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Synthesis of δ- and ε-Cyanoesters by Zinc-Catalyzed Ring-Opening of Cyclic Ethers with Acid Chlorides and Subsequent Cyanation

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Abstract In the present study, the zinc-catalyzed cleavage of cyclic ethers with acid halides as nucleophiles to yield chloroesters with different chain length has been investigated in detail. In the presence of straightforward and commercially available zinc salts as pre-catalysts excellent yields and selectivities were feasible. After studying the reaction conditions and the scope of the method, several efforts were carried out to understand the reaction mechanism. The obtained chloroesters were subsequently converted to δ- and ε-cyano esters, which are useful precursors in natural product synthesis.

Keywords Homogeneous catalysis · Zinc · Ether · Ring-opening · Nitriles · Cyanation

1 Introduction

Nitrile functionalities are extensively applied in organic chemistry and represent building blocks for the production of pharmaceuticals, agrochemicals, and polymers [1]. Especially, nitriles with additional functional groups allow for a broad scope of purposes. Here an interesting sub-class is represented by hydroxynitriles, which have been applied e.g. in the synthesis of natural products [2–5]. However, a general method for the synthesis of hydroxynitriles, which allows the easy adjustment of the carbon spacer between the hydroxyl and nitrile functionality is highly requested [6, 7]. In this regard, a three step synthesis based on the nucleophilic ring opening of ethers and subsequent cyanation can be an interesting possibility (Fig. 1). In more detail, on the one hand, a Lewis acid catalyzed ring-opening of cyclic ethers with acid chlorides as nucleophiles has the advantage of providing a variety of chloroesters with easy tunable chain lengths, since a great number of ethers are commercially available. During the years various methods based on Lewis acids have been introduced for the ring opening of cyclic ethers [8–20]. Among those protocols the application of zinc-salts as catalysts is advantageously, because it is abundant, cheap and low toxic. However, even if the zinc-catalyzed ring-opening of cyclic ethers has been reported a scope and limitations of the method is desired [21–27]. In addition, so far no mechanistical investigations have been accounted. On the other hand, the formation of a halide functionality allows a straightforward transformation to the corresponding nitriles [28, 29]. Finally, the cyanoesters are deprotected to provide the requested hydroxynitriles.

Herein we present based on our ongoing interest in zinc-chemistry an efficient and straightforward two step protocol based on zinc-catalyzed ring opening of cyclic ethers and subsequent cyanation to access protected hydroxynitriles with tunable chain length [30–36].

2 Results and Discussion

Initially, the ring-opening of THF with benzoyl chloride (**1**) was investigated as a model reaction to evaluate appropriate reaction conditions and to examine the influence of different reaction parameters (Table 1). As expected no formation of the δ-chloroester **2** was noticed in the absence of any zinc source applying THF as solvent at 70 °C (Table 1, entry 1). On the contrary, in the presence of

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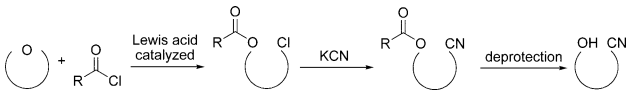


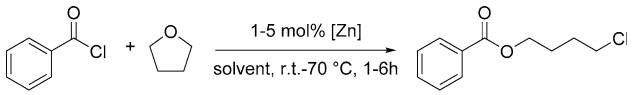
Fig. 1 Synthetic strategy for the synthesis of hydroxynitriles starting from cyclic ethers

5.0 mol% of commercially available $ZnCl_2$ an excellent yield (>99%) and chemoselectivity (>99%) was realized under non-inert conditions (Table 1, entry 2). Additionally, the effect of various zinc sources such as $ZnBr_2$, $Zn(OAc)_2$, $Zn(acac)_2$, and $Zn(OTf)_2$ on the formation of **2** was investigated (Table 1, entries 3–6). Interestingly, all applied zinc sources lead to a quantitative conversion of **1**. The loading of $Zn(OTf)_2$ was decreased to 1.0 and 0.5 mol% respectively, resulting in diminished yields of **2** for 0.5 mol% loading, while with 1.0 mol% excellent yields were feasible even after 1 h reaction time with turnover frequencies of >99 h^{-1} (Table 1, entry 6–8 and 11). Besides THF, toluene has been applied as solvent, but lower yields were achieved (Table 1, entry 10).

To explore the scope and limitation of the zinc catalyst, the ring-opening of a range of cyclic ethers with different benzoyl chlorides was performed (Table 2). The reaction conditions are in accordance to optimized conditions discovered in Table 1, means the corresponding ethers were converted in the presence of 1.0 mol% $ZnCl_2$. First an excess of THF was reacted with substituted benzoyl chlorides at 70 °C for 2 h (Table 2, entries 1–4). In all experiments excellent yields were observed. Furthermore, no difference was detected for electron-withdrawing as well as electron-donating groups (Table 2, entries 1–7). In addition the reaction of alkyl acid chlorides with THF resulted in excellent yields (Table 2, entries 8 and 9). By changing the source of cyclic ether towards tetrahydropyrane, 2,5-dimethyltetrahydrofuran and 3,3-dimethyloxetane lower yields were obtained (Table 2, entries 10–12). In case of **22** two isomers were found in a ratio of ~1:1. Moreover, sulfonic acid chlorides were reacted with THF in the presence of $ZnCl_2$. Moderate yields were monitored for p-toluenesulfonic acid chloride, whilst for p-nitrophenylsulfonic acid chloride no product formation was observed (Table 2, entries 13–14). Finally, also a heteroaromatic acid chloride was converted to the desired product in excellent yield (Table 2, entry 15).

After having established an appropriate catalyst system for the ring-opening of cyclic ethers to the corresponding chloroesters we became intrigued in studying the underlying reaction mechanism. As elucidated in Table 1 entry 1 catalytic amounts of zinc salts are necessary to promote the reaction, while in the absence of any zinc the reaction did not proceed. To investigate the effect of the anion connected to the zinc stoichiometric amounts of $ZnBr_2$ (1.0 equiv) or ZnF_2 (1.0 equiv), respectively, were added to a mixture of THF (excess) and **1** (1.0 equiv). After refluxing the reaction for 1 h the outcome was analyzed by GC–MS revealing the exclusive formation of chloroester **2**, while the corresponding bromo- or fluoroester was not observed. With respect to this result an abstraction of the chloride from the benzoyl chloride by the zinc is unlikely and the zinc acts probably as a Lewis acid [17]. Moreover, the

Table 1 Zinc-catalyzed synthesis of δ-chloroester **2**



1 **2**

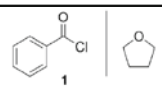
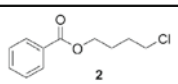
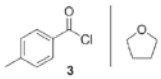
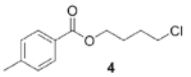
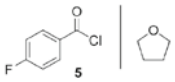
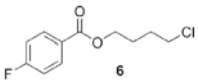
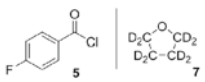
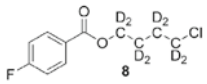
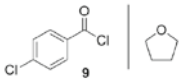
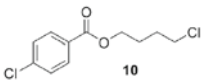
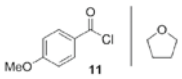
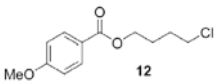
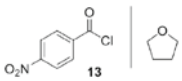
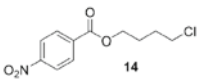
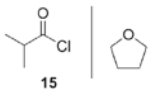
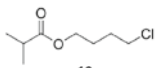
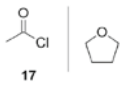
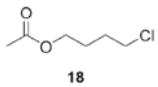
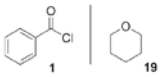
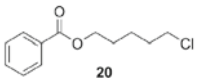
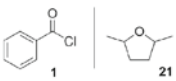
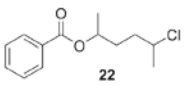
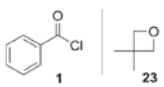
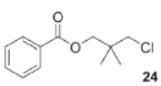
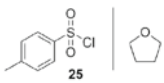
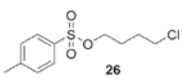
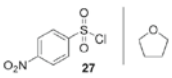
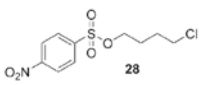
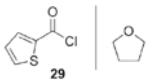
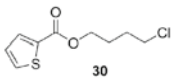
Entry	Zinc source (mol%)	Time (h)	T (°C)	Solvent	Yield (%)[a]
1	–	6	70	THF	<1
2	$ZnCl_2$ (5)	6	70	THF	>99
3	$ZnBr_2$ (5)	6	70	THF	>99
4	$Zn(OAc)_2$ (5)	6	70	THF	>99
5	$Zn(acac)_2$ (5)	6	70	THF	>99
6	$Zn(OTf)_2$ (5)	6	70	THF	>99
7	$Zn(OTf)_2$ (1.0)	6	70	THF	>99
8	$Zn(OTf)_2$ (0.5)	6	70	THF	72
9	$Zn(OTf)_2$ (5)	6	r.t.	THF	7
10[b]	$Zn(OTf)_2$ (1.0)	6	70	Toluene	59
11	$Zn(OTf)_2$ (1.0)	1	70	THF	>99

Reaction conditions: **1** (0.72 mmol), Zn-precursor (0.5–5.0 mol%), solvent (2.0 mL), THF (1.1 equiv.–excess), r.t.–70 °C, 1–6 h

[a] Determined by GC methods applying anisol as internal standard

[b] 1.1 equiv. of THF (0.79 mmol)

Table 2 Zinc-catalyzed synthesis of various chloroesters

Entry	Substrates	Product	Yield [%][a]
1			>99 (97)
2			>99 (89)
3			>99 (73)
4			>99
5			>99 (92)
6			>99 (85)
7			>99 (79)
8			>99 (90)
9			>99 (87)
10[b]			86 (77)
11			69 (60)
12			93 (84)
13			36
14			<1
15			>99 (98)

Reaction conditions: substrate (3.2–37 mmol), $ZnCl_2$ (1.0 mol%), ether (2.0–10 mL), 70 °C, 2 h

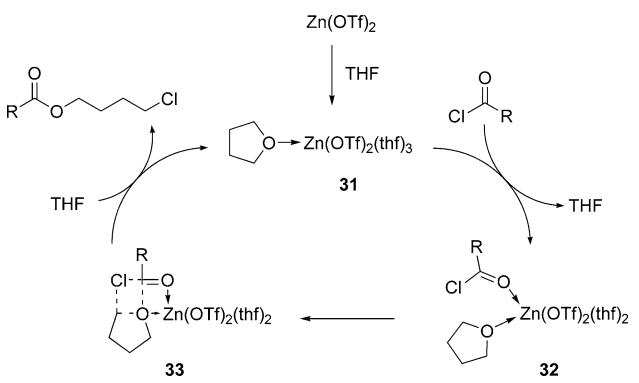
[a] In brackets the isolated yield is stated

[b] 24 h at 100 °C

function of the zinc was studied by NMR techniques. For this purpose $Zn(OTf)_2$ was applied as probe for ^{19}F NMR. $Zn(OTf)_2$ was dissolved in THF-d8 and a ^{19}F NMR spectrum was recorded showing a single peak at −79.1 ppm. The signal was assigned to the already known complex $Zn(OTf)_2(thf)_4$ (**31**), which was reported by Nefedov and

co-workers and more recently by us (Fig. 1) [33, 37]. The octahedral zinc is axial coordinated by the triflate groups and in the equatorial plane four THF molecules are located. Subsequently, acid chloride **5** (10 equiv.) was added to the solution at room temperature, resulting in the formation of a new signal for **5** at $\delta = -104.4$ ppm (sept, $J = 4.51$ Hz), while the signal for $Zn(OTf)_2$ ($\delta = -81.1$ ppm) is slightly shifted. Afterwards the mixture was heated to 70 °C for 1 h and cooled to room temperature followed by recording ^{19}F NMR spectrum. On the one hand the signal for $Zn(OTf)_2$ ($\delta = -81.1$ ppm) is unaltered on the NMR time-scale, which proves the assumption for a Lewis acid mechanism. On the other hand a new multiplet at $\delta = -109.3$ to -109.5 ppm occurred, which was dedicated to the product **8**. The product **8** was compared with the undeuterated compound **6** and affirmed by MS-methods. Based on the findings (vide supra) a reaction mechanism according to Scheme 1 is assumed. First the $Zn(OTf)_2$ is dissolved in THF and the complex **31** is formed. The coordination of the oxygen functionality of the ether to the zinc allows an activation of the oxygen and the adjacent carbon. In the next step one THF ligand dissociates and enables the coordination of the benzoyl chloride via the oxygen. Subsequently the chloride attacks the carbon and the benzoyl group is transferred to the former THF oxygen. The chloroester is discharged and a new molecule of THF coordinates to the zinc forming complex **31**, which can perform the next catalytic cycle.

After studying the zinc-catalyzed ring-opening of cyclic ethers we focused on the cyanation of the obtained chloroesters. In accordance to the work of Stirling and co-workers the chloroester and potassium cyanide were dissolved in dimethyl sulfoxide and stirred for 24 h at 80 °C [28]. In all experiments excellent yields have been observed for various substitution patterns (Table 3). Moreover, attempts to connect the zinc-catalyzed ring-opening and the cyanation protocol, means a one-pot procedure or a sequential process, failed so far.



Scheme 1 Proposed catalytic cycle for the synthesis of chloroesters

3 Conclusions

In summary, we have studied the zinc-catalyzed cleavage of cyclic ethers with acid halides as nucleophiles to yield chloroesters with different chain length. In the presence of straightforward and commercially available zinc salts as pre-catalysts excellent yields and selectivities were achieved. After studying the reaction conditions and the scope of the method, several efforts were carried out to understand the reaction mechanism. The obtained chloroesters were subsequently converted to δ- and ε-cyanoesters, which are useful precursors in natural product synthesis.

4 Experimental Section

4.1 General

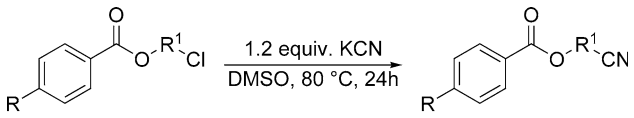
All compounds were used as received without further purification. THF and toluene were dried applying standard procedures. ^1H, ^{19}F and ^{13}C NMR spectra were recorded on a Bruker AFM 200 spectrometer (^1H: 200.13 MHz; ^{13}C: 50.32 MHz; ^{19}F: 188.31 MHz) using the proton signals of the deuterated solvents as reference. GC–MS measurements were carried out on a Shimadzu GC-2010 gas chromatograph (30 m Rxi-5 ms column) linked with a Shimadzu GCMA-QP 2010 Plus mass spectrometer. IR spectra were recorded on a Perkin Elmer Spectrum 100 FT-IR.

4.2 General Procedure for the Zinc-Catalyzed Ring-Opening of Cyclic Ethers

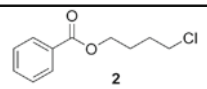
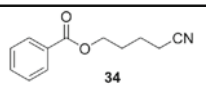
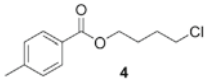
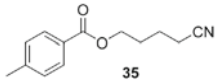
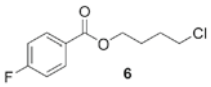
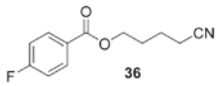
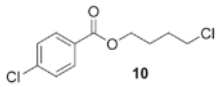
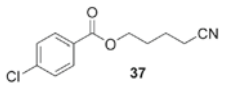
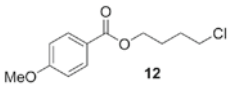
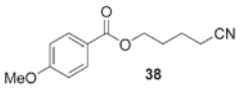
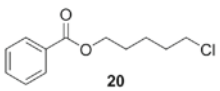
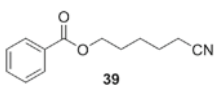
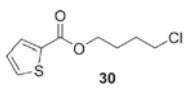
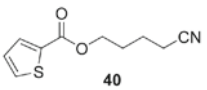
A pressure tube was charged with an appropriate amount of $ZnCl_2$ (1.0 mol%), the corresponding ether (2.0–10 mL) and the acid chloride (3.2–37 mmol). The reaction mixture was stirred in a preheated oil bath at 70 °C for 2 h. The mixture was cooled on an ice bath. The solvent was removed in vacuum and the residue was dissolved in dichloromethane (20 mL) and washed with water, brine and dried with Na_2SO_4. After filtration the solvent was removed to obtain colourless oils. The analytical properties of the corresponding chloroesters are in agreement with literature.

***δ*-Chlorobutyl benzoate (2)** [16] $m = 7.6$ g (97%); ^1H NMR ($CDCl_3$, 200 MHz) $\delta = 7.94–8.07$ (m, 2H); 7.33–7.58 (m, 3H), 4.26–4.40 (m, 2H), 3.50–3.65 (m, 2H), 1.84–1.98 (m, 4H) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) $\delta = 166.3$, 132.8, 130.1, 129.4, 128.2, 63.9, 44.3, 29.1, 26.2 ppm; IR (KBr): $\nu = 3805$ (w), 3660 (w), 3424 (m), 3065 (w), 2959 (m), 2871 (w), 2346 (w), 1720 (s), 1602 (w), 1584 (w), 1451 (s), 1387 (m), 1315 (s), 1275 (s), 1176

Table 3 Cyanation of chloroesters



2, 4, 20, 22, 24 **34, 35, 36, 37, 38**

Entry	Substrate	Product	Yield [%][a]
1	 **2**	 **34**	>99 (81)
2	 **4**	 **35**	>99 (87)
3	 **6**	 **36**	>99 (86)
4	 **10**	 **37**	>99 (91)
5	 **12**	 **38**	>99 (80)
6	 **20**	 **39**	>99 (94)
7	 **30**	 **40**	>99 (78)

Reaction conditions: substrate (4.7 mmol), KCN (5.7 mmol), DMSO (2.0 mL), 80 °C, 24 h

[a] In brackets the isolated yield is stated

(m), 1116 (s), 1070 (s), 1027 (s), 895 (w), 806 (w), 712 (s), 687 (m), 675 (m), 651 (m) cm^{-1}; MS (ESI) $m/z = 212$ (3, M^+), 177 (11), 122 (53), 105 (100), 77 (47) 51 (16).

***δ*-Chlorobutyl 4-methylbenzoate (4)** [18] $m = 6.0$ g (89%); ^{1}H NMR ($CDCl_3$, 200 MHz) $\delta = 7.84–7.94$ (m, 2H), 7.13–7.24 (m, 2H), 4.24–4.36 (m, 2H), 3.49–3.62 (m, 2H), 2.36 (s, 3H, CH_3), 1.82–1.96 (m, 4H) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) $\delta = 166.6$, 143.6, 129.6, 129.1, 127.5, 63.9, 44.5, 29.3, 26.2, 21.6 ppm; IR (KBr): $\nu = 3423$ (w), 2957 (s), 2867 (m), 2346 (w), 1717 (s), 1612 (s), 1578 (w), 1510 (m), 1446 (m), 1407 (m), 1385 (m), 1275 (s), 1208 (m), 1178 (s), 1110 (s), 1021 (m), 842 (m), 745 (s), 691 (w), 651 (w), 609 (w), 475 (w) cm^{-1}; MS (ESI) $m/z = 226$ (4, M^+), 191 (19), 136 (84), 119 (100), 91 (49), 65 (19), 55 (15).

***δ*-Chlorobutyl 4-fluorobenzoate (6)** $m = 533$ mg (73%); ^{1}H NMR ($CDCl_3$, 200 MHz) $\delta = 7.95–8.07$ (m, 2H), 6.99–7.13 (m, 2H), 4.24–4.35 (m, 2H), 3.32–3.62 (m, 3H), 1.84–1.96 (m, 3H) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) $\delta = 168.2$, 165.5, 132.1, 131.9, 126.5, 126.4, 115.6, 115.2, 64.2, 44.3, 29.2, 26.1 ppm; ^{19}F NMR ($CDCl_3$, 188 MHz) $\delta = -105.9$ to -105.6 (m); IR (KBr): $\nu = 2960$ (w), 2873 (w), 1718 (s), 1604 (s), 1508 (m), 1412 (w), 1274 (s), 1239 (m), 1154 (m), 1117 (m), 1091 (m), 1015 (w), 855 (m), 768 (m), 687 (w), 608 (w) cm^{-1}; MS (ESI) $m/z = 230$ (1, M^+), 195 (13), 140 (58), 123 (100), 96 (38), 75 (15), 55 (21).

***δ*-Chlorobutyl 4-chlorobenzoate (10)** [14] $m = 1.3$ g (92%); ^{1}H NMR ($CDCl_3$, 200 MHz) $\delta = 7.85–8.00$ (m, 2H), 7.31–7.43 (m, 2H), 4.23–4.39 (m, 2H), 3.35–3.82 (m, 2H), 1.62–2.01 (m, 4H) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) $\delta = 166.7$, 139.4, 131.0, 128.7, 128.6, 64.4, 44.4, 29.2, 26.2 ppm; IR (KBr): $\nu = 2959$ (m), 2871 (w), 1721 (s), 1595 (s), 1530 (m), 1488 (m), 1446 (w), 1402 (m), 1272 (s), 1172 (m), 1118 (s), 1015 (m), 895 (w), 850 (m), 760

(s), 721 (w), 685 (m), 652 (w), 524 (w), 479 (w) cm^{-1}; MS (ESI) m/z = 246 (3, M^+), 211 (14), 156 (78), 139 (100), 111 (34), 75 (21), 55 (38).

δ-Chlorobutyl 4-methoxybenzoate (12) [38] m = 6.2 g (85%); ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 7.90–8.01 (m, 2H), 6.84–6.92 (m, 2H), 4.23–4.34 (m, 2H), 3.82 (s, 3H, CH_3O), 3.36–3.63 (m, 3H), 1.84–1.94 (m, 3H) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 166.3, 163.4, 131.6, 122.7, 113.6, 63.8, 55.4, 44.5, 29.3, 26.3 ppm; IR (KBr): ν = 3851 (w), 3748 (w), 3736 (w), 3673 (w), 3650 (w), 3421 (w), 2959 (s), 2843 (m), 2346 (m), 1712 (s), 1607 (s), 1581 (m), 1512 (s), 1461 (s), 1421 (m), 1386 (m), 1312 (s), 1275 (s), 1253 (s), 1158 (s), 1103 (s), 1030 (s), 897 (w), 848 (m), 771 (s), 696 (m), 651 (w), 613 (m), 512 (w) cm^{-1}; MS (ESI) m/z = 242 (14, M^+), 207 (22), 152 (77), 135 (100), 107 (13), 92 (13), 77 (21), 56 (15).

δ-Chlorobutyl 4-nitrobenzoate (14) [14] m = 1.0 g (79%); ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 7.86–7.98 (m, 2H), 7.30–7.44 (m, 2H), 4.20–4.39 (m, 2H), 3.35–3.90 (m, 3H), 1.84–1.96 (m, 3H) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 165.7, 139.4, 131.0, 128.7, 128.6, 65.1, 44.4, 29.2, 26.2 ppm; IR (KBr): ν = 3112 (w), 2960 (m), 2870 (w), 1725 (s), 1608 (m), 1529 (s), 1446 (w), 1411 (w), 1350 (m), 1320 (w), 1275 (s), 1168 (w), 1104 (m), 1015 (w), 874 (m), 843 (w), 784 (w), 720 (s), 651 (w), 504 (w) cm^{-1}; MS (ESI) m/z = 257 (2, M^+), 168 (45), 150 (83), 120 (22), 104 (36), 92 (25), 76 (31), 65 (12), 54 (100).

δ-Chlorobutyl isobutyrate (16) [26] m = 4.0 g (90%); ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 3.98–4.13 (m, 2H), 3.31–3.70 (m, 2H), 2.35–2.60 (m, 1H), 1.65–1.90 (m, 4H), 1.05–1.17 (m, 6H) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 177.1, 63.4, 44.4, 34.0, 29.2, 26.1, 19.0 ppm; IR (KBr): ν = 2974 (m), 2877 (w), 2345 (w), 1735 (s), 1471 (m), 1390 (w), 1345 (w), 1259 (w), 1194 (m), 1157 (m), 1118 (w), 1078 (w), 890 (w), 754 (w), 669 (w), 653 (w) cm^{-1}; MS (ESI) m/z = 178 (1, M^+), 168 (45), 89 (70), 71 (91), 54 (79), 43 (100).

δ-Chlorobutyl 4-acetate (18) [39] m = 3.3 g (87%); ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 3.95–4.10 (m, 2H), 3.46–3.58 (m, 2H), 2.00 (s, 3H), 1.60–1.89 (m, 4H) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 171.0, 63.6, 44.4, 29.1, 26.1, 20.9 ppm; IR (KBr): ν = 2960 (m), 2871 (w), 1740 (s), 1446 (w), 1367 (m), 1241 (s), 1116 (m), 1047 (m), 755 (w), 650 (w), 607 (w) cm^{-1}; MS (ESI) m/z = 150 (1, M^+), 73 (14), 61 (16), 54 (36), 43 (100).

ε-Chloropentyl benzoate (20) [17] m = 6.2 g (77%); ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 7.94–8.06 (m, 2H), 7.30–7.55 (m, 3H), 4.21–4.34 (m, 2H), 3.41–3.57 (m, 2H), 1.40–1.90 (m, 6H) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 166.5, 132.9, 130.4, 129.5, 128.4, 64.6, 44.7, 32.2, 28.1, 23.5 ppm; IR (KBr): ν = 3360 (w), 3423 (w), 3065 (w), 2955 (s), 2868 (m), 2346 (w), 1720 (s), 1602 (m), 1584 (m), 1492 (w), 1452 (s), 1387 (m), 1314 (s), 1275 (s), 1176 (s), 1116 (s), 1070 (s), 1026 (s), 961 (w), 849 (w), 806 (w), 754 (w), 712 (s), 687 (m), 675 (m), 651 (m) cm^{-1}; MS (ESI) m/z = 226 (2, M^+), 123 (67), 105 (100), 77 (47), 51 (15).

1-Methyl-4-chloropentylbenzoate (22) [15] m = 2.9 g (60%); ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 7.80–8.17 (m, 2H), 7.35–7.68 (m, 3H), 5.07–5.23 (m, 1H), 3.95–4.15 (m, 1H), 1.28–2.04 (m, 10H) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 166.15, 166.18, 134.5, 133.7, 132.9, 130.7, 130.6, 130.2, 129.4, 128.9, 128.5, 128.4, 71.3, 70.8, 58.6, 58.5, 58.3, 57.9, 37.6, 36.9, 36.4, 36.0, 33.3, 33.1, 25.5, 25.4, 20.2, 20.16 ppm; IR (KBr): ν = 2975 (m), 1790 (w), 1717 (s), 1602 (w), 1584 (w), 1491 (w), 1451 (m), 1379 (w), 1354 (w), 1314 (m), 1276 (s), 1212 (w), 1176 (w), 1112 (m), 1070 (m), 1026 (m), 921 (w), 853 (w), 755 (w), 712 (s), 687 (w), 616 (w) cm^{-1}; MS (ESI) m/z = 240 (1, M^+), 123 (40), 105 (100), 82 (34), 77 (33), 55 (23).

4-Chloro-2,2-dimethylbutyl benzoate (24) m = 4.41 g (84%); ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 7.97–8.17 (m, 2H), 7.35–7.76 (m, 3H), 4.16 (s, 2H), 3.51 (s, 2H), 1.10 (s, 6H, 2xCH_3) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 166.3, 133.1, 131.4, 129.6, 128.5, 69.7, 52.2, 36.4, 22.7 ppm; IR (KBr): ν = 3065 (w), 2967 (m), 1721 (s), 1602 (w), 1528 (w), 1472 (w), 1451 (m), 1394 (w), 1373 (m), 1314 (w), 1273 (s), 1176 (w), 1114 (m), 1070 (w), 1026 (m), 972 (w), 935 (w), 851 (w), 805 (w), 772 (w), 711 (s), 687 (w), 672 (w) cm^{-1}; MS (ESI) m/z = 226 (1, M^+), 123 (25), 105 (100), 77 (29), 56 (13).

4-Chlorobutyl tosylate (26) MS (ESI) m/z = 262 (2, M^+), 172 (40), 155 (48), 107 (10), 91 (100), 65 (29), 54 (25).

δ-Chlorobutyl thiophenecarboxylate (30) m = 1.46 g (98%); ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 7.73–7.78 (m, 1H), 7.48–7.54 (m, 1H), 7.02–7.09 (m, 1H), 4.23–4.34 (m, 2H), 3.35–3.63 (m, 3H), 1.81–1.92 (m, 3H) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 162.0, 133.3, 132.2, 127.7, 64.2, 44.4, 29.1, 26.1 ppm; IR (KBr): ν = 2959 (w), 2871 (w), 1710 (s), 1526 (m), 1446 (w), 1420 (m), 1358 (m), 1260 (s), 1225 (w), 1153 (w), 1102 (s), 1076 (m), 1039 (w), 860 (w), 750 (m), 722 (m), 652 (w) cm^{-1}; MS (ESI) m/z = 218 (5, M^+), 183 (13), 128 (82), 111 (100), 55 (21).

4.3 General Procedure for the Cyanation of Chloroesters

The corresponding chloroester (4.7 mmol) and potassium cyanide (5.7 mmol, 1.2 equivalents) were dissolved in DMSO (2.0 mL) and stirred for 24 h at 80 °C. After cooling to room temperature water (20 mL) was added and the mixture was extracted with dichloromethane (2 × 20 mL). The organic layer was washed with water, brine and dried over Na_2SO_4. After filtration over a short plug of silica gel the solvent was removed in vacuum to obtain yellow oils.

δ-Cyanobutyl benzoate (**34**) [40] $m = 770$ mg (81%); ^{1}H NMR ($CDCl_3$, 200 MHz) $\delta = 7.96$–8.05 (m, 2H), 7.35–7.57 (m, 3H), 4.28–4.38 (m, 2H), 2.35–2.46 (m, 2H), 1.60–2.01 (m, 4H) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) $\delta = 166.5$, 133.1, 130.1, 129.6, 128.5, 128.4, 63.6, 527.8, 22.4, 17.0 ppm; IR (KBr): $\nu = 2958$ (m), 2346 (w), 2246 (w), 1718 (s), 1601 (w), 1684 (w), 1528 (w), 1452 (m), 1387 (w), 1315 (w), 1276 (s), 1176 (w), 1118 (m), 1071 (w), 1026 (w), 713 (s), 687 (w), 675 (w) cm^{-1}; MS (ESI) $m/z = 203$ (5, M^+), 122 (58), 105 (100), 77 (41), 51 (14).

δ-Cyanobutyl 4-methylbenzoate (**35**) $m = 890$ mg (87%); ^{1}H NMR ($CDCl_3$, 200 MHz) $\delta = 7.83$–7.92 (m, 2H), 7.14–7.23 (m, 2H), 4.25–4.35 (m, 2H), 2.35 (s, 3H), 2.32–2.44 (m, 2H), 1.68–1.97 (m, 4H) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) $\delta = 166.7$, 143.8, 129.6, 129.2, 127.3, 119.4, 63.5, 27.8, 22.4, 21.6, 16.9 ppm; IR (KBr): $\nu = 2956$ (m), 2342 (w), 2246 (w), 1717 (s), 1612 (m), 1509 (w), 1452 (w), 1375 (w), 1313 (w), 1276 (s), 1208 (w), 1178 (m), 1113 (m), 1071 (w), 1021 (w), 842 (w), 755 (m), 714 (m), 690 (w), 476 (w) cm^{-1}; MS (ESI) $m/z = 217$ (10, M^+), 136 (61), 114 (100), 91 (43), 65 (17).

δ-Cyanobutyl 4-fluorobenzoate (**36**) $m = 893$ mg (86%); ^{1}H NMR ($CDCl_3$, 200 MHz) $\delta = 7.92$–8.03 (m, 2H), 6.97–7.10 (m, 2H), 4.24–4.33 (m, 2H), 2.33–2.43 (m, 2H), 1.55–1.95 (m, 4H) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) $\delta = 168.3$, 165.4, 163.3, 132.2, 132.0, 126.3, 119.3, 115.8, 115.3, 63.8, 40.9, 27.7, 22.3, 16.9 ppm; ^{19}F NMR ($CDCl_3$, 188 MHz) $\delta = -105.6$ to -105.3 (m); IR (KBr): $\nu = 2959$ (w), 2874 (w), 1718 (s), 1604 (s), 1508 (s), 1458 (w), 1412 (w), 1388 (w), 1274 (s), 1239 (s), 1118 (s), 1091 (s), 1060 (w), 1015 (w), 951 (w), 929 (w), 856 (m), 768 (s), 688 (m), 608 (m), 504 (w) cm^{-1}; MS (ESI) $m/z = 221$ (3, M^+), 140 (57), 123 (100), 95 (37), 75 (13).

δ-Cyanobutyl 4-chlorobenzoate (**37**) $m = 1013$ mg (91%); ^{1}H NMR ($CDCl_3$, 200 MHz) $\delta = 7.85$–7.95 (m, 2H), 7.31–7.40 (m, 2H), 4.25–4.36 (m, 2H), 2.34–2.44 (m, 2H), 1.61–1.98 (m, 4H) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) $\delta = 165.5$, 139.5, 131.0, 128.8, 119.3, 63.9, 27.7, 22.3, 16.9 ppm; IR (KBr): $\nu = 2958$ (w), 2873 (w), 1718 (s), 1595 (m), 1489 (w), 1457 (w), 1421 (w), 1402 (w), 1274 (s), 1172 (m), 1126 (s), 1105 (s), 1092 (s), 1015 (m), 852 (m), 760 (m), 725 (w), 685 (w), 528 (w) cm^{-1}; MS (ESI) $m/z = 237$ (6, M^+), 156 (68), 141 (34), 139 (100), 111 (38), 75 (24).

δ-Cyanobutyl 4-methoxybenzoate (**38**) $m = 873$ mg (80%); ^{1}H NMR ($CDCl_3$, 200 MHz) $\delta = 7.85$–7.97 (m, 2H), 6.81–6.91 (m, 2H), 4.20–4.33 (m, 2H), 3.80 (s, 3H, OCH_3), 2.28–2.44 (m, 2H), 1.58–1.97 (m, 4H) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) $\delta = 166.0$, 163.3, 131.4, 122.3, 119.2, 113.5, 63.2, 55.3, 40.8, 27.2, 22.2, 16.8 ppm; IR (KBr): $\nu = 2958$ (w), 2873 (w), 1718 (s), 1595 (m), 1489 (w), 1457 (w), 1421 (w), 1402 (w), 1274 (s), 1172 (m), 1126 (s), 1105 (s), 1092 (s), 1015 (m), 852 (m), 760 (m), 725 (w), 685 (w), 528 (w) cm^{-1}; MS (ESI) $m/z = 233$ (20, M^+), 152 (56), 135 (100), 107 (11), 92 (12), 77 (18).

ε-Cyanopentyl benzoate (**39**) $m = 960$ mg (94%); ^{1}H NMR ($CDCl_3$, 200 MHz) $\delta = 7.95$–8.04 (m, 2H), 7.34–7.57 (m, 3H), 4.24–4.34 (m, 2H), 2.28–2.38 (m, 2H), 1.47–1.92 (m, 6H) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) $\delta = 166.5$, 133.0, 130.3, 129.5, 128.4, 119.5, 64.4, 28.0, 25.3, 25.1, 17.1 ppm; IR (KBr): $\nu = 2952$ (m), 2870 (w), 2246 (w), 1718 (s), 1602 (w), 1584 (w), 1452 (m), 1375 (w), 1315 (w), 1276 (s), 1176 (w), 1119 (m), 1071 (w), 1026 (w), 713 (s), 688 (w), 674 (w) cm^{-1}; MS (ESI) $m/z = 217$ (1, M^+), 177 (12), 122 (38), 105 (100), 77 (40), 55 (12).

δ-Cyanobutyl 3-thiophenecarboxylate (**40**) $m = 766$ mg (78%); ^{1}H NMR ($CDCl_3$, 200 MHz) $\delta = 7.69$–7.76 (m, 1H), 7.46–7.53 (m, 1H), 6.98–7.07 (m, 1H), 4.20–4.31 (m, 2H), 2.32–2.43 (m, 2H), 1.59–1.92 (m, 4H) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz) $\delta = 162.0$, 133.5, 132.6, 127.9, 119.3, 63.8, 27.7, 22.3, 16.9 ppm; IR (KBr): $\nu = 2957$ (w), 2873 (w), 1711 (s), 1604 (m), 1526 (m), 1508 (w), 1457 (m), 1420 (m), 1380 (w), 1358 (w), 1283 (s), 1262 (s), 1226 (m), 1154 (w), 1094 (s), 1076 (m), 1040 (w), 860 (m), 769 (m), 752 (m), 728 (m), 688 (w), 608 (w) cm^{-1}; MS (ESI) $m/z = 209$ (11, M^+), 128 (61), 111 (100).

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References

1. Larock RC (2010) Comprehensive organic transformations. Wiley, New York
2. McIver AL, Deiters A (2010) Org Lett 12:1288–1291
3. Deutsch HM, Ye X, Shi Q, Liu Z, Schweri MM (2001) Eur J Med Chem 36:303–312
4. Laronze JY, Cartier D, Laronze J (1980) J Levy Tetrahedron Lett 21:4441–4444
5. Meyers AI, Yamamoto Y, Mihelich ED, Bell RA (1980) J Org Chem 45:2792–2796
6. Quinet C, Sampoux L, Marko IE (2009) Eur. J. Org. Chem. 11:1806–1811
7. Miura K, Tomita M, Ichikawa J, Hosomi A (2008) Org Lett 10:133–136
8. Alper H, Edward JT (1970) Can J Chem 48:1623–1624
9. Goldsmith DJ, Kennedy E, Campbell RG (1975) J Org Chem 40:3571–3574
10. Brown HC, Lynch GJ (1981) J Org Chem 46:930–939
11. Yadav JS, Reddy BVS, Reddy PMK, Dash U, Gupta MK (2007) J Mol Catal A 271:266–269
12. Suresh V, Suryakiran N, Rajesh K, Selvam JJP, Srinivasulu M, Venkateswarlu Y (2008) Synth Commun 38:92–99
13. Suresh V, Suryakiran N, Venkateswarlu Y (2007) Can J Chem 85:1037–1040

14. Pasha MA, Manjula K (2007) Synth Commun 37:927–932
15. Costello JF, Draffin WN, Paver SP (2005) Tetrahedron 61:6715–6719
16. Coles SJ, Costello JF, Draffin WN, Hursthouse MB, Paver SP (2005) Tetrahedron 61:4447–4452
17. Guo Q, Miyaji T, Hara R, Shen B, Takahashi T (2002) Tetrahedron 58:7327–7334
18. Malladi RR, Kabalka GW (2002) Synth Commun 32:1997–2001
19. Kang J, Kim S-H (2000) Bull Korean Chem Soc 21:611–612
20. Tsonis CP (1988) J Mol Catal 45:145–150
21. Synerholm ME (1949) Org Synth 29:30–31
22. Helberger JH, Lantermann H (1954) Justus Liebigs Annalen der Chemie 586:158–164
23. Boberg F, Schultze GR (1955) Chem Ber 88:275–280
24. Birch SF, Dean RA, Hunter NJ, Whitehead EV (1955) J Org Chem 20:1178–1190
25. Pasha MA, Myint YY (2006) Ultrason Sonochem 13:175–179
26. Bhar S, Ranu BC (1995) J Org Chem 60:745–747
27. Qian C, Qiu A, Zhu D, Yang X (1994) J Mol Catal 87:357–359
28. Earl HA, Stirling CJM (1987) J Chem Soc 2:1273–1280
29. Neokosmidi A, Ragoussis V, Zikos C, Paravatou-Petsotas M, Livaniou E, Ragoussis N, Evangelatos G (2004) J. Agric Food Chem 52:4368–4374
30. Marinos NA, Enthaler S, Driess M (2010) ChemCatChem 2:846–853
31. Enthaler S, Eckhardt B, Inoue S, Irran E, Driess M (2010) Chem Asian J 5:2027–2035
32. Enthaler S, Schröder K, Inoue S, Eckhardt B, Junge K, Beller M, Driess M (2010) Eur J Org Chem 25:4893–4901
33. Enthaler S (2011) Catal Lett 141:55–61
34. Enthaler S (2011) Catal Sci Technol 1:104–110
35. Someya CI, Inoue S, Irran E, Krackl S, Enthaler S (2011) Eur J Inorg Chem 2691–2697
36. S. Enthaler, S. Inoue, *Chem. Asian J.* (2011). doi: 10.1002/asia.201100493
37. Amel'chenkova EV, Denisova TO, Nefedov SE (2006) Russ J Inorg Chem 51:1218–1263
38. Kotsuki H, Ichikawa Y, Nishizawa H (1988) Chem. Lett. 4:673–676
39. Fitch JW, Payne WG, Westmoreland D (1983) J Org Chem 48:751–753
40. Bose DS, Jayalakshmi B (1999) J Org Chem 64:1713–1714