Monatsh Chem
DOI 10.1007/s00706-015-1529-1

ORIGINAL PAPER

One-pot synthesis of heterocyclic compounds containing highly polarized double bond

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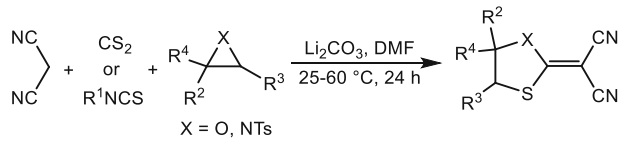
Received: 14 April 2015 / Accepted: 29 June 2015

Abstract Anionic adduct derived from malononitrile and heterocumulenes attacks on aziridines or oxiranes in regioselective manner to afford corresponding heterocycles containing highly polarized double bond. This transformation is carried out using Li_2CO_3 at 25–60 °C in DMF.
Graphical abstract



Keywords Heterocycles · Oxirane · Heterocumulenes · Aziridine · One-pot synthesis

Introduction

Push–pull alkenes are substituted alkenes with electron-donating substituent(s) on one side and of the other with electron-withdrawing substituent(s) [1–3]. Allowance for π-electron delocalization leads to the C–C double bond becoming polarized and the π-order of this double bond is reduced [4–6]. This effect is readily apparent by the restricted rotations about the C–Don and C–Acc partial double bonds which can be studied quantitatively by dynamic NMR spectroscopy [7–10]. Furthermore, the polarized structure of the double bond is discernible by ^{13}C NMR and measurement of the barriers to rotation about the C–C double bonds [11–16].

In continuation of our studies featuring synthesis of heterocyclic compounds [17–19], we have examined efficiency of malononitrile, heterocumulenes, and oxiranes or aziridines.

Results and discussion

In initial attempt, a solution of malononitrile (**1**, 1 mmol) and phenyl isothiocyanate (**2a**, 1 mmol) containing propene oxide (**3a**, 1.5 mmol) treated with Et_3N (1 mmol) in toluene at 25 °C for 18 h. No cyclization occurred and 2-[(2-hydroxypropylthio)(phenylimino)methyl]malononitrile (**4**) was obtained in 87 % yield. However, by increasing the reaction temperature to 60 °C 2-(5-methyl-1,3-oxathiolan-2-ylidene)malononitrile (**5a**) was achieved in 13 % yield. To optimize the reaction conditions, the effects of base and solvent were considered. Li-containing bases improved the yield likely due to better hard–hard interaction with amine moiety (Table 1). Other solvents such as DMF, $CHCl_3$, MeCN, and THF were also considered and the best result was achieved in DMF. The coupling constant of the two bridgehead hydrogens ($J = 11.8$ Hz) determined the *trans*-structure of product.

Under the optimum conditions, a number of oxiranes and aziridines were considered (Table 2). Alkyl substituted oxiranes were attacked at terminal position, exclusively, while styrene oxide afforded the benzylic-attacked product in high yield. *Cis*- and *trans*-2,3-diphenyloxirane gave acceptable yields. Acrylate containing oxirane also afforded a good yield. Cyclohexene oxide furnished the reaction with excellent yield, while cycloheptene oxide only gave

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Published online: 06 August 2015

Table 1 Optimization reaction conditions

Entry	Solvent	Base	Yield/%[a]
1	DMSO	Li_2CO_3	76
2	Toluene	Li_2CO_3	–
3	THF	Li_2CO_3	41
4	MeCN	Li_2CO_3	43
5	DMF	Li_2CO_3	81
6	DMF	Et_3N	20
7	DMF	K_2CO_3	53
8	DMF	LiOH	75

Reaction conditions: **1** (1.0 mmol), **2a** (1.0 mmol), **3a** (1.5 mmol), base (1.0 mmol), 3 cm^3 solvent, 60 °C, 18 h

[a] 79 % of **4** was achieved using Et_3N at room temperature in toluene

moderate success, likely due to the steric hindrance of the substrate. Alkyl isothiocyanate also yields the corresponding product in good yield.

To extend the scope of the transformation, tosylaziridines **6** were also considered using phenyl isothiocyanate or CS_2 (**7**) as the reaction partner and tosylthiazolidines **8** were synthesized in good yields (Table 3). It is worthwhile to mention that in the presence of **7** the reaction could be run at room temperature. The regioselectivity of these substrates is similar with those of oxiranes, although tosylaziridines need longer reaction times to complete the transformation.

The structures of products were confirmed by spectroscopic analyses. For example, the ^{1}H NMR spectrum of **5a** showed characteristic (AB)X spin system for the CH_2-CH H-atoms, together with a doublet for the methyl group. The ^{13}C NMR spectrum of **5a** exhibited 7 signals in agreement with the proposed structure. In the ^{13}C NMR spectrum, polarized character of central double bond is apparent, the deshielded position of the double bond is over 90–100 ppm at the lower field compared to the shielded position.

A plausible mechanism is proposed in Scheme 1. It is conceivable that the reaction starts with the formation of the intermediate **9**, followed by the addition of **3** to generate **10**. Cyclization of this intermediate leads to **11**, which is converted to **5** by elimination of $PhNH_2$.

In conclusion, we have described an efficient procedure to syntheses of 1,3-oxathiolanes and 1,3-thiazolidines containing highly polarized double bond. The reaction was in the most cases regioselective and only one regioisomer was detected in NMR analyses. In this transformation, amine moiety served as leaving group in the presence of Li salt.

Experimental

Epoxides, isothiocyanates, CS_2, malononitrile, bases, and solvents were obtained from Merck. Solvents were dried before use. *N*-Tosylaziridines were prepared using the literature procedures [20]. Melting points: Electrothermal-9100 apparatus. IR Spectra: Shimadzu IR-460 spectrometer. ^{1}H and ^{13}C NMR spectra: Bruker DRX-500 AVANCE instrument; in $CDCl_3$ at 500.1 and 125.7 MHz, resp; δ in ppm, J in Hz. EI-MS (70 eV): Finnigan-MAT-8430 mass spectrometer. Elemental analyses (C, H, N) were

Table 2 Synthesis of 1,3-oxathiolane containing highly polarized double bond

Isothiocyanate	R^1	Epoxide	R^2	R^3	R^4	Product, yield/%
2a	Ph	**3a**	CH_3	H	H	**5a**, 80
2b	*i*-Pr	**3b**	$ClCH_2$	H	H	**5b**, 83
		3c	CH_3CH_2	H	H	**5c**, 81
		3d	$(CH_3)_2CHOCH_2$	H	H	**5d**, 84
		3e	$CH_3C(CH_2)COOCH_2$	H	H	**5e**, 85
		3f	$CH_2CHCH_2OCH_2$	H	H	**5f**, 87
		3g	R^2, R^3 = –$(CH_2)_4$–		H	**5g**, 93
		3h	R^2, R^3 = –$(CH_2)_5$–		H	**5h**, 52
		3i	Ph	H	H	**5i**, 80[a]
		3j	$PhOCH_2$	H	H	**5j**, 87 (79)[b]
		3k	C_3H_7	H	CH_3	**5k**, 90
		3l	Ph	Ph (*cis*)	H	**5l**, 89
		3m	Ph	Ph (*trans*)	H	**5m**, 82
		3n	Bn	H	H	**5n**, 86

Reaction conditions: **1** (1.0 mmol), **2** (1.0 mmol), **3** (1.5 mmol), Li_2CO_3 (1.0 mmol), 3 cm^3 DMF, 60 °C, 18 h

[a] The yield of benzylic-attacked product

[b] **2b** was used as the isothiocyanate source

Table 3 Synthesis of 1,3-thiazolidine derivatives

Aziridine	R^2, R^3	Product, yield/%
6a	Ph, H	**8a**, 89 (78)[a]
6b	Bn, H	**8b**, 83 (76)
6c	C_3H_7, CH_3	**8c**, 86 (75)
6d	$-(CH_2)_4-$	**8d**, 89 (81)
6e	$-(CH_2)_5-$	**8e**, 52 (43)
6f	4-MeO–C_6H_4, H	**8f**, 91 (82)

Reaction conditions: **1** (1.0 mmol), **6** (1.5 mmol), **7** (3.0 mmol), Li_2CO_3 (1.0 mmol), 3 cm^3 DMF, 25 °C, 24 h

The values in parentheses are yields of the product using phenyl isothiocyanate (1.0 mmol) at 60 °C for 24 h

[a] The yield of the benzylic-attacked product

performed with a Heraeus CHN-O-Rapid analyzer. The results agreed favorably with the calculated values.

General procedure for the preparation of compounds 5

To a stirred solution of 0.061 g malononitrile (1 mmol), heterocumulene (1 mmol), and strained heterocycles (1.5 mmol) in 3 cm^3 DMF was added 0.07 g Li_2CO_3 (1 mmol, 0.07 g) in one portion. The mixture was stirred for 18–24 h at 25–60 °C. After completion of the reaction (monitored by TLC), 5 cm^3 EtOAc and 3 cm^3 H_2O were added to the reaction mixture. Two layers were seperated and aqueous layer was extracted with EtOAc (3 × 5 cm^3). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate 4:1). All the known compounds (**5a**–**5g**, **5i**, **5j**) [6] gave satisfactory spectroscopic values and are analog to spectroscopic data reported in literature.

2-(Hexahydro-3aH-cyclohepta[d][1,3]oxathiol-2-ylidene)malononitrile (**5h**, $C_{11}H_{12}N_2OS$)

The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 4/1, $R_f = 0.53$) affording 0.10 g (49 %) **5h**. Colorless crystals; m.p.: 90–92 °C; IR (KBr): $\bar{\nu}$ = 2972, 2247, 2231, 1568, 1318, 1124 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 1.54–2.28 (m, 5 CH_2), 3.13–3.20 (m, CH), 3.89–3.94 (m, CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 21.2 (CH_2), 24.5 (CH_2), 26.8 (CH_2), 31.4 (CH_2), 33.0 (CH_2), 48.1 (CH), 82.6 (CH), 86.2 (C), 111.2 (CN), 113.5 (CN), 190.3 (C) ppm; EI-MS (70 eV): *m/z* (%) = 220 (M^+, 3), 163 (58), 149 (100), 82 (86), 64 (40), 56 (35).

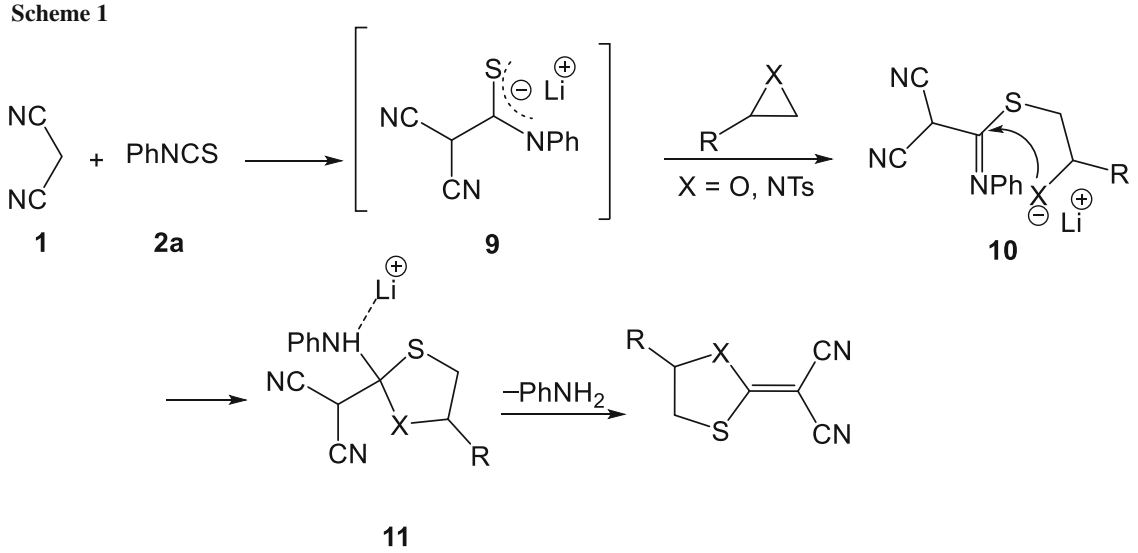
2-(5-Methyl-5-propyl-1,3-oxathiolan-2-ylidene)-malononitrile (**5k**, $C_{10}H_{12}N_2OS$)

The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 4/1, $R_f = 0.47$) affording 0.20 g (95 %) **5j**. Yellow oil; IR (KBr): $\bar{\nu}$ = 2967, 2248, 2235, 1563, 1315, 1124 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 0.90 (t, ^3J = 6.4 Hz, Me), 1.23 (s, Me), 1.32–1.37 (m, 2 CH_2), 3.25–3.36 (m, CH_2) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 12.5 (CH_2), 14.7 (Me), 23.1 (Me), 30.4 (CH_2), 37.6 (CH_2), 87.1 (C), 88.4 (C), 111.2 (CN), 113.7 (CN), 189.2 (C) ppm; EI-MS (70 eV): *m/z* (%) = 208.0 (M^+, 5), 191 (47), 165 (62), 139 (32), 116 (84), 108 (52), 78 (73).

2-((4R,5S and 4S,5R)-4,5-Diphenyl-1,3-oxathiolan-2-ylidene)malononitrile (**5l**, $C_{18}H_{12}N_2OS$)

The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 4/1, $R_f = 0.24$) affording 0.27 g

Scheme 1



(89 %) **5l**. Pale yellow crystals; m.p.: 121–123 °C; IR (KBr): $\bar{\nu} = 3025$, 2971, 2251, 2240, 1568, 1315, 1122 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 4.41$ (s, CH), 5.61 (s, CH), 7.11–7.28 (m, 10 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 56.4$ (CH), 83.2 (CH), 89.5 (C), 113.2 (CN), 114.1 (CN), 126.3 (2 CH), 126.7 (CH), 128.5 (CH), 128.7 (2 CH), 129.4 (2 CH), 130.2 (2 CH), 141.3 (C), 142.5 (C), 189.7 (C) ppm; EI-MS (70 eV): *m/z* (%) = 304 (M^+, 12), 197 (36), 181 (62), 93 (52), 77 (100), 54 (71).

2-((4R,5R and 4S,5S)-4,5-Diphenyl-1,3-oxathiolan-2-ylidene)malononitrile (**5m**, $C_{18}H_{12}N_2OS$)
The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 4/1, $R_f = 0.29$) affording 0.25 g (82 %) **5m**. Pale yellow crystals; m.p.: 169–171 °C; IR (KBr): $\bar{\nu} = 3043$, 2960, 2242, 2240, 1561, 1311, 1128 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 4.09$ (s, CH), 5.72 (s, CH), 7.08–7.25 (m, 10 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 54.2$ (CH), 85.9 (CH), 90.2 (C), 114.1 (CN), 114.4 (CN), 125.1 (2 CH), 126.2 (CH), 127.2 (2 CH), 127.9 (CH), 128.1 (2 CH), 130.4 (2 CH), 142.6 (C), 142.9 (C), 190.2 (C) ppm; EI-MS (70 eV): *m/z* (%) = 304 (M^+, 12), 197 (48), 181 (72), 93 (31), 77 (100), 54 (62).

2-(5-Benzyl-1,3-oxathiolan-2-ylidene)malononitrile (**5n**, $C_{13}H_{10}N_2OS$)
The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 4/1, $R_f = 0.53$) affording 0.21 g (86 %) **5n**. Pale yellow crystals; m.p.: 87–89 °C; IR (KBr): $\bar{\nu} = 3025$, 2981, 2260, 2243, 1554, 1310, 1107 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 2.86$–3.34 (m, 2 CH_2), 4.83–4.93 (m, CH), 7.08 (t, $^3J = 6.7$ Hz, CH), 7.14 (d, $^3J = 6.4$ Hz, 2 CH), 7.22 (t, $^3J = 6.8$ Hz, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 38.7$ (CH_2), 47.2 (CH_2), 87.2 (CH), 88.7 (C), 113.5 (CN), 114.2 (CN), 125.2 (CH), 127.2 (2 CH), 130.8 (2 CH), 139.5 (C), 191.0 (C) ppm; EI-MS (70 eV): *m/z* (%) = 242 (M^+, 7), 151 (43), 134 (64), 119 (37), 91 (100), 77 (56).

2-(4-Phenyl-3-tosylthiazolidin-2-ylidene)malononitrile (**8a**, $C_{19}H_{15}N_3O_2S_2$)
The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 2/1, $R_f = 0.46$) affording 0.34 g (89 %) **8a**. Pale yellow solid; m.p.: 144–146 °C; IR (KBr): $\bar{\nu} = 3024$, 2961, 1555, 1521, 1335, 1322, 1108 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 2.24$ (s, Me), 3.25 (dd, $^2J = 7.6$ Hz, $^3J = 6.8$ Hz, CH), 3.37 (dd, $^2J = 7.6$ Hz, $^3J = 11.4$ Hz, CH), 4.98–5.04 (m, CH), 7.12–7.35 (m, 5 CH), 7.38 (d, $^3J = 6.8$ Hz, 2 CH), 7.79 (d, $^3J = 6.7$ Hz, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 23.5$ (Me), 36.1 (CH_2), 64.1 (CH), 99.1 (C), 110.6 (CN), 113.2 (CN), 125.3 (CH), 126.5 (2 CH), 127.5 (2 CH), 129.3 (2 CH), 130.5 (2 CH), 135.5 (C), 140.5 (C), 145.1 (C), 193.7 (C) ppm; EI-MS (70 eV): *m/z* (%) = 381 (M^+, 1), 348 (35), 304 (68), 226 (79), 194 (82), 103 (42), 77 (100).

2-(4-Benzyl-3-tosylthiazolidin-2-ylidene)malononitrile (**8b**, $C_{20}H_{17}N_3O_2S_2$)
The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 4/1, $R_f = 0.26$) affording 0.33 g (83 %) **8b**. Pale yellow solid; m.p.: 147–149 °C; IR (KBr): $\bar{\nu} = 3029$, 2965, 1562, 1534, 1352, 1316, 1115 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 2.26$ (s, Me), 2.64 (dd, $^2J = 7.8$ Hz, $^3J = 6.3$ Hz, CH), 2.78 (dd, $^2J = 7.8$ Hz, $^3J = 10.5$ Hz, CH), 3.21 (dd, $^2J = 7.4$ Hz, $^3J = 6.5$ Hz, CH), 3.39 (dd, $^2J = 7.4$ Hz, $^3J = 10.5$ Hz, CH), 4.90–4.95 (m, CH), 7.10–7.38 (m, 5 CH), 7.40 (d, $^3J = 6.5$ Hz, 2 CH), 7.79 (d, $^3J = 6.3$ Hz, 2 CH) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 24.2$ (Me), 35.7 (CH_2), 40.2 (CH_2), 63.7 (CH), 98.5 (C), 111.4 (CN), 113.5 (CN), 124.7 (CH), 126.2 (2 CH), 127.1 (2 CH), 129.8 (2 CH), 131.0 (2 CH), 136.2 (C), 141.2 (C), 144.3 (C), 192.5 (C) ppm; EI-MS (70 eV): *m/z* (%) = 394 (M^+, 6), 362 (35), 337 (18), 246 (46), 117 (75), 91 (100), 77 (43).

2-(4-Methyl-4-propyl-3-tosylthiazolidin-2-ylidene)-malononitrile (**8c**, $C_{17}H_{19}N_3O_2S_2$)
The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 3/1, $R_f = 0.21$) affording 0.31 g (86 %) **8c**. Pale yellow solid; m.p.: 146–147.5 °C; IR (KBr): $\bar{\nu} = 3029$, 2965, 1562, 1534, 1352, 1316, 1115 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 0.90$ (t, $^3J = 6.4$ Hz, Me), 1.23 (s, Me), 1.32–1.37 (m, 2 CH_2), 2.32 (s, Me), 3.25–3.36 (m, CH_2), 7.41 (d, $^3J = 6.6$ Hz, 2 H), 7.83 (d, $^3J = 6.2$ Hz, 2 H) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 12.5$ (CH_2), 14.7 (Me), 22.8 (Me), 24.2 (Me), 30.4 (CH_2), 37.6 (CH_2), 63.7 (CH), 98.5 (C), 111.4 (CN), 113.5 (CN), 127.1 (2 CH), 129.8 (2 CH), 136.2 (C), 141.2 (C), 192.5 (C) ppm; EI-MS (70 eV): *m/z* (%) = 361 (M^+, 2), 287 (24), 212 (24), 206 (36), 155 (100).

2-(Hexahydro-3-tosylbenzo[d]thiazol-2(3H)-ylidene)-malononitrile (**8d**, $C_{17}H_{17}N_3O_2S_2$)
The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 2/1, $R_f = 0.37$) affording 0.32 g (89 %) **8d**. Pale yellow solid; m.p.: 213 °C; IR (KBr): $\bar{\nu} = 3049$, 2980, 1563, 1527, 1347, 1308, 1126 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 1.42$–1.85 (m, 3 CH_2), 2.11–2.20 (m, CH_2), 2.34 (s, Me), 3.12–3.20 (m, CH), 4.68–4.72 (m, CH), 7.34 (d, $^3J = 6.7$ Hz, 2 H), 7.80 (d, $^3J = 6.9$ Hz, 2 H) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 23.8$ (Me), 25.7 (CH_2), 28.2 (CH_2), 30.3 (CH_2), 32.7 (CH_2), 41.7 (CH_2), 68.9 (CH), 100.2 (C), 114.1 (CN), 115.2 (CN), 126.5 (2 CH), 130.3 (2 CH), 137.9 (C), 142.3 (C), 194.1 (C) ppm; EI-MS (70 eV): *m/z* (%) = 359 (M^+, 2), 251 (36), 170 (82), 155 (100), 109 (13), 82 (46).

2-(Octahydro-3-tosylcyclohepta[d]thiazol-2-ylidene)-malononitrile (**8e**, $C_{18}H_{19}N_3O_2S_2$)
The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 3/1, $R_f = 0.39$) affording 0.19 g (52 %) **8e**. Pale yellow solid; m.p.: 129–132 °C; IR (KBr): $\overline{\nu} = 3062, 2971, 1551, 1539, 1347, 1310, 1131\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 1.31–1.89$ (m, 4 CH_2), 2.23–2.28 (m, CH_2), 2.33 (s, Me), 3.04–3.21 (m, CH), 4.47–4.56 (m, CH), 7.32 (d, $^3J = 6.9$ Hz, 2 H), 7.81 (d, $^3J = 6.8$ Hz, 2 H) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 25.1$ (Me), 29.2 (CH_2), 30.5 (CH_2), 31.3 (CH_2), 34.2 (CH_2), 43.0 (CH_2), 47.2 (CH), 69.1 (CH), 101.7 (C), 113.5 (CN), 113.8 (CN), 127.1 (2 CH), 131.0 (2 CH), 135.2 (C), 143.1 (C), 192.8 (C) ppm; EI-MS (70 eV): *m/z* (%) = 373 (M^+, 2), 278 (11), 170 (71), 170 (43), 155 (100), 112 (47), 97 (62).

2-[5-(4-Methoxyphenyl)-3-tosylthiazolidin-2-ylidene]-malononitrile (**8f**, $C_{20}H_{17}N_3O_3S_2$)
The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 5/1, $R_f = 0.40$) affording 0.37 g (91 %) **8f**. Pale yellow solid; m.p.: 128–130 °C; IR (KBr): $\overline{\nu} = 3034, 2972, 1545, 1530, 1341, 1310, 1123\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 2.28$ (s, Me), 3.56 (s, OMe), 4.23 (dd, $^2J = 8.4$ Hz, $^3J = 6.6$ Hz, CH), 4.23 (dd, $^2J = 8.4$ Hz, $^3J = 12.1$ Hz, CH), 4.37–4.42 (m, CH), 6.89 (d, $^3J = 6.7$ Hz, 2 H), 7.01 (d, $^3J = 6.5$ Hz, 2 H), 7.32 (d, $^3J = 7.0$ Hz, 2 H), 7.79 (d, $^3J = 6.7$ Hz, 2 H) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 24.3$ (Me), 47.8 (CH), 56.5 (OMe), 64.2 (CH_2), 98.9 (C), 113.7 (CN), 113.9 (CN), 114.2 (2 CH), 126.2 (2 CH), 130.1 (2 CH), 131.4 (2 CH), 135.0 (C), 137.3 (C), 143.2 (C), 160.5 (C), 185.8 (C) ppm; EI-MS (70 eV): *m/z* (%) = 411 (M^+, 2), 256 (21), 169 (61), 134 (73), 155 (51), 107 (100).

2-[(2-Hydroxypropylthio)(phenylimino)methyl]-malononitrile (**4**, $C_{13}H_{13}N_3OS$)
The crude product was purified by column chromatography (SiO_2; hexane/EtOAc 3/1, $R_f = 0.27$) affording 0.23 g (87 %) **4**. Pale yellow solid; m.p.: 78–81 °C; IR (KBr): $\overline{\nu} = 3460, 3067, 2962, 1621, 1549, 1521, 1338, 1317, 1115\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 1.38$ (d, $^3J = 6.7$ Hz, Me), 3.09 (dd, $^2J = 7.1$ Hz, $^3J = 6.4$ Hz, CH), 3.22 (dd, $^2J = 7.2$ Hz, $^3J = 12.3$ Hz, CH), 4.21–4.24 (m, CH), 5.13 (s, CH), 6.42 (br s, OH), 7.07 (d, $^3J = 6.7$ Hz, 2 H), 7.11 (t, $^3J = 6.4$ Hz, H), 7.27 (t, $^3J = 6.5$ Hz, 2 H) ppm; ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 21.7$ (Me), 31.7 (CH), 36.8 (CH_2), 67.3 (CH), 114.1 (CN), 114.4 (CN), 122.5 (2 CH), 125.7 (CH), 131.3 (2 CH), 148.1 (C), 164.6 (C) ppm; EI-MS (70 eV): *m/z* (%) = 259 (M^+, 6), 241 (29), 194 (31), 167 (42), 92 (63), 77 (100).

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