Triethylamine-Catalyzed Efficient Synthesis of Oxathiolanes Containing a Highly Polarized Carbon-Carbon Double Bond from Reaction of Malononitrile, Carbon Disulfide (CS_2), and Oxiranes

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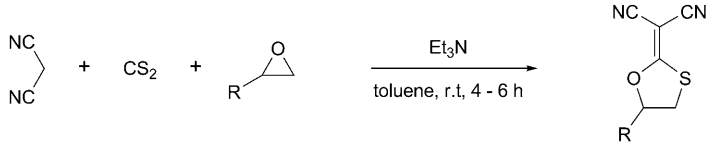
An efficient synthesis of functionalized 2-(1,3-oxathiolan-2-ylidene)malononitriles containing a push-pull C=C bond *via* a simple reaction between malononitrile, CS_2, and oxiranes in the presence of Et_3N is described (*Scheme 1*).

Introduction. – The concept of polarized (or push-pull) olefinic systems has played an important role in organic chemistry for four decades. Substitution of one C-atom of the C=C bond with electron-donating groups and of the other with electron-withdrawing groups diminishes the C=C bond order by charge separation [1–4]. The polarized structure of the C=C bond is discernible by ^{13}C-NMR spectroscopy due to the extreme deshielded position of the alkene C-atom on the donor side and the contrastingly shielded position of the C-atom on the acceptor side of the push-pull alkene.

As part of our current studies on the development of new routes in heterocycle synthesis [5–8], we report the synthesis of functionalized 2-(1,3-oxathiolan-2-ylidene)malononitriles **2** from malononitrile, CS_2, and oxiranes in the presence of Et_3N in high yields (*Scheme 1*). Structure **2** possesses a highly polarized push-pull C=C bond.

Scheme 1



1a	R = Me	**2a** R = Me	90
1b	R = $ClCH_2$	**2b** R = $ClCH_2$	87
1c	R = Et	**2c** R = Et	90
1d	R = Ph	**2d** R = Ph	88
1e	R = $PhOCH_2$	**2e** R = $PhOCH_2$	85
1f	R = CH_2=$CHCH_2OCH_2$	**2f** R = CH_2=$CHCH_2OCH_2$	92
1g	R = Me_2CHOCH_2	**2g** R = Me_2CHOCH_2	95
1h	R = CH_2=$C(Me)CO_2CH_2$	**2h** R = CH_2=$C(Me)CO_2CH_2$	86

Results and Discussion. – We began our study by looking at the reaction of malononitrile with CS_2 and oxiranes **1** in different solvent systems in the presence of Et_3N, and the results are shown in the *Table*. The desired product **2a** could be obtained in 37–90% yield in MeCN, CH_2Cl_2, toluene, and THF as solvent (*Table*), but toluene afforded the highest yield (*Table*, *Entries 1* and *5*). Other bases such as DBU (1,8-diazabicyclo[5.4.0]undec-7-ene), pyridine, and K_2CO_3 gave lower yields of **2a** (*Table*, *Entries 6–8*). Increasing the amount of the base reduced the reaction time to 4 h with a slight increase of the yield (*Table*, *Entry 5*).

Table. *Optimization of the Reaction Conditions for the Synthesis of Compound* **2a** *at Room Temperature*

Entry	Base	Sovent	Time [h]	Yield [%]
1	Et_3N (0.5 equiv.)	toluene	5	87
2	Et_3N (0.5 equiv.)	CH_2Cl_2	6	61
3	Et_3N (0.5 equiv.)	MeCN	6	48
4	Et_3N (0.5 equiv.)	THF	6	66
5	Et_3N (1.0 equiv.)	toluene	4	90
6	DBU (0.5 equiv.)	toluene	6	40
7	pyridine (0.5 equiv.)	toluene	6	51
8	K_2CO_3 (0.5 equiv.)	toluene	6	37

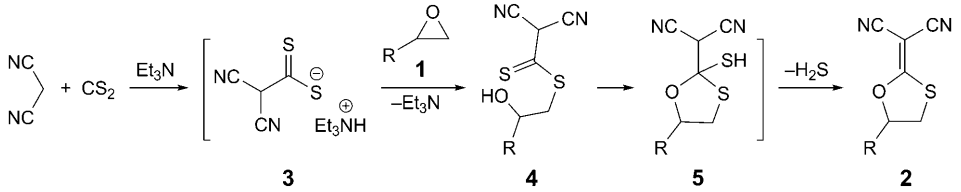
Under the optimized conditions, a wide range of oxiranes were successfully coupled to afford the corresponding oxathiolane derivatives **2** (*Scheme 1*). The structures of the latter were confirmed by spectroscopic analysis. For example, the ^{1}H-NMR spectrum of **2a** showed a characteristic *(AB)X* spin system for the CH_2CH H-atoms and a *d* for the Me group. The ^{13}C-NMR spectrum of **2a** exhibited 7 signals in agreement with the proposed structure. The polarized nature of the C=C bond of **2a** was discernible from its ^{13}C-NMR shifts. The deshielded position of the alkene C-atom on the donor side was δ(C) 188.3, which is more than 100 ppm at lower field compared to the shielded position of the C-atom on the acceptor side of this push-pull alkene. The ^{1}H- and ^{13}C-NMR spectra of compounds **2b–2h** were similar to those of **2a**, except for the signals of the substituent R at C(5) of the oxathiolane moiety, which showed characteristic signals in the appropriate regions of the spectra.

Electronic and steric variation of the oxiranes **1** showed no appreciable change in the efficiency of the reaction (*Scheme 1*). The reaction conditions were compatible with the presence of groups such as chloromethyl, phenoxy, and allyloxy groups, and of an α,β-unsaturated ester moiety at the oxirane ring. The reaction was completely regioselective so that only one regioisomer was obtained.

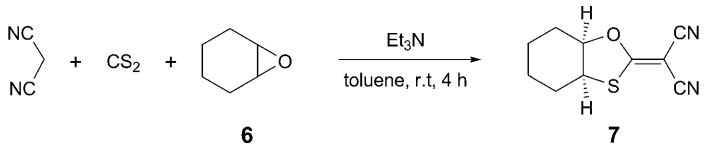
Although the mechanistic details of the formation of compounds **2** are not known, a plausible rationalization is proposed in *Scheme 2*. It is conceivable that the reaction starts with the formation of intermediate **3**, followed by addition of **1** to generate **4**. Cyclization of this intermediate leads to **5**, which is converted to **2** by elimination of H_2S.

When cyclohexene oxide (= 7-oxabicyclo[4.1.0]heptane; **6**) was used as the oxirane component in these reactions, the fused bicyclic oxathiolane derivative **7** was obtained in 82% yield (*Scheme 3*). The structure of compound **7** was again confirmed by its IR and NMR data.

Scheme 2



Scheme 3



In conclusion, we have described the use of malononitrile as a potential anionic nucleophile in a reaction involving CS_2 and oxiranes to produce functionalized 2-(1,3-oxathiolan-2-ylidene)malononitriles. Simple mixing of the starting materials and the potential diversity of this type of reaction are the advantages of this procedure.

Experimental Part

General. Oxiranes **1**, malononitrile, CS_2, and solvents were obtained from *Merck* and used without further purification. M.p.: *Electrothermal-9100* apparatus. IR Spectra: *Shimadzu-IR-460* spectrometer; KBr; $\tilde{\nu}$ in cm^{-1}. ^{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 rel. to Me_4Si as internal standard, J in Hz. MS: *Finnigan-MAT-8430* mass spectrometer; at 70 eV; in *m/z* (rel. %). Elemental analyses (C, H, N): *Heraeus-CHN-O-Rapid* analyzer.

Compounds **2**: *General Procedure.* To a stirred mixture of malononitrile (0.07 g, 1.0 mmol), oxirane **1** (1.0 mmol), and CS_2 (0.23 g, 3 mmol) in toluene (3 ml) was slowly added Et_3N (0.10 g, 1.0 mmol) at r.t. After completion of the reaction (4–6 h), as indicated by TLC (hexane/AcOEt 5:1), the solvent was evaporated, and the light brown residue was separated by CC (silica gel (230–400 mesh; *Merck*), hexane/AcOEt mixture): pure **2**.

2-(5-Methyl-1,3-oxathiolan-2-ylidene)propanedinitrile (**2a**): Yield 0.15 g (90%). Pale yellow oil. IR: 2910, 2242, 2239, 1555, 1175. ^{1}H-NMR: 1.56 (*d*, ^3J = 6.3, Me); 3.30 (*dd*, ^2J = 11.1, ^3J = 7.6, CH); 3.65 (*dd*, ^2J = 11.1, ^3J = 6.9, CH); 5.21–5.25 (*m*, CH). ^{13}C-NMR: 18.8 (Me); 38.6 (CH_2); 66.1 (CH); 88.7 (C); 111.0 (CN); 113.0 (CN); 188.3 (C). EI-MS: 166 (15, M^+), 151 (78), 123 (100), 102 (64), 64 (48). Anal. calc. for $C_7H_6N_2OS$ (166.20): C 50.59, H 3.64; found: C 50.7, H 3.7.

2-[5-(Chloromethyl)-1,3-oxathiolan-2-ylidene]propanedinitrile (**2b**): Yield 0.17 g (87%). Pale yellow oil. IR: 2930, 2221, 2218, 1565, 1185. ^{1}H-NMR: 2.61 (*d*, ^2J = 12.2, ^3J = 7.8, CH); 2.75 (*dd*, ^2J = 12.2, ^3J = 5.8, CH); 3.65–3.88 (*m*, CH_2); 5.28–5.38 (*m*, CH). ^{13}C-NMR: 36.7 (CH_2); 43.5 (CH_2); 69.6 (CH); 88.1 (C); 111.4 (CN); 113.8 (CN); 188.5 (C). EI-MS: 199 (8, M^+), 151 (80), 123 (100), 102 (62), 64 (55), 36 (56). Anal. calc. for $C_7H_5ClN_2OS$ (199.98): C 41.90, H 2.51; found: C 42.0, H 2.6.

2-(5-Ethyl-1,3-oxathiolan-2-ylidene)propanedinitrile (**2c**): Yield 0.16 g (90%). Pale yellow oil. IR: 2960, 2251, 2247, 1585, 1179. ^{1}H-NMR: 1.12 (*t*, ^3J = 7.4, Me); 1.88–2.08 (*m*, CH_2); 3.42 (*dd*, ^2J = 11.9, ^3J = 7.5, CH); 3.65 (*dd*, ^2J = 11.9, ^3J = 5.5, CH); 5.05–5.09 (*m*, CH). ^{13}C-NMR: 9.6 (Me); 26.3 (CH_2); 36.8 (CH_2); 57.7 (CH); 93.7 (C); 111.0 (CN); 113.0 (CN); 188.4 (C). EI-MS: 180 (10, M^+), 151 (79), 123 (100), 102 (65), 64 (53), 29 (33). Anal. calc. for $C_8H_8N_2OS$ (180.04): C 53.31, H 4.47; found: C 53.4, H 4.5.

2-(5-Phenyl-1,3-oxathiolan-2-ylidene)propanedinitrile (**2d**): Yield 0.20 g (88%). Colorless crystals. M.p. 102–104°. IR: 2965, 2260, 2257, 1560, 1165. ^{1}H-NMR: 4.90 (*dd*, ^2J = 12.0, ^3J = 5.6, CH); 5.10 (*dd*,

$^2J = 12.0$, $^3J = 7.8$, CH); 5.77 (*dd*, $^3J = 7.8$, $^3J = 5.6$, CH); 7.37–7.44 (*m*, 3 CH); 7.50 (*d*, $^3J = 7.2$, 2 CH). ^{13}C-NMR: 54.1 (CH_2); 83.2 (CH); 92.6 (C); 110.7 (CN); 112.7 (CN); 127.3 (2 CH); 129.3 (2 CH); 130.4 (CH); 133.7 (C); 188.6 (C). EI-MS: 228 (10, M^+), 151 (76), 123 (85), 91 (55), 77 (100). Anal. calc. for $C_{12}H_8N_2OS$ (228.04): C 63.14, H 3.53; found: C 63.2, H 3.6.

2-[5-(Phenoxymethyl)-1,3-oxathiolan-2-ylidene]propanedinitrile (**2e**): Yield 0.22 g (85%). Pale yellow crystals. M.p. 92–94°. IR: 2924, 2250, 2246, 1540, 1180. ^{1}H-NMR: 3.74 (*dd*, $^2J = 12.3$, $^3J = 6.5$, CH); 3.81 (*dd*, $^2J = 12.3$, $^3J = 5.5$, CH); 4.32–4.40 (*m*, CH_2); 5.42–5.44 (*m*, CH); 6.93 (*d*, $^3J = 7.5$, 2 CH); 7.02 (*t*, $^3J = 7.5$, CH); 7.33 (*t*, $^3J = 7.5$, 2 CH). ^{13}C-NMR: 34.5 (CH_2); 65.9 (CH); 70.2 (CH); 88.7 (C); 110.7 (CN); 112.8 (CN); 114.7 (2 CH); 121.9 (CH); 129.7 (2 CH); 157.8 (C); 188.1 (C). EI-MS: 258 (10, M^+), 165 (42), 151 (78), 123 (64), 93 (100), 65 (76). Anal. calc. for $C_{13}H_{10}N_2O_2S$ (258.05): C 60.45, H 3.90; found: C 60.6, H 4.0.

2-[5-[(Prop-2-en-1-yloxy)methyl]-1,3-oxathiolan-2-ylidene]propanedinitrile (**2f**): Yield 0.20 g (92%). Pale yellow oil. IR: 2915, 2235, 2229, 1535, 1165. ^{1}H-NMR: 3.46 (*dd*, $^2J = 9.8$, $^3J = 5.8$, CH); 3.79–3.81 (*m*, CH); 3.94 (*dd*, $^2J = 12.1$, $^3J = 4.7$, CH); 4.04 (*d*, $^3J = 5.6$, 2 CH); 4.07 (*dd*, $^2J = 12.1$, $^3J = 5.7$, CH); 5.12–5.17 (*m*, CH); 5.20–5.30 (*m*, 2 CH); 5.83–5.91 (*m*, CH). ^{13}C-NMR: 34.9 (CH_2); 46.8 (CH); 69.2 (CH_2); 72.1 (CH_2); 90.1(C); 110.9 (CN); 113.1 (CN); 118.4 (CH_2); 134.3 (CH); 188.9 (C). EI-MS: 222 (15, M^+), 158 (68), 151 (85), 123 (100), 98 (46), 71 (73), 64 (33). Anal. calc. for $C_{10}H_{10}N_2O_2S$ (22.05): C 54.04, H 4.53; found: C 54.2, H 4.4.

2-[5-[(1-Methylethoxy)methyl]-1,3-oxathiolan-2-ylidene}propanedinitrile (**2g**): Yield 0.21 g (95%). Colorless crystals. M.p. 81–83°. IR: 2910, 2220, 2216, 1542, 1190. ^{1}H-NMR: 1.12 (*d*, $^3J = 6.1$, 2 Me); 3.53–3.62 (*m*, CH_2); 3.73 (*m*, CH); 3.89 (*dd*, $^2J = 12.0$, $^3J = 5.9$, CH); 4.01 (*dd*, $^2J = 12.0$, $^3J = 6.7$, CH); 5.40 (*sept.*, $^3J = 6.1$, CH). ^{13}C-NMR: 21.8 (Me); 21.9 (Me); 32.6 (CH_2); 66.6 (CH_2); 70.3 (CH); 73.1 (CH); 90.4 (C); 111.5 (CN); 113.2 (CN); 189.1 (C). EI-MS: 224 (5, M^+), 209 (73), 151 (84), 123 (100), 100 (52), 73 (36). Anal. calc. for $C_{10}H_{12}N_2O_2S$ (224.06): C 53.55, H 5.39; found: C 53.85, H 5.26.

[2-(Dicyanomethylene)-1,3-oxathiolan-5-yl]methyl 2-Methylprop-2-enoate (**2h**): Yield 0.20 g (86%). Pale yellow oil. IR: 2985, 2270, 2264, 1703, 1580, 1183. ^{1}H-NMR: 2.01 (*s*, Me); 3.66 (*dd*, $^2J = 14.0$, $^3J = 7.0$, CH_2); 4.08 (*m*, CH); 4.15 (*dd*, $^2J = 12.0$, $^3J = 4.9$, CH); 4.49 (*dd*, $^2J = 12.0$, $^3J = 5.7$, CH); 7.13–7.15 (*m*, CH); 7.23–7.25 (*m*, CH). ^{13}C-NMR: 31.2 (Me); 45.1 (CH_2); 63.3 (CH_2); 69.3 (CH); 90.4 (C); 111.5 (CN); 113.2 (CN); 124.1 (C); 136.0 (CH_2); 171.2 (COO); 188.4 (C). EI-MS: 236 (5, M^+), 151 (84), 123 (100), 112 (52), 85 (90), 55 (61). Anal. calc. for $C_{11}H_{10}N_2O_3S$ (236.03): C 52.79, H 4.03; found: C 53.1, H 4.0.

rel-*2-[(3a*R*,7a*S*)-Hexahydro-1,3-benzooxathiol-2-ylidene]propanedinitrile* (**7**): Yield 0.17 g (82%). Colorless crystals. M.p. 260° (dec.). IR: 2912, 2222, 2217, 1555, 1179. ^{1}H-NMR: 1.43–1.48 (*m*, CH_2); 1.68–1.75 (*m*, CH_2); 1.93–1.97 (*m*, CH_2); 2.17–2.22 (*m*, CH_2); 3.32–3.35 (*m*, CH); 3.47–3.56 (*m*, CH). ^{13}C-NMR: 18.8 (CH_2); 23.2 (CH_2); 25.8 (CH_2); 28.2 (CH_2); 47.8 (CH); 74.0 (CH); 95 (C); 113.3 (CN); 115.1 (CN); 188.6 (C). EI-MS: 206 (35, M^+), 149 (78), 123 (100), 82 (64), 64 (48), 56 (45). Anal. calc. for $C_{10}H_{10}N_2OS$ (206.05): C 58.23, H 4.89; found: C 58.1, H 4.9.

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