Regioselective Synthesis of 5-(2-Cyanoethyl)-1,1′-biphenyl-2-carboxylates by Formal [3 + 3] Cyclocondensations of 1,3-Bis[(trimethylsilyl)oxy]buta-1,3-dienes

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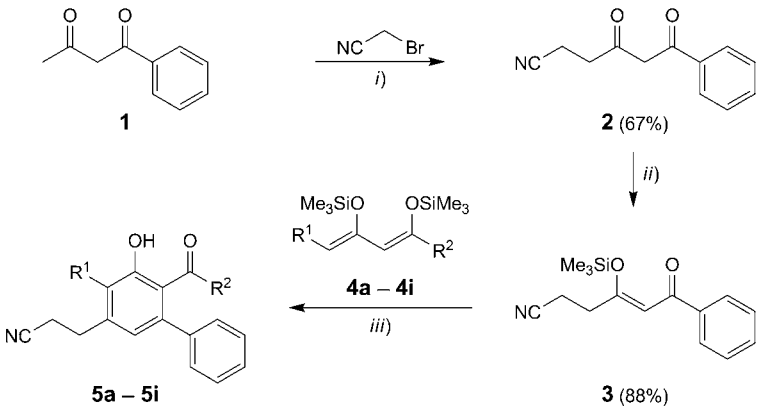
5-(2-Cyanoethyl)-1,1′-biphenyl-2-carboxylates were prepared by regioselective formal [3 + 3] cyclocondensations of 1,3-bis[(trimethylsilyl)oxy]buta-1,3-dienes.

Introduction. – Phenols, salicylates, and biarlys can be prepared by formal [3 + 3] cyclization reactions of 1,3-bis[(trimethylsilyl)oxy]buta-1,3-dienes with suitable 1,3-dielectrophiles [1]. This building-block strategy allows the synthesis of highly functionalized and substituted products from readily available starting materials. Some years ago, we reported the regioselective synthesis of 5-cyanosalicylates, highly functionalized benzonitriles, by this approach [2]. Herein, we report a new and convenient synthesis of 5-(2-cyanoethyl)-1,1′-biphenyl-2-carboxylates, which are difficult to prepare by other methods.

Results and Discussion. – The reaction of the dianion of benzoylacetone (**1**), generated from 2.5 equiv. of LDA (lithium diisopropylamide), and 2-bromoacetonitrile, afforded, following a methodology reported by our group [3], 4,6-dioxo-6-phenylhexanenitrile (**2**) in good yield (*Scheme*). The reaction of **2** with Et_3N and Me_3SiCl gave 6-oxo-6-phenyl-4-[(trimethylsilyl)oxy]hex-4-enenitrile (**3**). The reaction of **3** with 1,3-bis[(trimethylsilyl)oxy]buta-1,3-dienes **4a**–**4i** [4] (1.5–2.0 equiv.), carried out in a highly concentrated soln. of CH_2Cl_2 (2 ml/mmol) at −78° in the presence of $TiCl_4$ (1.1 equiv.), afforded the 5-(2-cyanoethyl)-1,1′-biphenyl-2-carboxylates **5a**–**5i**, respectively, in 30–75% yields (*Table*).

The cyclizations proceeded with excellent regioselectivity. Only the products, which contain the Ph group in *ortho*-position to the ester group, were formed. The two possible regioisomers **A** and **B** of **5h** are depicted in *Fig. 1*. The best yields were obtained for the reactions of **4a**–**4c**, which contain no substituent at the terminal C-atom of the diene. The yields of the other products are lower, presumably due to steric reasons. It is important to note that the other regioisomers could not be detected in the

Scheme. *Synthesis of* **5a**–**5i**



i) 1. 2.5 equiv. LDA, THF, 0°, 1 h; 2. $NCCH_2Br$, −78–20°, 16 h; 3. 10% HCl [3]. *ii*) Et_3N, Me_3SiCl, pentane, 20°, 72 h. *iii*). 1. $TiCl_4$, CH_2Cl_2, −78–20°, 12–14 h; 2. 10% HCl.

Table. *Synthesis of* **5a**–**5i**

4/**5**	R^1	R^2	Yield of **5** [%][a])	**4**/**5**	R^1	R^2	Yield of **5** [%][a])
a	H	MeO	75	**f**	Pr	MeO	41
b	H	EtO	69	**g**	MeO	MeO	30
c	H	^{i}PrO	58	**h**	$Cl(CH_2)_3$	MeO	50
d	Me	MeO	54	**i**	Allyl	MeO	35
e	Et	MeO	36				

[a]) Yields of isolated products.

product mixtures before the chromatographic purification (^{1}H-NMR evidence). The moderate yields might be explained by hydrolysis or oxidative dimerization of the dienes which were previously reported [5]. Besides the steric hindrance, the purity of each individual diene also plays a role.

The structure of **5h** was confirmed by ^{1}H,^{1}H-NOESY experiments (*Fig. 2*). Diagnostic correlations were observed between the H-atoms of the phenyl with those of the MeO group, and between the CH_2 groups of the 3-chloropropyl chain with those of the 2-cyanoethyl moiety. The structure of **5f** was independently confirmed by X-ray crystal-structure analysis (*Fig. 3*)[1]). Comparison of the spectroscopic data of **5f** and **5h** with those of the other derivatives indicate that all products are formed with the same pattern of regioselectivity.

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[1]) CCDC-918957 contains the supplementary crystallographic data for **5f**. These data can be obtained free of charge *via* http://www.ccdc.cam.ac.uk/data_request/cif or from the *Cambridge Crystallographic Data Centre*, 12 Union Road, Cambridge CB21EZ, UK; fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk).

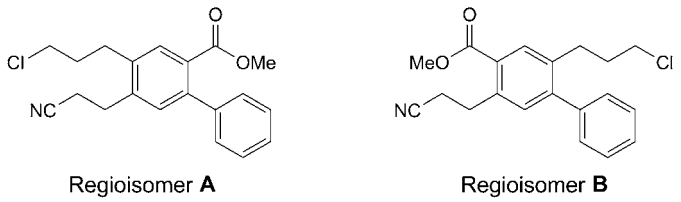

Fig. 1. *Possible regioisomers of* **5h**

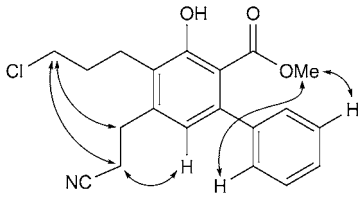

Fig. 2. *^{1}H,^{1}H-NOESY Correlations of* **5h**

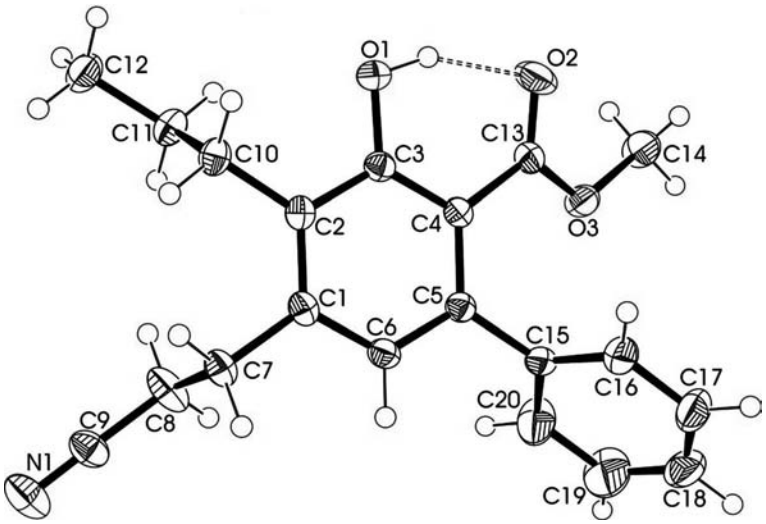

Fig. 3. *ORTEP Plot of* **5f** (50% probability level)

In conclusion, we have developed the synthesis of 5-(2-cyanoethyl)-1,1′-biphenyl-2-carboxylates by formal [3 + 3] cyclocondensations of 1,3-bis[(trimethylsilyl)oxy]buta-1,3-dienes with readily available 6-oxo-6-phenyl-4-[(trimethylsilyl)oxy]hex-4-enenitrile. The cyclizations proceeded with excellent regioselectivity.

Experimental Part

General. The solvents CH_2Cl_2, pentane, heptane, and AcOEt were purchased directly from *ACROS* and used without further purification. TLC: Silica-gel *60* F_{254} plates (SiO_2; *Merck*). Column chromatography (CC): *60 A* SiO_2 (60–200 mesh, *Merck*). IR Spectra: *Perkin-Elmer FT-IR 1600 ATR*

apparatus; $\tilde{\nu}$ in cm^{-1}. NMR Spectra: *Bruker Avance 250 II*, *Bruker DPX 300*, and *Bruker DPX 500*; δ in ppm rel. to solvent ($CDCl_3$, 7.26 and 77.0 ppm; (D_6)DMSO, 2.49 and 39.7 ppm) as internal standard, *J* in Hz. MS: *Hewlett-Packard HP GC/MS 5890/5972* instrument by electron ionization (EI, 70 eV), chemical ionization (CI, isobutane), or electrospray ionization (ESI); in *m/z* (rel. %).

Synthesis of (4Z)-6-Oxo-6-phenyl-4-[(trimethylsilyl)oxy]hex-4-enenitrile (**3**). To a soln. of *4,6-dioxo-6-phenylhexanenitrile* (**2**; 4.100 g, 20.29 mmol) in pentane (1 ml/mmol) and CH_2Cl_2 (1 ml/mmol) was added Et_3N (3.80 ml, 27.0 mmol) at 20°, and the soln. was stirred for 30 min. Subsequently, Me_3SiCl (4.15 ml, 30.50 mmol) was added, and the soln. was stirred for 74 h at 20°. The solvent was removed *in vacuo*, and to the residue was added pentane (50 ml). The mixture was filtered, and the filtrate was concentrated *in vacuo*. The residue was again washed with pentane (50 ml), the suspension was filtered, and the filtrate was concentrated *in vacuo* to give **3** (4.87 g, 88%) as a red oil. Due to the unstable nature of the product, it was only characterized by ^{1}H-NMR and directly used after its preparation. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.06–0.44 (*m*, Me_3Si); 2.62–3.19 (*m*, 2 CH_2); 5.96–6.30 (*m*, CH); 7.36–7.92 (*m*, 5 arom. H).

General Procedure for the Synthesis of 5-(2-Cyanoethyl)-3-hydroxy-1,1′-biphenyl-2-carboxylates **5a**–**5i**: To a soln. of **3** (1.0 mmol) and of **4a**–**4i** (1.5–2.0 mmol) in dry CH_2Cl_2 (2 ml/mmol **3**) was added $TiCl_4$ (1.1 mmol) at −78°. The soln. was allowed to warm to 20° within 6 h and was stirred for 6–8 h at 20°. To the soln. was added HCl (10%, 10 ml/mmol), and the mixture was extracted with CH_2Cl_2 (3 × 50 ml). The combined org. layers were dried (Na_2SO_4), filtered, and the filtrate was concentrated *in vacuo*. The residue was puried by CC (SiO_2).

Methyl 5-(2-Cyanoethyl)-3-hydroxy-1,1′-biphenyl-2-carboxylate (**5a**). From **3** (0.50 mmol, 137 mg), **4a** (1.00 mmol, 260 mg), and $TiCl_4$ (0.55 mmol, 0.06 ml) in 1 ml of CH_2Cl_2, **5a** was isolated by CC (heptane/AcOEt 13:1): 105 mg (75%). Colorless solid. M.p. 84–86°. IR (ATR): 3237*s*, 3036*w*, 3023*w*, 2953*w*, 2921*w*, 2849*w*, 2247*m*, 1668*s*, 1608*s*, 1573*s*, 1504*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.66 (*t*, ^3J = 7.6, CH_2); 2.95 (*t*, ^3J = 7.6, CH_2); 3.48 (*s*, MeO); 6.67 (*d*, ^4J = 1.9, H–C(6)); 6.87 (*d*, ^4J = 1.9, H–C(4)); 7.19–7.23 (*m*, 2 arom. H); 7.32–7.40 (*m*, 3 arom. H); 10.76 (*s*, OH). ^{13}C-NMR (63 MHz, $CDCl_3$): 18.4, 31.3 (CH_2); 51.7 (MeO); 111.0 (C_q); 116.1 (C(4)); 118.6 (C_q); 122.7 (C(6)); 127.0, 127.6, 128.0 (arom. CH); 142.3, 144.1, 145.6 (C_q); 161.8 (C(3)); 171.0 (C=O). EI-MS (70 eV): 281 (30, M^+), 250 (20), 249 (100), 181 (43), 152 (26). HR-ESI-MS: 282.11260 ($[M + H]^+$, $C_{17}H_{16}NO_3^+$; calc. 282.11247).

Ethyl 5-(2-Cyanoethyl)-3-hydroxy-1,1′-biphenyl-2-carboxylate (**5b**). From **3** (1.00 mmol, 273 mg), **4b** (2.00 mmol, 550 mg), and $TiCl_4$ (1.10 mmol, 0.12 ml) in 2 ml of CH_2Cl_2, **5b** was isolated by CC (heptane/AcOEt 15:1): 201 mg (69%). Colorless solid. M.p. 69–70°. IR (ATR): 3061*w*, 3031*w*, 2983*w*, 2936*m*, 2873*w*, 2242*m*, 1665*s*, 1612*s*, 1569*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.75 (*t*, ^3J = 7.2, Me); 2.65 (*t*, ^3J = 7.6, CH_2); 2.94 (*t*, ^3J = 7.6, CH_2); 3.98 (*q*, ^3J = 7.2, MeCH_2O); 6.66 (*d*, ^4J = 1.7, H–C(6)); 6.87 (*d*, ^4J = 1.7, H–C(4)); 7.20–7.23 (*m*, 2 arom. H); 7.32–7.37 (*m*, 3 arom. H); 10.92 (*s*, OH). ^{13}C-NMR (63 MHz, $CDCl_3$): 12.9 (Me); 18.5, 31.4 (CH_2); 61.0 (MeCH_2O); 111.1 (C_q); 116.1 (C(4)); 118.6 (C_q); 122.5 (C(6)); 126.9, 127.6, 128.1 (arom. CH); 142.6, 143.9, 145.7 (C_q); 161.9 (C(3)); 170.6 (C=O). EI-MS (70 eV): 295 (26, M^+), 250 (20), 249 (100), 181 (39), 152 (24). Anal. calc. for $C_{18}H_{17}NO_3$ (295.332): C 73.20, H 5.80, N 4.74; found: C 72.74, H 5.95, N 4.56.

1-Methylethyl 5-(2-Cyanoethyl)-3-hydroxy-1,1′-biphenyl-2-carboxylate (**5c**). From **3** (1.00 mmol, 273 mg), **4c** (2.00 mmol, 578 mg), and $TiCl_4$ (1.10 mmol, 0.12 ml) in 2 ml of CH_2Cl_2, **5c** was isolated by CC (heptane/AcOEt 13:1): 178 mg (58%). Colorless oil. IR (ATR): 3057*w*, 3027*w*, 2981*m*, 2936*w*, 2873*w*, 2247*m*, 1724*w*, 1654*s*, 1612*s*, 1570*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.85 (*d*, ^3J = 6.3, 2 Me); 2.65 (*t*, ^3J = 7.3, CH_2); 2.94 (*t*, ^3J = 7.3, CH_2); 4.93 (*sept.*, ^3J = 6.3, Me_2CH); 6.63 (*d*, ^4J = 1.9, H–C(6)); 6.86 (*d*, ^4J = 1.9, H–C(4)); 7.18–7.22 (*m*, 2 arom. H); 7.33–7.37 (*m*, 3 arom. H); 11.06 (*s*, OH). ^{13}C-NMR (75 MHz, $CDCl_3$): 18.5 (CH_2); 20.9 (2 Me); 31.5 (CH_2); 69.2 (Me_2CH); 111.5 (C_q); 116.1 (C(4)); 118.6 (C_q); 122.5 (C(6)); 126.8, 127.6, 128.2 (arom. CH); 142.8, 143.7, 145.7 (C_q); 162.0 (C(3)); 170.1 (C=O). EI-MS (70 eV): 309 (20, M^+), 250 (21), 249 (100), 181 (26), 152 (16). Anal. calc. for $C_{19}H_{19}NO_3$ (309.359): C 73.77, H 6.19, N 4.53; found: 73.75, H 6.35, N 4.18.

Methyl 5-(2-Cyanoethyl)-3-hydroxy-4-methyl-1,1′-biphenyl-2-carboxylate (**5d**). From **3** (1.00 mmol, 273 mg), **4d** (1.50 mmol, 412 mg), and $TiCl_4$ (1.10 mmol, 0.12 ml) in 2 ml of CH_2Cl_2, **5d** was isolated by CC (heptane/AcOEt 15:1): 159 mg (54%). Slightly yellow solid. M.p. 86–87°. IR (ATR): 3069*w*, 3036*w*, 3002*w*, 2976*w*, 2949*m*, 2244*m*, 1651*s*, 1611*s*, 1601*s*, 1564*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.28 (*s*, Me); 2.61

(t, $^3J = 7.6$, CH_2); 3.00 (t, $^3J = 7.6$, CH_2); 3.48 (s, MeO); 6.65 (s, H–C(6)); 7.20–7.23 (m, 2 arom. H); 7.31–7.39 (m, 3 arom. H); 11.10 (s, OH). ^{13}C-NMR (75 MHz, $CDCl_3$): 11.2 (Me), 17.7, 29.4 (CH_2); 51.7 (MeO); 110.3, 118.7 (C_q); 122.7 (C(6)); 123.6 (C_q); 126.8, 127.6, 128.1 (arom. CH); 141.9, 142.2, 142.5 (C_q); 159.9 (C(3)); 171.6 (C=O). EI-MS (70 eV): 295 (31, M^+), 264 (21), 263 (100), 209 (30), 165 (20), 152 (15). HR-EI-MS: 295.12062 (M^+, $C_{18}H_{17}NO_3^+$; calc. 295.12029).

Methyl 5-(2-Cyanoethyl)-4-ethyl-3-hydroxy-1,1′-biphenyl-2-carboxylate (**5e**). From **3** (0.95 mmol, 260 mg), **4e** (1.90 mmol, 548 mg), and $TiCl_4$ (1.00 mmol, 0.11 ml) in 2 ml of CH_2Cl_2, **5e** was isolated by CC (heptane/AcOEt 70:1): 105 mg (36%). Yellow solid. M.p. 111–112°. IR (ATR): 3062*w*, 3028*w*, 2979*w*, 2964*w*, 2953*w*, 2932*w*, 2873*m*, 2243*m*, 1651*s*, 1611*m*, 1600*m*, 1564*m*, 1538*w*, 1500*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.21 (t, $^3J = 7.6$, $MeCH_2$); 2.62 (t, $^3J = 7.7$, CH_2); 2.74 (q, $^3J = 7.6$, $MeCH_2$); 3.02 (t, $^3J = 7.7$, CH_2); 3.48 (s, MeO); 6.65 (s, H–C(6)); 7.12–7.26 (m, 2 arom. H); 7.31–7.39 (m, 3 arom. H); 11.04 (s, OH). ^{13}C-NMR (75 MHz, $CDCl_3$): 13.9 ($MeCH_2$); 18.4 (CH_2); 19.3 ($MeCH_2$); 28.6 (CH_2); 51.7 (MeO); 110.5, 118.7 (C_q); 122.8 (C(6)); 126.8, 127.6, 128.1 (arom. CH); 129.7, 141.3, 142.3, 142.5 (C_q); 159.8 (C(3)); 171.6 (C=O). EI-MS (70 eV): 309 (58, M^+), 277 (76), 223 (100), 219 (55), 165 (49). Anal. calc. for $C_{19}H_{19}NO_3$ (309.359): C 73.77, H 6.19, N 4.53; found: C 73.54, H 6.04, N 4.67.

Methyl 5-(2-Cyanoethyl)-3-hydroxy-4-propyl-1,1′-biphenyl-2-carboxylate (**5f**). From **3** (1.00 mmol, 273 mg), **4f** (1.50 mmol, 605 mg), and $TiCl_4$ (1.10 mmol, 0.12 ml) in 2 ml of CH_2Cl_2, **5f** was isolated by CC (heptane/AcOEt 15:1): 132 mg (41%). Yellow solid. M.p. 106–107°. IR (ATR): 3081*w*, 3033*w*, 2958*m*, 2867*m*, 2245*m*, 1660*s*, 1627*w*, 1598*m*, 1557*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.05 (t, $^3J = 7.4$, $MeCH_2CH_2$); 1.61–1.63 (m, $^3J = 7.4$, $^3J = 7.9$, $MeCH_2CH_2$); 2.61 (t, $^3J = 7.6$, CH_2); 2.69–2.71 (m, $^3J = 7.9$, $MeCH_2CH_2$); 3.01 (t, $^3J = 7.6$, CH_2); 3.47 (s, MeO); 6.64 (s, H–C(6)); 7.20–7.23 (m, 2 arom. H); 7.31–7.36 (m, 3 arom. H); 11.04 (s, OH). ^{13}C-NMR (75 MHz, $CDCl_3$): 14.4 ($MeCH_2CH_2$); 18.4 (NC–CH_2CH_2); 22.9 ($MeCH_2CH_2$); 28.1 ($MeCH_2CH_2$); 28.7 (NC–CH_2CH_2); 51.7 (MeO); 110.5, 118.7 (C_q); 122.7 (C(6)); 126.8, 127.6, 128.0 (arom. CH); 128.4, 141.6, 142.3, 142.5 (C_q); 159.9 (HO–C(3)); 171.6 (C=O). EI-MS (70 eV): 323 (61, M^+), 273 (22), 262 (56), 237 (100), 165 (49). HR-EI-MS: 323.15176 (M^+, $C_{20}H_{21}NO_3^+$; calc. 323.15160).

Methyl 5-(2-Cyanoethyl)-3-hydroxy-4-methoxy-1,1′-biphenyl-2-carboxylate (**5g**). From **3** (1.00 mmol, 273 mg), **4g** (1.50 mmol, 436 mg), and $TiCl_4$ (1.10 mmol, 0.12 ml) in 2 ml of CH_2Cl_2, **5g** was isolated by CC (heptane/AcOEt 10:1): 91 mg (30%). Brown oil. IR (ATR): 3055*w*, 3025*w*, 2999*w*, 2949*m*, 2836*w*, 2246*m*, 1731*m*, 1661*s*, 1601*m*, 1564*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.66 (t, $^3J = 7.6$, CH_2); 2.98 (t, $^3J = 7.6$, CH_2); 3.49 (s, COOMe); 3.98 (s, MeO); 6.65 (s, H–C(6)); 7.19–7.22 (m, 2 arom. H); 7.30–7.37 (m, 3 arom. H); 10.85 (s, OH). ^{13}C-NMR (75 MHz, $CDCl_3$): 17.7, 26.8 (CH_2); 51.8 ($COOMe$); 60.6 (MeO); 112.5 (C_q); 122.8 (C(6)); 126.8, 127.6, 128.1 (arom. CH); 135.8, 139.7, 142.0, 145.6 (C_q); 154.6 (HO–C(3)); 171.2 (C=O). EI-MS (70 eV): 311 (36, M^+), 280 (21), 279 (100), 225 (26), 139 (22). HR-EI-MS: 311.11467 (M^+, $C_{18}H_{17}NO_4^+$; calc. 311.11521).

Methyl 4-(3-Chloropropyl)-5-(2-cyanoethyl)-3-hydroxy-1,1′-biphenyl-2-carboxylate (**5h**). From **3** (1.00 mmol, 273 mg), **4h** (1.50 mmol, 503 mg), and $TiCl_4$ (1.10 mmol, 0.12 ml) in 2 ml of CH_2Cl_2, **5h** was isolated by CC (heptane/AcOEt 10:1): 181 mg (50%). Colorless oil. IR (ATR): 3036*w*, 3008*w*, 2954*m*, 2918*w*, 2244*m*, 1745*m*, 1716*m*, 1653*s*, 1600*s*, 1556*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.04–2.14 (m, $^3J = 7.7$, $^3J = 6.2$, $ClCH_2CH_2CH_2$); 2.64 (t, $^3J = 7.6$, $NCCH_2CH_2$); 2.86–2.91 (m, $^3J = 7.7$, $ClCH_2CH_2CH_2$); 3.05 (t, $^3J = 7.6$, $NCCH_2CH_2$); 3.48 (s, MeO); 3.65 (t, $^3J = 6.2$, $ClCH_2CH_2CH_2$); 6.67 (s, H–C(6)); 7.20–7.26 (m, 2 arom. H); 7.33–7.39 (m, 3 arom. H); 11.12 (s, OH). ^{13}C-NMR (75 MHz, $CDCl_3$): 18.4 ($NCCH_2CH_2$); 23.4 ($ClCH_2CH_2CH_2$); 28.6 ($NCCH_2CH_2$); 32.0 ($ClCH_2CH_2CH_2$); 45.1 ($ClCH_2CH_2CH_2$); 51.7 (MeO); 110.6, 118.6 (C_q); 123.0 (C(6)); 126.6 (C_q); 126.9, 127.6, 128.0 (arom. CH); 141.9, 142.3, 142.9 (C_q); 160.0 (C(3)); 171.6 (C=O). EI-MS (70 eV): 359 (8, $M(^{37}Cl)^+$), 357 (15, $M(^{35}Cl)^+$), 321 (17), 290 (100), 271 (20), 165 (21). Anal. calc. for $C_{20}H_{20}ClNO_3$ (358.831): C 67.13, H 5.63, N 3.91; found: C 66.83, H 5.82, N 3.87.

Methyl 5-(2-Cyanoethyl)-3-hydroxy-4-(prop-2-en-1-yl)-1,1′-biphenyl-2-carboxylate (**5i**). From **3** (1.00 mmol, 273 mg), **4i** (1.50 mmol, 412 mg), and $TiCl_4$ (1.10 mmol, 0.12 ml) in 2 ml of CH_2Cl_2, **5i** was isolated by CC (heptane/AcOEt 15:1): 110 mg (35%). Colorless solid. M.p. 95–96°. IR (ATR): 3083*w*, 3062*w*, 3030*w*, 2956*w*, 2897*w*, 2848*w*, 2243*m*, 1651*s*, 1633*m*, 1600*s*, 1564*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.62 (t, $^3J = 7.6$, $NCCH_2CH_2$); 3.00 (t, $^3J = 7.6$, $NCCH_2CH_2$); 3.48 (s, MeO); 3.52–3.54 (m, $CH_2CH{=}CH_2$); 4.96–5.09 (m, $CH_2CH{=}CH_2$); 5.96–6.09 (m, $CH_2CH{=}CH_2$); 6.68 (s, C(6)); 7.21–7.24 (m, 2 arom. H); 7.32–7.29 (m, 3 arom. H); 11.09 (s, OH). ^{13}C-NMR (75 MHz, $CDCl_3$): 18.2 (NC–CH_2CH_2); 28.8

(NC–CH_2CH_2); 30.0 (CH_2CH=CH_2); 51.7 (MeO); 110.7 (C_q); 115.3 (CH_2CH=CH_2); 118.7 (C_q); 123.0 (C(6)); 125.1 (C_q); 126.9, 127.7, 128.1 (arom. CH); 135.8 (CH_2CH=CH_2); 142.4, 142.4, 143.1 (C_q); 159.8 (C(3)); 171.6 (C=O). EI-MS (70 eV): 321 (82, M^+), 289 (73), 274 (35), 235 (100), 221 (57). Anal. calc. for $C_{20}H_{19}NO_3$ (321.370): C 74.75, H 5.96, N 4.36; found: C 74.39, H 6.20, N 4.06.

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REFERENCES

[1] P. Langer, *Synthesis* **2002**, 441; H. Feist, P. Langer, *Synthesis* **2007**, 327; G. Karapetyan, T. T. Dang, M. Sher, T. V. Ghochikyan, A. Saghyan, P. Langer, *Curr. Org. Chem.* **2012**, *16*, 557.
[2] A. Riahi, O. Fatunsin, M. Shkoor, R. Dede, H. Reinke, C. Fischer, P. Langer, *Synthesis* **2009**, 1623.
[3] E. Holtz, P. Langer, *Synth. Commun.* **2007**, *37*, 2959.
[4] T. H. Chan, P. Brownbridge, *J. Am. Chem. Soc.* **1980**, *102*, 3534; G. A. Molander, K. O. Cameron, *J. Am. Chem. Soc.* **1993**, *115*, 830; V. T. H. Nguyen, E. Bellur, B. Appel, *Synthesis* **2006**, 2865.
[5] P. Brownbridge, T. H. Chan, M. A. Brook, G. J. Kang, *Can. J. Chem.* **1983**, *61*, 688; K. Hirai, I. Ojima, *Tetrahedron Lett.* **1983**, *24*, 785.

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