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Synthesis of 1*H*-1-alkyl-8-X-2,2-dioxoisothiazolo[5,4,3-*d,e*]-quinolines via tandem cyclization of *N*-alkyl-*N*-(2-X-5-nitrophenyl)prop-2-enyl sulfonamides

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Abstract

Tandem five- and six-membered ring closure reactions to afford tricyclic sultams from *N*-alkyl-*N*-(2-X-5-nitrophenyl) prop-2-enyl sulfonamides is described.

Keywords: allyl nitroarylsulfonamides; tandem double cyclization; intramolecular.

Recently we reported a new method of synthesis of 2-aryl or alkyl substituted 4-arylsulfonyl-quinolines from nitroarenes and allyl or cinnamyl sulfones on treatment with base and Lewis acid or silylating agent in an aprotic solvent. The reaction is considered to proceed via addition of a carbanion derived from the sulfone to the nitroarene to form a σ^H adduct, then the nitroso compound which undergoes cyclization to the final product.[1]

Now we would like to report the intramolecular version of this reaction applied to sulfonamides and leading to sultams, namely 1*H*-1-alkyl-8-X-2,2-dioxoisothiazolo[5,4,3-*de*]quinolines, which may be interesting as potentially biologically active compounds.[2]

N-Alkyl-*N*-(2-X-5-nitrophenyl) propen-3-yl sulfonamides **3** suitable for cyclization were obtained from commercial 2-X-5-nitroanilines **1** (X = H, Cl) via a sulfonylation reaction with propen-3-yl sulfonyl chloride (Py/CH_2Cl_2, –30°C to rt; 55–76%) to yield **2**, followed by the alkylation with alkyl halide (K_2CO_3/DMF/ cat. KI, rt; 70–90%). Tandem five- and six-membered ring closure was accomplished under the action of base in the presence of a catalytic amount of $MgCl_2$ in DMSO in moderate yields (Scheme 1).

Thus, 1 mmol of **2** dissolved in 10 mL of DMSO was treated with $MgCl_2$ (60 mg, 0.625 mmol) for 20 min at rt then DBU (746 μL, 5 mmol) was added and the reaction mixture was stirred at rt for approximately 24 h. Work-up, followed by column chromatography gave **4** and **5**.[3]

Other solvents were less effective in these conditions, (solvent/time/**4**[%]/**5**[%]): MeCN/30 days/6/8; Py/7 days/43/9; CH_2Cl_2/21 days/3/6; DMF/1 day/59/12).

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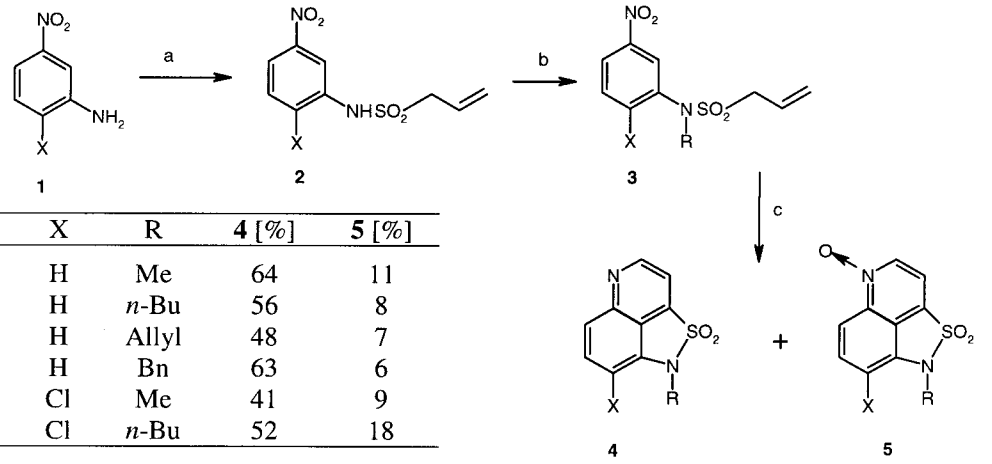
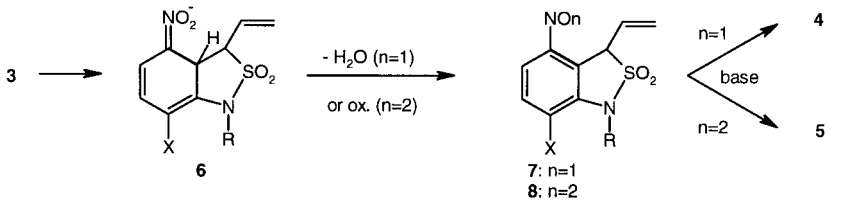


3	X	R	4 [%]	5 [%]
a	H	Me	64	11
b	H	*n*-Bu	56	8
c	H	Allyl	48	7
d	H	Bn	63	6
e	Cl	Me	41	9
f	Cl	*n*-Bu	52	18

Scheme 1. Reagents and conditions: (a) $AllylSO_2Cl$, Py, CH_2Cl_2, –30°C to rt, 3–5 h; (b) RX, K_2CO_3KI (cat.), DMF, rt, 24 h–7 days; (c) DBU, $MgCl_2$ (cat.), DMSO, rt, 24 h

Formation of products could be rationalized according to Scheme 2. Deprotonation of **3** at the position adjacent to the SO_2 group followed by the intramolecular addition to the nitroaromatic ring led to σ^H adduct **6** which is stabilized either by formal elimination of the OH^- anion[1] to form **7,** or oxidatively[4] to **8**. Further base-catalyzed intramolecular condensation[1,5] led to **4** and **5**.



Scheme 2. Possible formation of products

Acknowledgements

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References

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2. For example see: Hanson, P. R.; Probst, D. A.; Robinson, R. E.; Yau, M. A. *Tetrahedron Lett*. **1999**, *40*, 4761–4766 and references cited herein.
3. The structures of products confirmed by ^1H NMR and MS spectra, for example: **4a**: NMR ($CDCl_3$): 3.39 (s, 3H), 6.78, 7.72, 7.80 (ABX, $J_{AB}=8.8$, $J_{BX}=0.5$, $J_{AX}=7.4$, 3H), 7.81 (d, J = 4.5, 1H), 9.24 (d, J = 4.5, 1H); MS (*m*/*z*, %): 221 (12.4), 220 (100), 156 (9.9), 155 (78.9), 129 (40.6), 128 (55.3); **5a**: NMR ($CDCl_3$): 3.39 (s, 3H), 6.81 (d, J = 7.4, 1H), 7.70 (d, J = 6.4, 1H), 7.75 (dd, J = 8.9, 7.4, 1H), 7.94 (d, J = 8.9, 1H), 8.59 (d, J = 6.4, 1H); MS (*m*/*z*, %): 237 (11.1), 236 (100), 220 (26.6), 189 (35.5), 171 (8.8), 155 (17.5).
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