C*H*), 6.66 (d, *J* = 16.0 Hz, 1 H, PhC*H*=CH), 6.82 (d, *J* = 16.0 Hz, 1 H, PhC*H*=CH), 7.27–7.46 (m, 5 H, Ar-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.2, 17.2, 17.7, 20.5, 55.6, 55.8, 64.7, 65.5, 118.4, 118.5, 123.2, 126.2, 126.6, 126.8, 128.5, 128.5, 128.6, 128.7, 134.6, 134.9, 135.3, 135.4.

Anal. Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.08; H, 6.48; N, 6.78.

2-Methyl-1-oxaspiro[2.5]oct-4-ene-2-carbonitrile (25)
Yield: 2.65 g (36%); colorless oil; bp 109–114 °C (15 Torr); mixture of diastereoisomers.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.63 (s, 1 H, CH_3 major), 1.64 (s, 1 H, CH_3 minor), 1.76–2.25 (m, 6 H, CH_2), 5.22–5.32 (m, 1 H, CC*H*=CH major), 5.50–5.60 (m, 1 H, CC*H*=CH minor), 6.22–6.40 (m, 1 H, CCH=C*H*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.9, 17.2, 20.6, 20.8, 24.6, 24.9, 26.7, 29.9, 55.1, 55.4, 63.5, 64.1, 118.4, 118.5, 121.8, 124.7, 139.0, 139.9.

Anal. Calcd for $C_9H_{11}NO$: C, 72.46; H, 7.43; N, 9.39. Found: C, 72.41; H, 7.47; N, 9.28.

Synthesis of Compounds 26–30; General Procedure
Powdered NaOH (3.00 g, 75 mmol) and THF (25 mL) were stirred with a magnetic stirrer while a mixture of α-chloroester **3** (5.12 g, 37.5 mmol) or **4** (4.52 g, 30 mmol) and the carbonyl compound **5**–**8** (25 mmol) was added dropwise at 10–30 °C (Table 2) over 10 min. The mixture was stirred at the same temperature for the time indicated in Table 2 (until GC analyses indicated the total consumption of the starting carbonyl compound) and worked up as described above. The products **26**–**30** were isolated either by vacuum distillation or by crystallization from MeOH (Table 2).

Isopropyl 3-(1-Methylstyryl)oxirane-2-carboxylate (26)
Yield: 1.97 g (32%); yellowish oil; bp 141–145 °C (1.5 Torr).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31 [d, *J* = 6.4 Hz, 3 H, $CH(CH_3)_2$], 1.32 (d, *J* = 6.4 Hz, 3 H, $CH(CH_3)_2$], 1.75 (d, *J* = 1.6 Hz, 3 H, CH_3), 3.50 (d, *J* = 1.6 Hz, 1 H, C2-H), 3.72 (dd, *J* = 1.6, 0.8 Hz, 1 H, C3-H), 5.14 [qq, *J* = 6.4, 6.4 Hz, 1 H, $CH(CH_3)_2$], 6.72 (s, 1 H, PhC*H*=CCH_3), 7.22–7.38 (m, 5 H, Ar-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.9, 21.6, 21.7, 52.7, 61.8, 69.4, 127.1, 128.1, 128.2, 128.9, 130.9, 131.7, 136.5, 168.4.

Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.12; H, 7.37.

***tert*-Butyl 3-(1-Propenyl)oxirane-2-carboxylate (27)**
Yield: 1.40 g (30%); colorless oil; bp 57–60 °C (0.2 Torr); mixture of diastereoisomers.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 [s, 9 H, $C(CH_3)_3$ *E*], 1.45 [s, 9 H, $C(CH_3)_3$ *Z*], 1.70–1.75 (m, 3 H, CH_3 *E* + *Z*), 3.20 (d, *J* = 2.0 Hz, 1 H, C2-H *E*), 3.43 (dd, *J* = 8.0, 2.0 Hz, 1 H, C3-H *E*), 3.48–3.52 (m, 2 H, C2-H + C3-H *Z*), 5.13 (ddq, *J* = 15.6, 8.0, 1.6 Hz, 1 H, CH_3CH=C*H E*), 5.34–5.42 (m, 1 H, CH_3CH=C*H Z*), 5.94–6.08 (m, 1 H, CH_3C*H*=CH *E* + *Z*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.8, 18.0, 27.8, 28.0, 54.6, 55.1, 57.2, 57.7, 82.2, 82.3, 123.6, 126.5, 133.7, 135.1, 166.9, 167.7.

HRMS (EI): *m*/*z* [M^+] calcd for $C_{10}H_{16}O_3$: 184.1099; found: 184.1099.

***tert*-Butyl 3-(1-Methylenepentyl)oxirane-2-carboxylate (28)**
Yield: 3.89 g (69%); colorless oil; bp 75–76 °C (0.5 Torr); mixture of diastereoisomers.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (t, *J* = 7.2 Hz, 3 H, CH_3 *E*), 0.90 (t, *J* = 7.2 Hz, 3 H, CH_3 *Z*), 1.26–1.53 (m, 4 H, CH_2 *E* + *Z*), 1.42 [s, 9 H, $C(CH_3)_3$ *Z*], 1.48 [s, 9 H, $C(CH_3)_3$ *E*], 1.87–2.01 (m, 2 H, CH_2C=C *E*), 2.06–2.12 (m, 2 H, CH_2C=C *Z*), 3.24 (d, *J* = 1.6 Hz, 1 H, C2-H *E*), 3.48 (d, *J* = 1.6 Hz, 1 H, C3-H *E*), 3.52–3.56 (m, 2 H, C2-H + C3-H *Z*), 4.97–4.99 (m, 1 H, C=CH_2 *Z*), 5.01 (q, *J* = 1.2 Hz, 1 H, C=CH_2 *E*), 5.12 (s, 1 H, C=CH_2 *Z*), 5.19 (s, 1 H, C=CH_2 *E*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9 (*E* + *Z*), 22.3, 22.5, 27.9, 28.0, 30.0, 30.4, 33.3, 54.2, 55.3, 57.6, 59.2, 82.1, 82.4, 112.2, 113.9, 140.4, 143.6, 165.8, 167.8.

Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 69.14; H, 9.71.

***tert*-Butyl 3-Styryl-oxirane-2-carboxylate (29)**
Yield: 2.48 g (40%); colorless oil; bp 147 °C (0.6 Torr); mixture of diastereoisomers.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.50 [s, 9 H, $C(CH_3)_3$ *Z*], 1.52 [s, 9 H, $C(CH_3)_3$ *E*], 3.39 (d, *J* = 2.0 Hz, 1 H, C2-H *E*), 3.66 (d, *J* = 4.4 Hz, 1 H, C2-H *Z*), 3.69 (dd, *J* = 8.0, 2.0 Hz, 1 H, C3-H *E*), 3.75 (dd, *J* = 8.4, 4.4 Hz, 1 H, C3-H *Z*), 5.87 (dd, *J* = 16.0, 8.0 Hz, 1 H, PhCH=C*H E*), 6.16 (dd, *J* = 16.0, 8.4 Hz, 1 H, PhCH=C*H Z*), 6.85 (d, *J* = 16.0 Hz, 1 H, PhC*H*=CH *E*), 6.89 (d, *J* = 16.0 Hz, 1 H, PhC*H*=CH *Z*), 7.24–7.42 (m, 5 H, Ar-H *E* + *Z*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.9, 28.0, 55.0, 55.6, 57.5, 58.0, 82.5 (*E* + *Z*), 121.6, 124.2, 126.5, 128.4, 128.6, 135.5, 136.1, 137.5, 166.8, 167.5.

Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 72.91; H, 7.20.

***tert*-Butyl 3-(1-Methylstyryl)oxirane-2-carboxylate (30)**
Yield: 4.75 g (73%); white solid; mp 66–67 °C (MeOH).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.52 [s, 9 H, $C(CH_3)_3$], 1.74 (d, *J* = 1.2 Hz, 3 H, CH_3), 3.42 (d, *J* = 2.0 Hz, 1 H, C2-H), 3.67 (dd, *J* = 2.0, 0.4 Hz, 1 H, C3-H), 6.72 (s, 1 H, PhC*H*=CCH_3), 7.23–7.38 (m, 5 H, Ar-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.9, 27.9, 53.1, 61.6, 82.5, 127.0, 128.2, 128.9, 130.9, 131.9, 136.5, 167.9.

Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.68; H, 7.85.

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