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Conversion of 3-nitroanilines into tricyclic systems: 1*H*-1-alkyl-8-X-2,2-dioxoisothiazolo[5,4,3-*d*,*e*]quinolines

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Abstract—The route leading to the tricyclic 2,2-dioxoisothiazolo[5,4,3-*d*,*e*]quinolines from 3-nitroanilines has been described. The scope and limitation factors as well as some mechanistic features are discussed.

1. Introduction

In 1997 we reported the reaction of nitroarenes with some allylic systems to obtain 4-substituted quinoline derivatives, which took place in the presence of a base and Lewis acid. The postulated transformation mechanism consisted in the initial formation of a σ^H-adduct of a carbanion derived from the allylic compound to the nitroaromatic system, followed by its conversion to the nitroso compound, which subsequently underwent intramolecular cyclization to the final product.[1–3] Recently we presented a communication[4] describing the intramolecular version of this reaction, namely direct transformation of *N*-alkyl-*N*-3-nitroaryl allylsulfonamides **1** to tricyclic 1*H*-1-alkyl-8-X-2,2-dioxoisothiazolo[5,4,3-*d*,*e*]quinolines **2**. Small amounts of quinoline *N*-oxides **3** accompanied formation of **2** (Scheme 1).[4]

Since **2** are expected to be useful intermediates in the synthesis of pyrroloquinoline[5] or pyridoquinoline[6] type natural products and some other fused nitrogen heterocycles[7] we undertook more detailed investigations of this transformation. Here we present a full report.

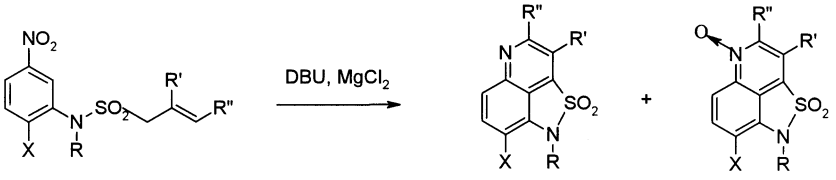
2. Results

Simple allyl sulfonamides **1a**–**h** with an unsubstituted terminal CC double bond, suitable for cyclization step

Table 1. Preparation of **1a**–**h** from **4** via sulfonylation followed by alkylation with alkyl iodides

X	4	Time[a]	6	Yield (%)	R	Time[a]	1	Yield (%)[b]
H	**a**	3 h	**a**	76	Me	2 h	**a**	90
					n-Bu[c]	4 d	**b**	70
					Allyl[d]	1 d	**c**	84
					Bn[d]	2 d	**d**	78
Cl	**b**	1 d	**b**	55[e]	Me	2 d	**e**	87
					n-Bu[c]	4 d	**f**	89
Me	**c**	3 h	**c**	76	Me	2 h	**g**	89
MeO	**d**	3 h	**d**	90	Me	1 d	**h**	89

[a] h=hours, d=days.
[b] Isolated.
[c] 3 equiv.
[d] RCl and cat. KI.
[e] 3-Nitro *N*,*N*-di(prop-2-enylsulfonyl)aniline isolated in 20% yield as a byproduct.



1 **2** **3**

Scheme 1.

Keywords: 3-nitroanilines; σ^H-adducts; intramolecular cyclization; nitroso compounds; 1*H*-1-alkyl-8-X-2,2-dioxoisothiazolo[5,4,3-*d*,*e*]quinolines.
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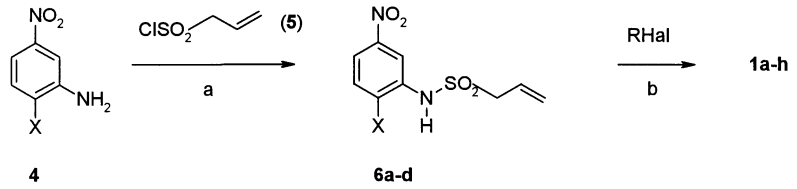
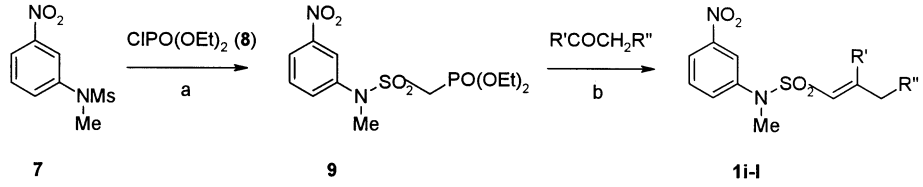


Scheme 2. *Reagents and conditions:* (a) py., DCM, −30°C to rt; (b) K_2CO_3, KI (cat. for Hal=Cl), DMF, rt.



Scheme 3. *Reagents and conditions:* (a) 2LDA, THF, TMEDA, −78°C; (b) DBU, LiBr, THF, rt.

Table 2. Preparation of **1i–l** from **9** and carbonyl compounds in Horner–Wadsworth–Emmons reaction

R′	R″	**1**	Isolated yield (%)
$(CH_2)_4$		**i**	72
Me	H	**j**	62
H	Ph	**k**	63
Ph	H	**l**	60

were synthesized from commercial 3-nitroanilines **4** (Scheme 2).

The sulfonylation of **4** with allylsulfonyl chloride **5**[8] in the presence of pyridine in dry dichloromethane (DCM) gave *N*-(3-nitroaryl)prop-2-enyl sulfonamides **6** with 55–90% yield. The reaction proceeded smoothly and selectively with more nucleophilic nitroanilines (X=H, Me, MeO: **4a**, **4c**, **4d**, respectively) whereas in the case of less nucleophilic 2-chloro-5-nitroaniline **4b** it was slower and was accompanied with the formation of bissulfonylated 3-nitro-*N*,*N*-di(prop-2-enylsulfonyl)aniline. Alkylation of the sulfonamide nitrogen atom with an alkyl chloride or iodide was performed in the presence of K_2CO_3 in DMF at room temperature.[9] KI was added as a catalyst in the case of alkyl chlorides. NMR spectra revealed that both transformations occurred with the preservation of the terminal double bond position.

Allyl sulfonamides **1i–l** with substituted allylic double bonds were synthesized from *N*-methyl-*N*-(3-nitrophenyl)-methanesulfonamide **7**[9] according to Scheme 3 (Table 2).

Attempts to perform a direct addition of the lithiated **7** to cyclohexanone were unsuccessful and led to mixture of products. Alternatively **7** was treated with 2 equiv. of LDA and successively phosphorylated with diethyl chlorophosphate **8** according to the Craig procedure[10] to give in moderate 47% yield phosphonate **9** suitable for Horner–Wadsworth–Emmons reaction. Condensation of **9** with carbonyl compounds was accomplished under the modified Rathke conditions[11] (DBU/LiBr/THF) to yield **1i–l**. In this case the unsaturated bond occurred mainly at α,β position to SO_2 group.

N-(3-Nitrophenyl)prop-2-enyl sulfonamide **1a** treated with DBU and $MgCl_2$ in DMSO underwent cyclization to **2a** with subsequent five- and six-membered ring closure in moderate yield. Quinoline *N*-oxide **3a** was isolated as a byproduct (Scheme 1 R′=R″=H).

The tricyclic structure of **2a** was confirmed by ^{1}H NMR spectrum.[4] None of the signals derived from allylic part of **1a** was observed. Instead, two new aromatic protons at 7.81 and 9.24 ppm could be observed with coupling constant J=4.5 Hz characteristic for protons at positions 2 and 3 of the quinoline ring. Also a four-proton pattern characteristic for 1,3-disubstituted benzene ring in **1a** was replaced in **2a** by eight signals in 7.69–7.85 ppm region with pattern characteristic for ABX system.

Dimethyl sulfoxide turned out to be the solvent of choice although other dipolar aprotic solvents such as DMF or HMPA gave comparable results (Table 3).

The reaction carried out in HMPA was faster than in DMSO or DMF but the total yield of **2a** and **3a** was not higher. The use of less polar solvents retarded the reaction and reduced the yields of both products. Interestingly, despite the rather poor material balance of the reaction (even in the best case) only a little tarry material was observed. Presumably some water-soluble side-products were formed which have not yet been isolated. The optimum amounts of $MgCl_2$ and DBU were 0.6 and 5 equiv., respectively, as was found for similar

Table 3. Cyclization of **1a** in various conditions

Entry	Amount of $MgCl_2$	Solvent	Time[a]	Yields (%)[b]	
				2a	**3a**
1	None	DMSO	1 d	27	Traces
2	0.625	DMSO	1 d	64	11
3	2.5	DMSO	1 d	50	9
4	0.625	DMF	1 d	59	12
5	1.0	MeCN	30 d	6	8
6	0.625	Py	7d	43	9
7	0.625	HMPA	3 h	60	3

5 equiv. of DBU as a base.
[a] h=hours, d=days.
[b] Isolated.

Table 4. Cyclization of **1a–j** under optimized conditions

1	X	R	R′	R″	Procedure[a]	Time[b]	**2** (%)[c]	**3** (%)[c]
a	H	Me	H	H	A	1 d	64	11
					B	1 d (1 h)	63	–
b	H	*n*-Bu	H	H	A	1 d	64	8
c	H	Allyl	H	H	A	1 d	61	7
d	H	Bn	H	H	A	1 d	70	9
e	Cl	Me	H	H	A	1 d	41	11
					B	1 d (30 min)	57	–
f	Cl	*n*-Bu	H	H	A	1 d	52	18
g	Me	Me	H	H	A	60 d	21	5
h	MeO	Me	H	H	A	2 d[d]	14	–
						14 d[e]	33	–
i	H	Me	$(CH_2)_4$		A	1 d	7	35
					B	1 d (30 min)	35	–
j	H	Me	Me	H	A	1 d	28	27
					B	1 d (30 min)	63	–
k	H	Me	H	Ph	A	1 d	46	23
l	H	Me	Ph	H	A	2 h	31[f]	16

[a] A: 5 equiv. DBU, 0.625 equiv. $MgCl_2$, DMSO solution rt, B: 1-st stage A, then refluxing with an excess of $P(OEt)_3$.
[b] d=days, h=hours, time of refluxing with $P(OEt)_3$ in parentheses.
[c] Isolated.
[d] Reaction at 80°C, no reaction at 20°C.
[e] HMPA instead DMSO.
[f] **10l** (3.5%) also isolated.

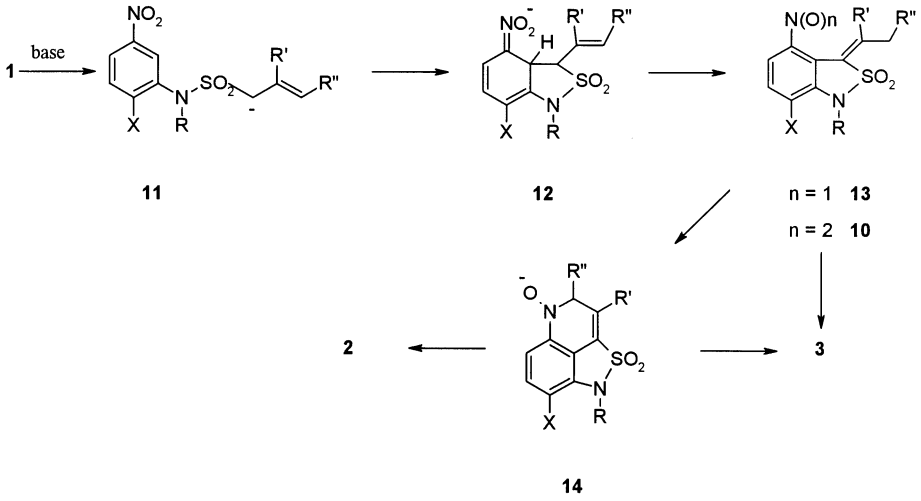
intermolecular processes.[1–3] However, unlike the later ones the reaction proceeded even in the absence of Lewis acid although significantly less effectively.

A variety of *N*-(3-nitroaryl)-*N*-methyl allylsulfonamides **1b–l** were subjected to the cyclization reaction under optimum conditions (Table 4).

The results presented above lead to the following observations:

1. The reaction is of general character with respect to substituents X, R, R′, and R″.
2. The reaction course (rate and **2**/**3** ratio) does not practically depend on R.
3. The substituent in the aromatic ring (X) has an impact on the rate of the reaction rather than on the products ratio. In the cases of X=H and Cl the reaction was completed within a day whereas for X=Me, it needed several weeks for completion. For X=OMe, no reaction was observed at room temperature. To accomplish the transformation, it was necessary to raise the temperature or replace DMSO with HMPA. In such conditions small amounts of some other products were observed.
4. The substitution of the allylic part of the molecule had the dramatic influence on the product **2** and **3** ratio, although it had only little influence on the overall rate of the reaction. The introduction of substituents in both 2 and 3 positions resulted in the formation of substantial amounts of quinoline *N*-oxide **3** which appeared to be the main product in cyclization of the cyclohexylidene derivative **1i**. Unexpectedly **1l** turned out to be the most reactive substrate. Its full conversion was achieved in 2 h (see Table 4). The formation of **2l** and **3l** was accompanied by small amounts of **10l** which could be considered as an intermediate in the formation of **3l** (see Scheme 4).

Since **3** are the oxidized forms of quinolines **2**, some efforts



Scheme 4.

Table 5. Influence of oxygen on cyclization of **1j** to **2j** and **3j**

Conditions	**2j** (%)[a]	**3j** (%)[a]
[b]	25	35
Ar[c]	59	21
O_2[d]	9	50

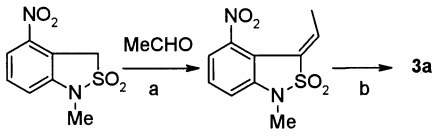
[a] Isolated.
[b] DMSO dried by distillation from CaH_2, 100 ml of DMSO per 1 mmol of **1j**, reaction at rt conducted until **1j** was consumed (ca. 20 h, HPLC control).
[c] As in (b) but special grade Ar bubbled through the reaction mixture for 3 days prior to the addition of DBU and then until the end of the reaction (ca. 20 h).
[d] As in (c) but O_2 used instead of Ar.

were undertaken to transform **3** in the crude mixtures of **2** and **3** to pure **2** thus improving the total yields of **2** and simplifying the isolation procedure. In a control experiment it was found that pure **3a** on action of refluxing $P(OEt)_3$[12] gave **2a** with 90% isolated yield. Thus, some crude mixtures of **2** and **3** after the cyclization step were refluxed with excess of $P(OEt)_3$ and then separated on silica gel (Table 4, procedure B).

Mechanistic details of the reaction are under investigation. Nevertheless the following general scheme seems plausible.

Deprotonation at the α position to SO_2 group with DBU followed by the intramolecular addition of carbanionic centre of **11** to the nitroaromatic part of the molecule would lead to σ^H-adduct **12**.[13] The loss of a molecule of water (Lewis acid mediated) would lead to the nitroso derivative **13**. The intramolecular base-induced Ehrlich–Sachs condensation[14,15] of the latter (via intermediate **14**) would terminate the reaction leading to product **2**. The mechanism of formation of oxidized product **3** is not clear. It may have been derived from nitro compound **10** (isolated from the reaction mixture in cyclization of **1l**, Table 4) which in turn could originate either from σ^H-adduct **12** or from the nitroso compound **13** as well as from **14** in a spontaneous oxidation process. Unlike σ^H adducts[13] aromatic nitroso compounds were not reported to undergo spontaneous oxidation to the nitro compounds. The oxidizing agent has not been recognized so far. It could not have been DMSO since similar results were obtained in DMF or HMPA. Experiments conducted in the presence of oxygen or in inert atmosphere showed that oxygen is involved in the formation of **3** (Table 5).

On the other hand, the potential intermediate in formation of **3a**, namely, **10a** (R=Me, X=R′=R″=H), prepared independently via condensation of cyclic sultam **15**[9] with acetaldehyde according to the described procedure,[16]



15 **10a** X = H, R = Me, R' = R'' = H

Scheme 5. *Reagents and conditions:* (a) DMF, K_2CO_3 (cat.), rt, 1 h; (b) DBU (5 equiv.), DMSO, rt, 4 min.

subjected to the standard cyclization conditions was consumed within 4 min (compared with several hours needed for the conversion of **1a** to **2a** and **3a**, Table 4) giving **3a** with 69% yield (Scheme 5).

This means that **10a** cannot be excluded as an intermediate in the formation of **3a**. Taking both electronic and steric reasons into consideration one could expect the cyclization of **13** to **2** to proceed even faster than **10** to **3**, meaning that the former cannot be the rate-limiting step in the transformation of **1** to **2**. The dominating impact of R on **2/3** ratio (see Table 4) is hard to explain without more information about the oxidation step which precedes formation of **3**.

Further investigation on the mechanistic details of the reaction as well as on application of 1*H*-1-alkyl-8-X-2,2-dioxoisothiazolo[5,4,3-*d*,*e*]quinolines as the intermediates in the synthesis of other heterocyclic compounds are in progress.

3. Experimental

Melting points are uncorrected. The ^1H and ^{13}C NMR spectra were recorded on Varian Gemini (200 MHz) in $CDCl_3$ solutions with TMS as an internal standard. Chemical shifts were expressed in ppm, coupling constants in hertz. The mass spectra were obtained on AMD-604 (AMD Intectra GmbH Germany) spectrometer with electron impact technique (70 eV). IR spectra were recorded on Spectrum 2000 as films or in KBr pellets. Silica gel (230–400 mesh, Merck) was used for column chromatography. All starting 3-nitroanilines were commercial. Allylsulfonyl chloride **5** was prepared according to the literature.[8]

3.1. Sulfonylation of 3-nitroanilines 4 with allylsulfonyl chloride 5 (general procedure)

To 3-nitro-4-X-aniline (25 mmol) dissolved in the mixture of dry DCM (50 ml) and pyridine (ca. 30 mmol; 2.5 ml), cooled to −20°C, allylsulfonyl chloride (ca. 27.5 mmol; 4 g) was added with stirring. The mixture was slowly heated to the room temperature and stirred until the substrate was consumed (TLC control). Then the mixture was poured onto cold diluted aq. HCl solution, the layers were separated and the aqueous layer was extracted with DCM (3×20 ml). Combined organic layers were washed with water, dried ($MgSO_4$), the solvent was evaporated and the residue was recrystallized or purified on silica gel with hexane–ethyl acetate mixture as eluent.

3.1.1. Compound 6a. From **4a**; yield 76%; yellow crystals; mp 104–105°C (AcOEt–hexane); [Found: C, 44.52; H, 4.14; N, 11.41%. $C_9H_{10}N_2O_4S$ requires C, 44.62; H, 4.16; N, 11.56%]: δ_H: 3.91 (dt, *J*=7.2, 1.0 Hz, 2H), 5.35 (ddt, *J*=17.0, 2.4, 1.0 Hz, 1H), 5.50 (ddt, *J*=10.0, 2.4, 1.0 Hz, 1H), 5.82–6.03 (m, 1H), 7.23 (broad s, $\nu_{1/2}$=4.75, 1H), 7.50–7.64 (m, 2H), 8.00–8.10 (m, 2H); *m*/*z* (int. %): 242 (9.2), 179 (2.5), 178 (23.8), 177 (8.5), 151 (12.6), 131 (11.8), 117 (7.9), 105 (6.3), 91 (22.5); ν_{max} (KBr): 1531.5, 1485.2, 1414.1, 1348.4, 1316.8, 1150.8, 1080.7.

3.1.2. Compound 6b. From **4b**: yield 55%; light-brown

crystals; mp 137–138°C (AcOEt); [Found: C, 39.10; H, 3.21; N, 10.14%. $C_9H_9N_2O_4SCl$ requires C, 39.07; H, 3.28; N, 10.12%]; δ_H: 3.93 (ddt, *J*=7.2, 1.6, 0.8 Hz, 2H), 5.32 (ddd, *J*=17.0, 1.6, 0.8 Hz, 1H), 5.47 (ddt, *J*=10.1, 1.6, 0.8 Hz, 1H), 5.80–6.01 (m,1H), 7.02 (broad s, $\nu_{1/2}$=4.50, 1H), 7.60 (d, *J*=8.8 Hz, 1H), 7.98 (dd, *J*=8.8, 2.6 Hz, 1H), 8.59 (d, *J*=2.6 Hz, 1H); *m/z* (int. %): 278 (11.9), 276 (32.3), 214 (11.5), 213 (7.4), 212 (37.2), 211 (11.8), 187 (8.6), 185 (28.5), 178 (6.7), 177 (50.4), 168 (5.0), 167 (5.2), 166 (8.0), 165 (12.7); ν_{max} (KBr): 1524.2, 1479.4, 1400.5, 1347.2, 1331.9, 1244.7, 1221.7, 1155.2, 1139.2, 1044.0; accompanied with 3-nitro-*N*,*N*-di(prop-2-enylsulfonyl)aniline: light-yellow crystals; mp 109–111°C (AcOEt–hexane); δ_H: 4.22 (ddt, *J*=13.8, 6.3 Hz, 1.1, 2H), 4.62 (ddt, *J*=13.8, 7.0, 0.8 Hz, 2H), 5.62 (m, 2H), 5.68 (m, 2H), 5.82–6.02 (m, 2H), 7.70 (dd, *J*=8.8, 0.5 Hz, 1H), 8.26 (dt, *J*=8.8, 2.6 Hz, 1H), 8.33 (dd, *J*=2.6, 0.5 Hz, 1H); ν_{max} (KBr): 1529.7, 1379.8, 1351.0, 1227.0, 1156.1, 1063.9; *m/z* (int. %): 380 (<1.0), 350 (<1.0), 318 (2.1), 276 (5.6), 337 (6.3), 225 (5.5), 217 (12.4), 212 (10.9), 211 (10.8): LSIMS: 381 $(M+H)^+$.

3.1.3. Compound 6c. From **4c**: yield 76%; light-yellow crystals; mp 130–135°C (AcOEt–hexane); [Found: C, 46.67; H, 4.84; N, 11.00%. $C_{10}H_{12}N_2O_4S$ requires C, 46.87; H, 4.72; N, 10.93%]: δ_H: 2.40 (s, 3H), 3.94 (dt, *J*=7.2, 1.2 Hz, 2H), 5.33 (ddd, *J*=17.0, 2.3, 1.2 Hz, 1H), 5.49 (ddd, *J*=10.1, 2.3, 1.2 Hz, 1H), 5.83–6.05 (m, 1H), 7.38 (d, *J*=8.4 Hz, 1H), 7.97 (dd, *J*=8.4, 2.4 Hz, 1H), 8.39 (d, *J*=2.4 Hz, 1H); δ_C: 147.16, 136.33, 136.02, 131.69, 125.02, 124.92, 119.97, 115.70, 56.81, 18.25; (*m/z*, %): 257 (1.9), 256 (11.9), 192 (10.8), 177 (6.1), 175 (5.2), 165 (14.9), 163 (8.0), 151 (6.2), 146 (7.8), 145 (12.6), 144 (4.7), 117 (12.5); ν_{max} (KBr): 1642.7, 1595.3, 1519.2, 1496.8, 1416.8, 1349.5, 1334.9, 1312.2, 1277.5, 1150.3, 1092.4.

3.1.4. Compound 6d. From **4d**; yield 90%; dark-yellow crystals; mp 126–127°C (AcOEt–hexane); [Found: C, 44.12; H, 4.54; N, 10.40%. $C_{10}H_{12}N_2O_5S$ [272.05]: C, 44.11; H, 4.44; N, 10.29%]: δ_H: 3.87 (dt, *J*=7.2, 1.2 Hz, 2H), 4.01 (s, 3H), 5.26 (ddt, *J*=17.0, 2.4, 1.2 Hz, 1H), 5.43 (ddt, *J*=10.2, 2.4, 1.2 Hz, 1H), 5.79–6.00 (m, 1H), 6.98 (d, *J*=9.1 Hz, 1H), 6.99 (broad s, 1H), 8.06 (dd, *J*=9.1, 2.7 Hz, 1H), 8.46 (d, *J*=2.7 Hz, 1H); *m/z* (int. %): 274 (4.9), 273 (9.9), 272 (79.3), 209 (4.8), 208 (41.3), 207 (6.0), 181 (18.2), 179 (12.2), 168 (10.5), 167 (100.0), 151 (12.2); ν_{max} (KBr): 1593.3, 1521.3, 1401.5, 1342.5, 1267.9, 1151.9, 1084.8.

3.2. Preparation of 1 by alkylation of 6 (general procedure)

To the solution of **6** (10 mmol) in DMF (25 ml), K_2CO_3 (50 mmol, 6.9 g) was added (in some cases acompanied with addition of KI, 1 mmol, ca. 170 mg) followed by the addition of alkyl halide (50 or 30 mmol, see Table 1). The reaction flask was stoppered and the mixture stirred vigorously until the starting material was consumed (TLC control). The mixture was poured into cold aq. HCl solution and extracted with AcOEt (3×50 ml). The combined organic layers were washed with diluted NaCl solution, dried with $MgSO_4$, the solvent was evaporated and the residue recrystallized. The mother liquor was purified on silica gel with hexane–ethyl acetate mixture as eluent.

3.2.1. Compound 1a. Light-yellow crystals; mp 66°C, (aq. MeOH); [Found: C, 46.90; H, 4.78; N, 11.06%. $C_{10}H_{12}N_2O_4S$ requires C, 46.87: H, 4.72; N, 10.93%]; δ_H: 3.44 (s, 3H), 3.83 (dt, *J*=7.2, 1.0 Hz, 2H), 5.43 (ddd, *J*=16.9, 2.3, 1.1 Hz, 1H), 5.48 (ddt, *J*=10.1, 2.3, 1.1 Hz, 1H), 5.80–6.01 (m, 1H), 7.57 (t, *J*=8.1 Hz, 1H), 7.80 (ddd, *J*=8.1, 2.1, 1.0 Hz, 1H), 8.14 (ddd, *J*=8.1, 2.1, 1.0 Hz, 1H), 8.22 (t, *J*=2.1 Hz, 1H); *m/z* (int. %): 256 (20.3), 192 (7.8), 191 (10.1), 177 (15.0), 165 (37.9), 146 (12.5), 145 (14.5), 105 (35.9), 104 (23.7); ν_{max} (KBr): 1641.3, 1578.9, 1531.6, 1479.0, 1347.3, 1313.0, 1261.5, 1179.5, 1150.2, 1088.5, 1052.9.

3.2.2. Compound 1b. Brown oil; [Found: C, 52.32; H, 6.28; N, 9.51%. $C_{13}H_{18}N_2O_4S$ requires C, 52.33; H, 6.08; N, 9.39%]; δ_H: major β,γ isomer (>90%): 0.88 (t, *J*=7.5 Hz, 3H), 1.24–1.52 (m, 4H), 3.73–3.81 (m, 4H), 5.44 (ddt, *J*=11.3, 2.4, 1.2 Hz, 1H), 5.50 (ddt, *J*=4.7, 2.4, 1.2 Hz, 1H), 5.82–6.03 (m, 1H), 7.75 (ddd, *J*=8.0, 2.1, 1.2 Hz, 1H), 8.16 (m, 2H); minor, α,β isomer (<10%): 1.94 (dd, *J*=6.8, 1.6 Hz, 3H), 3.58–3.66 (m, 4H), 6.20 (ddd, *J*=15.0, 3.3, 1.6 Hz, 1H), 6.61–6.79 (m, 1H), other signals overlapped with those of the major isomer; *m/z* (int. %): 298 (17.5), 255 (26.8), 193 (8.6), 192 (9.2), 191 (74.7), 151 (19.8); ν_{max} (film): 1640.5, 1614.3, 1532.1, 1477.8, 1423.8, 1350.5, 1303.8, 1247.1, 1144.2, 1099.1, 1072.4.

3.2.3. Compound 1c. Brown oil; [Found: C, 51.40; H, 5.25; N, 10.03%. $C_{12}H_{14}N_2O_4S$ requires C, 51.05; H, 5.00; N, 9.92%]: δ_H: major β,γ isomer (>96%): 3.84 (dt, *J*=7.1, 1.0 Hz, 2H), 4.36 (dt, *J*=6.3, 1.2 Hz, 2H), 5.11–5.21 (m, 2H), 5.45 (ddt, *J*=13.3, 2.4, 1.2 Hz, 1H), 5.52 (ddt, *J*=6.6, 2.4, 1.2 Hz, 1H), 5.68–6.05 (m, 2H), 7.53–7.62 (m, 1H), 7.70–7.76 (m, 1H), 8.13–8.19 (m, 2H); minor, α,β isomer (traces): 1.96 (dd, *J*=6.9, 1.7 Hz, 3H), 4.26 (dt, *J*=6.2, 1.3 Hz, 2H), 6.18–6.28 (m, 1H), 6.65–6.83 (m, 1H); *m/z* (int. %): 282 (6.1), 217 (3.5), 203 (6.5), 191 (16.9), 189 (5.9), 177 (15.9), 176 (8.7), 172 (5.9), 171 (8.4), 150 (6.2), 149 (20.3); ν_{max} (KBr): 1641.8, 1613.4, 1532.0, 1480.1, 1422.6, 1351.3, 1227.4, 1197.6, 1153.2, 1067.4.

3.2.4. Compound 1d. Light-brown crystals; mp 127–128°C (AcOEt–hexane); [Found: C, 58.01: H, 4.87; N, 8.41%. $C_{16}H_{16}N_2O_4S$ requires C, 57.83; H, 4.85; N, 8.43%]: δ_H: major β,γ isomer (>96%): 3.86 (dt, *J*=7.2, 1.0 Hz, 2H), 4.93 (s, 2H), 5.44–5.57 (m, 2H), 5.88–6.09 (m, 1H), 7.21–7.26 (m, 5H), 7.48 (dd, *J*=8.1, 0.3 Hz, 1H), 7.66 (ddd, *J*=8.1, 2.1, 1.2 Hz, 1H), 8.06–8.12 (m 1H), 8.14–8.17 (m, 1H); minor, α,β isomer (traces): 1.97 (dd, *J*=6.9, 1.6 Hz, 3H), 4.81 (s, 2H), 6.28 (dq, *J*=15.0, 1.6 Hz, 1H), 6.69–6.87 (m, 1H); *m/z* (int. %): 332 (2.5), 227 (7.6), 226 (14.9); ν_{max} (KBr): 1527.9, 1455.5, 1344.1, 1300.1, 1247.6, 1221.3, 1140.7, 1061.9.

3.2.5. Compound 1e. Light-yellow crystals; mp 83–84°C (AcOEt–hexane); [Found: C, 41.32; H, 3.88; N, 9.60%. $C_{10}H_{11}N_2O_4SCl$ requires C, 41.31; H, 3.81; N, 9.63%]: δ_H: 3.33 (s, 3H), 3.94 (dt, *J*=7.1, 1.0 Hz, 2H), 5.49–5.60 (m, 2H), 5.90–6.10 (m, 1H), 7.67 (d, *J*=8.3 Hz, 1H), 8.18 (dd, *J*=8.8, 2.6 Hz, 1H); *m/z* (int. %): 278 (5.2), 276 (13.4), 216

(6.2), 212 (19.1), 185 (10.4), 177 (20.5); ν_{max} (KBr): 1522.1, 1473.5, 1353.9, 1337.8, 1206.7, 1189.9, 1139.3, 1088.3.

3.2.6. Compound 1f. Light-yellow crystals; mp 60–61°C (AcOEt–hexane); [Found: C, 46.93; H, 5.30; N, 8.24%. $C_{13}H_{17}N_2O_4SCl$ requres C, 46.92; H, 5.15; N, 8.42%]: δ_H: 0.89 (t, *J*=7.1 Hz, 3H), 1.23–1.52 (m, 4H), 3.68 (broad s, 2H), 3.90 (d, *J*=7.1 Hz, 2H), 5.45–5.50 (m, 1H), 5.52–5.58 (m, 1H), 5.87–6.08 (m, 1H), 7.67 (d, *J*=8.8 Hz, 1H), 8.19 (dd, *J*=8.8, 2.7 Hz, 1H), 8.30 (d, *J*=2.7 Hz, 1H); *m/z* (int. %): 334 (1.6), 332 (4.6), 291 (13.0), 289 (34.2), 227 (34.8), 226 (10.5), 225 (77.6), 186 (24.7), 139 (12.5); ν_{max} (KBr): 1528.4, 1469.1, 1343.4, 1203.5, 1142.5, 1081.3, 1048.3.

3.2.7. Compound 1g. Light-yellow crystals; mp 70–71°C (MeOH); [Found: C, 48.87; H, 5.29; N, 10.40%. $C_{11}H_{14}N_2O_4S$ requires C, 48.88; H, 5.22; N, 10.36%]: δ_H: 2.53 (s, 3H), 3.29 (s, 3H), 3.93 (dt, *J*=7.2, 1.1 Hz, 2H), 5.52–5.64 (m, 2H), 5.92–6.12 (m, 1H), 7.48 (dt, *J*=8.3, 0.6 Hz, 1H), 8.13 (dd, *J*=8.3, 2.3 Hz, 1H), 8.17 (d, *J*=2.3 Hz, 1H); δ_H: 147.49, 146.58, 140.83, 132.25, 125.48, 124.75, 123.72, 123.29, 55.87, 39.40, 18.86; *m/z* (int. %): 271 (4.9), 270 (36.9), 191 (12.3), 189 (11.2), 179 (14.2), 166 (10.7) 165 (100.0), 160 (12.7), 119 (81.7), 118 (38.6); ν_{max} (KBr): 1587.4, 1519.2, 1351.5, 1341.4, 1293.4, 1183.9, 1139.2, 1054.3.

3.2.8. Compound 1h. Light-brown crystals; mp 119–120°C (aq. MeOH); [Found: C, 46.16; H, 5.05; N, 9.76%. $C_{11}H_{14}N_2O_5S$ requires C, 46.15; H, 4.93; N, 9.78%]: δ_H: major β,γ isomer: 3.27 (s, 3H), 3.85 (dt, *J*=7.3, 1.0 Hz, 2H), 4.03 (s, 3H), 5.51–5.57 (m, 2H), 5.85–6.04 (m, 1H); minor, α,β isomer: 6.23 (ddd, *J*=15.0, 3.4, 1.7 Hz, 1H), 6.64–6.83 (m, 1H); aromatic part for both isomers: 6.99–7.04 (m, 1H), 8.22–8.27 (m, 2H); *m/z* (int. %): 287 (3.00), 286 (22.6), 182 (10.2), 181 (100.0), 166 (18.9), 165 (13.5), 136 (6.5), 135 (43.5); ν_{max} (KBr): 1588.8, 1511.4, 1498.7, 1332.0, 1287.6, 1190.8, 1140.4, 1057.1, 1018.2.

3.3. Synthesis of phosphonosulfonamide 9 (similiar to lit.[10])

To the solution of LDA prepared from diisopropylamine (12.4 ml, 88 mmol) and *n*-BuLi (8.8 ml of 10 M solution in hexane, 88 mmol) in dry THF (350 ml) and TMEDA (8 ml) a solution of *N*-methyl-*N*-3-nitrophenyl methanesulfonamide **7**[9] (9.2 g, 40 mmol) in THF (50 ml) was added quickly at −70°C under nitrogen. The dark-red mixture was then stirred 5 min and treated with diethyl chlorophosphate (2.7 ml, 15 mmol). After stirring for 10 min. at −70°C the mixture was quenched with aq. HCl and extracted with DCM (3×50 ml). Combined organic extracts were washed with water, dried ($MgSO_4$), the solvent was evaporated and the residue chromatographed on silica gel with DCM as eluent to yield the substrate (1.86 g; 20% recovery) and product **9** (6.90 g; 47%).

3.3.1. Compound 9. Light-yellow crystals; mp 67–69°C (AcOEt–hexane); [Found: C, 39.21; H, 5.55; N, 7.41%. $C_{12}H_{19}N_2O_7SP$ requires C, 39.35; H, 5.23; N, 7.65%]: δ_H: 1.36 (dt, *J*=7.1 Hz, $^3J_{PH}$=0.6 Hz, 6H), 3.50 (s, 3H), 3.60 (d, $^1J_{PH}$=17 Hz, 2H), 4.22 (dq, *J*=7.1 Hz, $^2J_{PH}$=8.3 Hz, 4H), 7.6 (t, 8.2, 1H), 7.89 (ddd, *J*=8.2, 2.2, 1.1 Hz, 1H), 8.18 (ddd, *J*=8.2, 2.2, 1.1 Hz, 1H), 8.36 (t, *J*=2.2 Hz, 1H); *m/z* (int. %): 367 (1.1), 321 (3.7), 302 (2.4), 293 (2.6), 215 (2.9), 159 (15.9), 153 (6.3), 152 (100.0); ν_{max} (KBr): 1611.8, 1533.7, 1479.9, 1463.3, 1359.1, 1291.3, 1252.5, 1214.2, 1183.3, 1159.5, 1067.8, 1012.4.

3.4. Synthesis of 1i–l by condensation of phosphonosulfonamide 9 with carbonyl compounds (general procedure)

Phosphonosulfonamide **9** (1830 mg, 5 mmol), LiBr (653 mg, 7.5 mmol) and the carbonyl compound (7.5 mmol) were dissolved in dry THF and cooled to −20°C then treated with DBU (900 μl, 6 mmol). The mixture turned deep-red and yellow solid precipitated immediately. The cooling bath was removed and the mixture stirred at rt until the starting **9** was consumed (TLC control). After pouring into ice-cold aq. HCl solution, extraction with DCM (3×50 ml), drying the extracts with $MgSO_4$ and evaporation of the solvent, the residue was purified on silica gel with hexane–ethyl acetate mixture as eluent to yield products **1i–l**.

3.4.1. Compound 1i. From **9** and cyclohexanone; yield 72%; yellow crystals, mp 61–62°C; [Found: C, 54.46; H, 6.08; N, 8.96%. $C_{14}H_{18}N_2O_4S$ requires C, 54.19; H, 5.85; N, 9.03%]: δ_H: 1.40–1.71 (m, 6H), 2.21 (t, *J*=6.2 Hz, 2H), 2.46 (t, *J*=6.2 Hz, 2H), 3.33 (s, 3H), 5.90 (s, 1H), 7.55 (ddd, *J*=8.1, 7.7, 1.0 Hz, 1H), 7.79 (ddd, *J*=8.1, 2.2, 1.1 Hz, 1H), 8.08–8.17 (m, 2H); *m/z* (int. %): 310 (18.3), 246 (15.4), 229 (13.0), 203 (18.1), 190 (19.3), 152 (44.5); ν_{max} (KBr): 1525.6, 1338.4, 1317.9, 1146.2, 1098.4.

3.4.2. Compound 1j. From **9** and Me_2CO; yield 62%; light-yellow oil; [Found: 48.83; H, 5.15; N, 10.42%. $C_{11}H_{14}N_2O_4S$ requires C, 48.88; H, 5.22; N, 10.36%]: δ_H: major, α,β isomer: 1.94 (s, 3H), 1.95 (s, 3H), 3.32 (s, 3H), 5.94–5.97 (m, 1H); minor, β,γ isomer: 1.94 (s, 3H), 3.45 (s, 3H), 3.76 (s, 2H), 5.06–5.09 (m, 1H): aromatic part for both: 7.50–7.60 (m, 1H), 7.75–7.84 (m, 1H), 8.10–8.23 (m, 2H); *m/z* (int. %): 271 (3.6), 270 (25.8), 207 (6.4), 206 (40.7), 205 (6.8), 192 (7.8), 191 (68.5), 189 (4.6), 174 (8.6), 166 (9.2), 165 (100.0), 160 (12.4), 152 (27.9); ν_{max} (film): 1631.9, 1531.8, 1479.2, 1444.1, 1350.9, 1316.4, 1166.4, 1146.9, 1100.6, 1067.6.

3.4.3. Compound 1k. From **9** and $PhCH_2CHO$: yield 63%; yellow crystals; mp 85°C (EtOH); [Found: C, 57.95; H, 4.52; N, 8.37%. $C_{16}H_{16}N_2O_4S$ requires C, 57.82; H, 4.85; N, 8.43%]: δ_H: 3.44 (s, 3H), 3.99 (dd, *J*=6.5, 1.1 Hz, 2H), 6.15 (dt, *J*=15.9, 7.4 Hz, 1H), 6.64 (dt, *J*=15.9, 1.1 Hz, 1H), 7.28–7.37 (m, 5H), 7.51 (t, *J*=8.2 Hz, 1H), 7.80 (ddd, *J*=8.2, 2.3, 1.0 Hz, 1H), 8.07 (ddd, *J*=8.2, 2.3, 1.0 Hz, 1H), 8.19 (t, *J*=2.3 Hz, 1H); LSIMS: 355 $(M+Na)^+$; ν_{max} (KBr): 1524.0, 1483.1, 1448.2, 1404.4, 1351.6, 1295.2, 1274.0, 1238.6, 1143.6, 1066.8.

3.4.4. Compound 1l. From **9** and PhCOMe; yield 60%; in this case 10 equiv. of carbonyl compound and MeCN as a solvent were used; yellow oil; [Found: C, 57.92; H, 4.92; N, 8.41%. $C_{16}H_{16}N_2O_4S$ [332.39]: C, 57.82; H, 4.85; N, 8.43%]: two isomers (separated from a small sample); δ_H: major, α,β isomer: 2.23 (d, *J*=1.3 Hz, 3H), 3.39 (s, 3H),

6.36 (q, *J*=1.3 Hz, 1H), 7.33–7.44 (m, 5H), 7.57 (td, *J*=8.2, 0.4 Hz, 1H), 7.8 (ddd, *J*=8.2, 2.2, 1.1 Hz, 1H), 8.15 (ddd, *J*=8.2, 2.2, 1.1 Hz, 1H), 8.21 (td, *J*=2.2, 0.4 Hz, 1H); *m/z* (int. %): 332 (2.7), 270 (2.0), 269 (17.9), 268 (100.0), 253 (15.9), 210 (7.5); minor, β,γ isomer: 3.25 (s, 3H), 4.27 (d, *J*=0.7 Hz, 2H), 5.54 (d, *J*=0.7 Hz, 1H), 5.73 (d, *J*=0.7 Hz, 1H), 7.28–7.35 (m, 5H), 7.46 (t, *J*=8.1 Hz, 1H), 7.64 (ddd, *J*=8.1, 2.2,1.1 Hz, 1H), 7.85 (t, *J*=2.2 Hz, 1H), 8.04 (ddd, *J*=8.2, 2.2, 1.1 Hz, 1H); *m/z* (int. %): 332 (0.5), 296 (2.6), 270 (12.0), 269 (14.9), 268 (78.9), 206 (12.7); ν_{max} (film): 1604.4, 1573.4, 1531.4, 1479.2, 1444.4, 1351.2, 1167.7, 1148.8, 1100.7, 1067.4.

3.5. Reaction of 3-nitroarylallylsulfones 1 with DBU and $MgCl_2$

Procedure A. Compound **1** (1 mmol) and $MgCl_2$ (0.625 mmol, 60 mg) were dissolved in dry DMSO (10 ml), DBU (746 μl, 5 mmol) was added in one portion, the reaction vial stoppered and the mixture stirred for the time indicated in Table 4 until the starting material disappeared (TLC control). In the selected experiments (Scheme 5, Table 5) Ar or O_2 was bubbled through the reaction mixture for indicated time prior to the addition of DBU and then during the reaction. After completion, the mixture was poured into saturated aq. NH_4Cl solution and extracted with AcOEt (3×20 ml). The combined extracts were washed with dil. NaCl solution, dried with $MgCl_2$ the solvent was evaporated and the residue separated on silica gel with hexane–ethyl acetate mixture as eluent.

Procedure B. After performing procedure A, the crude mixture was heated to reflux with triethylphosphite for 30 min to 1 h (Table 4). The volatiles were removed under vacuum and the residue chromatographed on silica gel with hexane–ethyl acetate mixture as eluent.

The following products were isolated:

3.5.1. From the reaction of 1a. *Compound* **2a**: Yellow crystals; mp 143–144°C (AcOEt–hexane); [Found: C, 54.62; H, 3.48; N, 12.76%. $C_{10}H_8N_2O_2S$ requires C, 54.53; H, 3.66; N, 12.72%]: δ_H lit.[4]; *m/z* (int. %): 222 (5.7), 221 (12.4), 220 (100.0), 156 (9.9), 155 (78.6), 129 (40.6), 128 (55.3), 102 (19.7), 101 (19.2); ν_{max} (KBr): 1626.3, 1597.2, 1466.1, 1362.5, 1315.1, 1277.4, 1192.4, 1153.7, 1135.3, 1036.1. *Compound* **3a**: Light green crystals; mp 228–229°C (MeOH); [Found: 50.66, H, 3.31; N, 11.95%. $C_{10}H_8N_2O_3S$ requires C, 50.84; H, 3.41; N, 11.86%]: δ_H lit.[4]; *m/z* (int. %): 238 (5.3), 237 (11.1), 236 (100.0), 221 (5.0), 220 (26.6), 188 (35.5), 171 (8.8), 155 (17.5), 143 (9.8), 128 (16.1), 116 (19.1), 115 (12.3), 114 (7.8); ν_{max} (KBr): 1631.8, 1561.3, 1498.8, 1462.4, 1418.1, 1388.5, 1322.1 1285.1, 1223.3, 1169.3, 1154.7.

3.5.2. From the reaction of 1b. *Compound* **2b**: Dark-green crystals; mp 68–69°C (CCl_4–hexane); [Found: C, 59.64; H, 5.49; N, 10.65%. $C_{13}H_{14}N_2O_2S$ requires C, 59.52; H, 5.38; N, 10.68%]: δ_H: 1.01 (t, *J*=7.3 Hz, 3H), 1.38–1.62 (m, 2H), 1.84–1.98 (m, 2H), 3.82 (t, *J*=7.5 Hz, 2H), 6.78 (dd, *J*=7.1, 0.8 Hz, 1H), 7.69 (dd, *J*=8.8, 0.8 Hz, 1H), 7.79 (dd, *J*=8.8, 7.1 Hz, 1H), 7.80 (d, *J*=4.6 Hz, 1H), 9.23 (d, *J*=4.6 Hz, 1H); *m/z* (int. %): 264 (4.9), 263 (12.9), 262 (81.5), 221 (5.7), 220 (12.3), 219 (100.0), 207 (8.5), 206 (60.9), 142 (21.6), 128 (48.1); ν_{max} (KBr): 1621.0, 1594.6, 1470.2, 1410.1, 1364.6, 1326.5, 1208.5, 1157.1, 1137.5. *Compound* **3b**: Light-brown crystals; mp 102–103°C (aq. EtOH); [Found: C, 56.15; H, 5.13; N, 10.06%. $C_{13}H_{14}N_2O_3S$: C, 56.10; H, 5.07; N, 10.06%]: δ_H: 1.02 (t, *J*=7.4 Hz, 3H), 1.42–1.60 (m, 2H), 1.82–1.97 (m, 2H), 3.81 (t, *J*=7.5 Hz, 2H), 6.82 (d, *J*=7.5 Hz, 1H), 7.68 (d, *J*=6.4 Hz, 1H), 7.73 (dd, *J*=8.9, 7.5 Hz, 1H), 7.92 (d, *J*=8.9 Hz, 1H), 8.57 (d, *J*=6.4 Hz, 1H); *m/z* (int. %): 280 (6.0), 279 (16.4), 278 (100.0), 262 (11.7), 236 (8.80), 235 (10.7), 222 (63.2), 219 (15.3), 206 (9.9), 154 (19.1), 128 (18.3); ν_{max} (KBr): 1632.7, 1562.1, 1499.1, 1431.6, 1391.7, 1326.5, 1225.0, 1170.9.

3.5.3. From the reaction of 1c. *Compound* **2c**: Light-brown crystals; mp 112°C (AcOEt–hexane); [Found: C, 58.29; 3.99; N, 11.40%. $C_{12}H_{10}N_2O_2S$: C, 58.52; H, 4.09; N, 11.37%]: δ_H: 4.44 (dt, *J*=5.5, 1.6 Hz, 2H), 5.38 (ddt, *J*=10.2, 1.6, 1.0 Hz, 1H), 5.50 (ddt, *J*=17.1, 1.6, 1.0 Hz, 1H), 5.92–6.11 (m, 1H), 6.79 (dd, *J*=6.5, 1.4 Hz, 1H), 7.69–7.83 (m, 2H), 7.82 (d, *J*=4.5 Hz, 1H), 9.25 (d, *J*=4.5 Hz, 1H); *m/z* (int. %): 248 (5.8), 247 (15.2), 246 (100.0), 206 (7.5), 182 (7.2), 181 (31.8), 155 (10.6), 154 (7.2), 142 (9.7), 128 (16.9); ν_{max} (KBr): 1621.6, 1594.8, 1468.5, 1405.9, 1360.0, 1320.8, 1259.8, 1206.7, 1160.3, 1134.6. *Compound* **3c**: Yellow crystals; mp 174–175°C (MeOH); [Found: C, 55.09; H, 3.78; N, 10.69%. $C_{12}H_{10}N_2O_3S$ requires C, 54.95; H, 3.84; N, 10.62%]: δ_H: 4.42 (dt, *J*=5.6, 1.5 Hz, 2H), 5.40 (ddd, *J*=10.2, 2.4 Hz, 1H), 5.50 (ddd, *J*=16.1, 2.4, 1.5 Hz, 1H), 5.90–6.10 (m, 1H), 6.81 (d, *J*=7.5 Hz, 1H), 7.70 (d, *J*=6.3 Hz, 1H), 7.72 (dd, *J*=8.9, 7.5 Hz, 1H), 7.93 (d, *J*=8.9 Hz, 1H), 8.58 (d, *J*=6.3 Hz, 1H); *m/z* (int. %): 264 (3.1), 263 (6.9), 262 (46.5), 221 (6.7), 197 (4.6), 181 (8.3); ν_{max} (KBr): 1631.0, 1561.1 1499.0, 1432.0, 1391.4, 1225.4, 1169.8, 1156.5, 1129.3, 1080.4.

3.5.4. From the reaction of 1d. *Compound* **2d**: Light-brown crystals; mp 127–128°C (AcOEt–hexane); [Found: C, 64.77; H, 3.97; N, 9.46%. $C_{16}H_{12}N_2O_2S$ requires C, 64.85; H, 4.08; N, 9.45%]: δ_H: 4.99 (s, 2H), 6.54 (dd, *J*=6.2, 1.7 Hz, 1H), 7.30–7.45 (m, 3H), 7.47–7.55 (m, 2H), 7.60–7.73 (m, 2H), 7.86 (d, *J*=4.5 Hz, 1H), 9.26 (d, *J*=4.5 Hz, 1H); *m/z* (int. %): 297 (5.6), 296 (28.0), 92 (7.3), 91 (100.0); ν_{max} (KBr): 1624.3, 1595.8, 1482.2, 1468.9, 1266.9, 1317.2, 1211.1, 1158.2, 1139.5. *Compound* **3d**: Brown crystals; mp 181–182°C (AcOEt); [Found: C, 61.27; H, 3.83; N, 8.88%. $C_{16}H_{12}N_2O_3S$ requires C, 61.53; H, 3.87; N, 8.97%]: δ_H: 4.97 (s, 2H), 6.56 (d, *J*=7.5 Hz, 1H), 7.33–7.52 (m, 5H), 7.58 (dd, *J*=8.8, 7.5 Hz, 1H), 7.74 (d, *J*=6.3 Hz, 1H), 7.89 (d, *J*=8.8 Hz, 1H), 8.59 (d, *J*=6.3 Hz, 1H); *m/z* (int. %): 313 (3.1), 312 (15.5), 296 (3.4), 92 (8.2), 91 (100.0); ν_{max} (KBr): 1633.3, 1604.4, 1559.3, 1498.2, 1456.1, 1432.5, 1391.1, 1361.5, 1316.6, 1291.3, 1172.8, 1147.4, 1127.7, 1074.6.

3.5.5. From the reaction of 1e. *Compound* **3e**: Pale-yellow crystals; mp 214–215°C (AcOEt); [Found: C, 43.10; H, 2.72; N, 11.21%. $C_{10}H_7N_2O_2SCl$: C, 47.16; H, 2.77; N, 11.00%]: δ_H: 3.67 (s, 3H), 7.70 (s, 2H), 7.85 (d, *J*=4.5 Hz, 1H), 9.23 (d, *J*=4.5 Hz, 1H); *m/z* (int. %): 257 (4.7), 256 (37.3), 255 (12.6), 254 (100.0), 191 (14.1), 190 (5.5), 189 (43.5), 163 (14.7), 162 (18.5), 155 (16.2); ν_{max} (KBr): 1616.2, 1595.0, 1469.6, 1437.0, 1405.7, 1349.2,

1321.9, 1247.4, 1207.8, 1168.0, 1142.3, 1114.6. *Compound* **3e**: Yellow crystals; mp 252–257°C (dec., $ClCH_2CH_2Cl$–AcOEt); [Found: 44.47; H, 2.31; N, 10.28%. $C_{10}H_7N_2O_3SCl$ requires C, 44.47; H, 2.61; N, 10.37%]: δ_H: 3.68 (s, 3H), 7.63 (d, *J*=9.4 Hz, 1H), 7.74 (d, *J*=6.4 Hz, 1H), 7.93 (d, *J*=9.4 Hz, 1H), 8.55 (d, *J*=6.4 Hz, 1H); *m/z* (int. %): 272 (37.8), 271 (12.5), 270 (100.0), 256 (10.4), 254 (27.8); ν_{max} (KBr): 1564.7, 1490.7, 1372.3, 1328.9, 1223.3, 1201.9, 1166.8, 1139.4.

3.5.6. From the reaction of 1f. *Compound* **2f**: Light-brown crystals; mp 107–108°C (AcOEt–hexane);[Found: C, 52.71; H, 4.42; N, 9.46%. $C_{10}H_7N_2O_2SCl$ requires C, 52.61; H, 4.42; N, 9.44%]: δ_H: 1.00 (t, *J*=7.3 Hz, 3H), 1.40–1.52 (m, 2H), 1.81–1.95 (m, 2H), 4.07–4.16 (m, 2H), 7.69 (s, 2H), 7.83 (d, *J*=4.5 Hz, 1H), 9.22 (d, *J*= 4.5 Hz, 1H); *m/z* (int. %): 298 (16.3), 297 (6.6), 296 (42.9), 255 (14.7), 254 (5.2), 253 (39.1), 242 (35.9), 241 (11.7), 240 (100.0), 189 (8.3), 176 (30.8); ν_{max} (KBr): 1615.5, 1595.3, 1469.0, 1404.5, 1325.1, 1250.7, 1202.0, 1165.6, 1114.4. *Compound* **3f**: Yellow crystals; mp 174°C (AcOEt–hexane); [Found: C, 49.90; H, 4.15; N, 8.96%. $C_{13}H_{13}N_2O_3SCl$ requires C, 49.92; H, 4.19; N, 8.96%]: δ_H: 1.00 (t, *J*=7.3 Hz, 3H), 1.38–1.61 (m, 2H), 1.78–1.96 (m, 2H), 4.07–4.15 (m, 2H), 7.62 (d, *J*=9.4 Hz, 1H), 7.72 (d, *J*=6.4 Hz, 1H), 7.93 (d, *J*=9.4 Hz, 1H), 8.55 (d, *J*=6.4 Hz, 1H); *m/z* (int. %): 315 (4.0), 314 (25.2), 313 (10.1), 312 (64.1), 302 (6.2), 298 (5.9), 296 (15.2), 271 (12.9), 270 (5.0), 269 (33.4), 259 (8.2), 258 (37.4), 257 (11.8), 256 (100.0), 253 (14.5), 242 (12.6), 240 (34.6); ν_{max} (KBr): 1627.0, 1586.1, 1565.3, 1495.1, 1470.1, 1434.9, 1398.1, 1365.6, 1336.1, 1286.0, 1217.6, 1185.0, 1164.6, 1142.7, 1070.4.

3.5.7. From the reaction of 1g. *Compound* **2g**: Yellow crystals; mp 222–226°C (AcOEt–hexane); [Found: C, 56.44; H, 4.27; N, 12.13%. $C_{11}H_{10}N_2O_2S$ requires C, 56.40; H, 4.30; N, 11.96%]: δ_H: 2.64 (s, 3H), 3.52 (s, 3H), 7.58–7.75 (ABq: δ_A=7.72, δ_B=7.60, *J*=8.8 Hz, 2H), 7.79 (d, *J*=4.6 Hz, 1H), 9.16 (d, *J*=4.6 Hz, 1H); *m/z* (int. %): 236 (5.5), 235 (12.8), 234 (100.0), 170 (11.4), 169 (81.4), 168 (9.6), 155 (25.5), 143 (9.8), 142 (24.0); ν_{max} (KBr): 1588.6, 1483.6, 1463.8, 1413.0, 1401.7, 1344.9, 1314.0, 1249.3, 1216.7, 1197.3, 1155.4, 1131.6, 1064.6. *Compound* **3g**: Yellow crystals; mp 251–252°C (AcOEt); [Found: C, 52.05; H, 4.09; N, 11.10%. $C_{11}H_{10}N_2O_3S$ requires C, 52.79; H. 4.03; N, 11.19%]: δ_H: 2.63 (s, 3H), 3.53 (s, 3H), 7.57 (d, *J*=9.0 Hz, 1H), 7.69 (d, *J*=6.3 Hz, 1H), 7.88 (d, *J*=9.0 Hz, 1H), 8.47 (d, *J*=6.3 Hz, 1H); *m/z* (int. %): 251 (8.8), 250 (58.4), 235 (12.5), 234 (88.9), 202 (16.2), 186 (13.8), 173 (11.9), 170 (13.9), 169 (100.0), 168 (20.9), 155 (33.5); ν_{max} (KBr): 1621.5, 1304.5, 1569.5, 1493.7, 1483.1, 1461.8, 1421.7, 1391.5, 1367.5, 1308.4, 1282.0, 1226.5, 1204.1, 1162.1, 1147.9, 1125.7, 1076.5.

3.5.8. From the reaction of 1h. *Compound* **2h**: Yellow crystals; mp 178°C (MeOH): [Found: C, 52.76; H, 3.94; N, 11.16%. $C_{11}H_{10}N_2O_3S$ requires C, 52.79; H, 4.03; N, 11.19%]: δ_H: 3.55 (s,1H), 4.03 (s, 3H), 7.63 (d, *J*=9.3 Hz, 1H), 7.78 (d, *J*=4.5 Hz, 1H), 7.80 (d, *J*=9.3 Hz, 1H), 9.10 (d, *J*=4.5 Hz, 1H); *m/z* (int. %): 286 (5.9), 252 (5.8), 251 (13.7), 250 (100.0), 235 (26.0), 185 (7.0), 181 (24.2), 172 (4.8), 171 (44.6), 166 (5.0); ν_{max} (KBr): 1627.3, 1586.0, 1490.8, 1473.3, 1405.8, 1348.8, 1314.7, 1301.0, 1204.6, 1156.0, 1129.5, 1080.2.

3.5.9. From the reaction of 1i. *Compound* **2i**: Yellow crystals; mp 181°C (EtOH); [Found: C, 61.12; H, 4.98; N, 10.21%. $C_{14}H_{14}N_2O_2S$ requires C, 61.29; H, 5.14; N, 10.21%]: δ_H: 1.93–2.13 (m, 4H), 3,24 (t, *J*=6.3 Hz, 2H), 3.33 (s, 3H), 3.38 (t, *J*=6.3 Hz, 2H), 6.64 (d, *J*=7.1 Hz, 1H), 7.53 (dd, *J*=8.8 Hz, 0.8, 1H), 7.64 (dd, *J*=8.8, 7.1 Hz, 1H); *m/z* (int. %): 276 (6.3), 275 (16.7), 274 (100.0), 209 (22.1), 182 (11.5), 181 (7.2), 169 (6.0); ν_{max} (KBr): 1627.2, 1602.9, 1594.2, 1482.6, 1466.5, 1432.4, 1364.4, 1353.3, 1320.3, 1278.4, 1240.2, 1215.5, 1186.8, 1151.7. *Compound* **3i**: Brown crystals; mp 203–204°C (EtOH); [Found: C, 57.83; H, 4.89; N, 9.61%. $C_{14}H_{14}N_2O_3S$ requires C, 57.92; H, 4.86; N, 9.65%]: δ_H: 1.85–2.10 (m, 4H), 3.12 (t, *J*= 6.4 Hz, 2H), 3.32 (t, *J*=6.4 Hz, 2H), 3.34 (s, 3H), 6.68 (d, *J*=7.5 Hz, 1H), 7.61 (dd, *J*=8.8, 7.5 Hz, 1H), 7.88 (d, *J*= 8.8 Hz, 1H); *m/z* (int. %): 292 (6.2), 291 (16.2), 290 (100.0), 275 (9.0), 274 (35.9), 273 (89.9), 272 (4.5), 227 (6.4), 226 (8.5), 225 (47.8), 224 (4.9), 210 (11.6), 209 (49.1), 208 (15.2); ν_{max} (KBr): 1636.6, 1608.6, 1579.1, 1494.4, 1465.4, 1423.1, 1393.6, 1349.7, 1315.4, 1290.4, 1242.7, 1174.8, 1150.8, 1108.2, 1073.9.

3.5.10. From the reaction of 1j. *Compound* **2j**: Yellow crystals; mp 147–148°C (aq. MeOH); [Found: C, 56.52; H, 4.34; N, 11.84%. $C_{11}H_{10}N_2O_2S$ requires C, 56.39; H, 4.30; N, 11.96%]: δ_H: 2.83 (s, 3H), 3,36 (s, 3H), 6.75 (dd, *J*=6.2, 1.8 Hz, 1H), 7.62–7.75 (m, 2H), 9.00 (s, 1H); *m/z* (int. %): 236 (5.4), 235 (13.6), 234 (100.0), 186 (7.3), 185 (6.1), 170 (16.0), 169 (47.7), 155 (16.5), 142 (11.2); ν_{max} (KBr): 1610.0 1597.2, 1475.4, 1445.2, 1417.0, 1404.0, 1312.5, 1291.2, 1261.5, 1208.2, 1190.0, 1155.6, 1131.4, 1033.3. *Compound* **3j**: Yellow crystals; mp 237–238°C (MeOH); [Found: C, 52.70; H, 3.88; N, 11.09%. $C_{11}H_{10}N_2O_3S$ requires C, 52.79; H, 4.03; N, 11.19%]: δ_H: 2.72 (s, 3H), 3.35 (s, 3H), 6.76 (d, *J*=7.4 Hz, 1H), 7.65 (dd, *J*=8.9, 7.4 Hz, 1H), 7.87 (d, *J*=8.7 Hz, 1H), 8.41 (s, 1H); *m/z* (int. %): 252 (5.8), 251 (13.7), 250 (100.0), 235 (3.2), 234 (22.9), 202 (23.8), 169 (15.1); ν_{max} (KBr): 1636.4, 1604.3, 1588.3, 1491.2, 1470.1, 1431.5, 1394.5, 1384.1, 1365.0, 1313.9, 1299.5, 1219.4, 1159.0, 1105.0, 1059.7, 1034.3.

3.5.11. From the reaction of 1k. *Compound* **2k**: Yellow crystals; mp 208–209°C (AcOEt); [Found: C, 64.81; H, 3.97; N, 9.55%. $C_{16}H_{12}N_2O_2S$ requires C, 64.85; H, 4.08; N, 9.45%]: δ_H: 3.40 (s, 3H), 6.75 (dd, *J*=6.5, 1.5 Hz, 1H), 7.52–7.63 (m, 3H), 7.71–7.85 (m 2H), 8.13–8.19 (m, 2H), 8.24–8.26 (m, 1H); *m/z* (int. %): 297 (18.8), 296 (100.0), 232 (6.3), 231 (19.3), 204 (10.3); ν_{max} (KBr): 1622.8, 1600.2, 1573.4, 1503.1, 1482.9, 1462.3, 1424.0, 1375.9, 1329.0, 1247.2, 1201.7, 1182.8, 1157.1. *Compound* **3k**: Light-orange crystals; mp 237–238°C (MEK); [Found: C, 61.22; H, 3.77; N, 8.83%. $C_{16}H_{12}N_2O_3S$ requires C, 61.53; H, 3.87; N, 8.97%]: δ_H: 3.40 (s, 3H), 6.82 (d, *J*=7.5 Hz, 1H), 7.52–7.59 (m, 3H), 7.77 (dd, *J*=8.9, 7.5 Hz, 1H), 7.85–7.90 (m, 2H), 7.91 (s, 1H), 8.01 (d, *J*=8.9 Hz, 1H); *m/z* (int. %): 313 (13.1), 312 (61.4), 311 (31.9), 298 (6.6), 297 (18.6), 296 (100.0), 248 (7.5), 247 (16.1), 232 (7.7), 231 (22.8), 219 (14.3). ν_{max} (KBr): 1633.5, 1564.7, 1509.0, 1492.5, 1448.9, 1394.3, 1374.7, 1327.7, 1314.7, 1180.4, 1152.5, 1079.3.

3.5.12. From the reaction of 1l. *Compound* **2l**: Green crystals; mp 220–222°C (dec., 1,2-dichloroethane–AcOEt–MeOH); [Found: C, 64.58; H, 3.74; N, 9.55%. $C_{16}H_{12}N_2O_2S$ requires C, 64.85; H, 4.08; N, 9.45%]: δ_H: 3.39 (s, 3H), 6.79 (dd, *J*=6.3, 1.6 Hz, 1H), 7.51–7.67 (m, 3H), 7.71–7.82 (m, 2H), 7.91–7.97 (m, 2H), 9.26 (s, 1H); *m/z* (int. %): 298 (6.5), 297 (19.1), 296 (100.0), 250 (6.9), 249 (4.8), 248 (7.5), 247 (6.4), 232 (18.9), 231 (36.2), 205 (10.5), 204 (18.7); ν_{max} (KBr): 1619.6, 1590.2, 1574.4, 1522.2, 1499.2, 1445.7, 1468.0, 1408.7, 1319.3, 1222.0, 1191.2, 1155.5, 1136.3, 1090.2, 1036.1. *Compound* **3l**: Deep-red crystals; mp 195–200°C (1,2-dichloroethane–AcOEt); δ_H: 3.37 (s, 3H), 6.81 (d, 1H), 7.59–7.65 (m, 3H), 7.70 (dd, *J*=8.8, 7.4 Hz, 1H), 7.83–7.89 (m, 2H), 7.94 (d, *J*=8.8 Hz, 1H), 8.69 (s, 1H); *m/z* (int. %): 314 (6.8), 313 (19.5), 312 (100.0), 297 (11.8), 296 (62.9), 264 (22.3), 248 (6.4), 247 (10.9), 232 (12.0), 231 (28.3), 219 (10.0), 204 (17.2); HRMS: calcd for $C_{16}H_{12}N_2SO_3$ [312.0569]; Found: 312.0568; ν_{max} (KBr): 1631.8, 1601.3, 1580.0, 1564.7, 1489.6, 1469.5, 1431.3, 1444.6, 1393.6, 1359.9, 1322.1, 1232.3, 1211.4, 1187.6, 1164.6, 1153.6, 1136.1, 1098.1, 1039.3. *Compound* **10l**: Yellow crystals; mp 201–202°C (dec.); [Found: C, 58.11; H, 4.26; N, 8.30%. $C_{16}H_{14}N_2SO_4$ requires C, 58.17; H, 4.27; N, 8.48%]: δ_H: 2.74 (s, 3H), 3.28 (s, 3H), 6.36 (d, *J*=9.2 Hz, 1H), 7.27–7.34 (m, 2H), 7.44–7.54 (m, 5H); *m/z* (int. %): 332 (6.3), 331 (18.8), 330 (100.0), 301 (2.7), 300 (13.8), 266 (10.1), 265 (7.2), 238 (3.5), 237 (5.4), 236 (26.9), 235 (8.9), 221 (11.3), 220 (39.4), 219 (19.8), 218 (14.9); ν_{max} (KBr): 1620.0, 1605.0, 1590.4, 1522.0, 1467.7, 1444.3, 1418.7, 1339.2, 1319.3, 1300.7, 1269.5, 1193.9, 1162.2, 1125.0, 1100.1.

3.5.13. Synthesis of 10a. The reaction was carried out according to the described procedure.[16] Sultam **15**[9] (1140 mg, 5 mmol) was dissolved in dry DMF (6 ml), K_2CO_3 (30 mg) and the large excess of acetaldehyde (6 ml, ca. 200 mmol), were added. The mixture was stirred until the substrate was consumed (about 1 h). The mixture was poured onto ice-cold aq. dil. HCl, extracted with AcOEt (3×30 ml), extracts washed with water, dried with $MgSO_4$ and the solvent was evaporated. The residue containing the mixture of alcohols was dissolved in dry pyridine and cooled to −20°C. MsCl (excess, ca. 2 ml) was added, the cooling bath was removed and the reaction stirred at rt until completion (TLC control). The mixture was poured onto ice-cold aq. HCl, extracted with AcOEt (3×50 ml), extracts washed with water, dried with $MgSO_4$, solvent was evaporated and the residue flash-chromatographed on silica gel with hexane–ethyl acetate mixture (2:1) to give **10a** (560 mg, 44%): light-brown crystals; mp 139–142°C (aq. MeOH); [Found: C, 47.28; H, 3.96; N, 10.82%. $C_{10}H_{10}N_2SO_4$ requires C, 47.24; H, 3.96; N, 11.02%]: δ_H: 2.42 (d, *J*=7.6 Hz, 3H), 3.22 (s, 3H), 6.89 (dd, *J*=8.0, 1.3 Hz, 1H), 7.1 (q, *J*=7.6 Hz, 1H), 7.32 (dd, *J*=8.2, 1.3 Hz, 1H), 7.41 (q, *J*=8.1 Hz, 1H); *m/z* (int. %): 256 (6.1), 255 (12.4), 254 (100.0), 237 (11.2), 236 (6.3), 220 (9.2), 173 (16.0), 161 (8.1), 160 (5.7), 148 (7.0), 147 (7.8), 145 (13.7); ν_{max} (KBr): 1639.9, 1606.7, 1525.6, 1469.3, 1449.8, 1362.6, 1329.3, 1304.2, 1203.6, 1169.0, 1154.6, 1121.6.

3.5.14. Conversion of 10a to 3a. 10a (254 mg, 1 mmol) and $MgCl_2$ (60 mg, 0.625 mmol) were dissolved in DMSO (10 ml), DBU (746 μl, 5 mmol) was added, the mixture was stirred for 4 min at rt, and then quenched with saturated aq. NH_4Cl solution. After work up followed by flash chromatography **3a** was isolated (162 mg, 69%).

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