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Transformation of 2,2-dioxoisothiazolo[5,4,3-*d*,*e*]quinolines to pyrrolo[4,3,2-*d*,*e*]quinolin-2(1*H*)-ones

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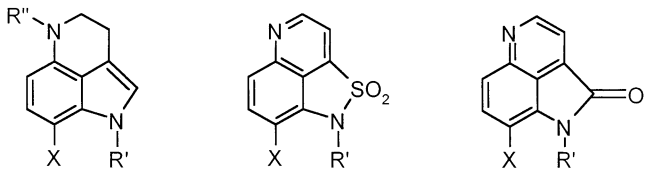
Abstract—The sulfonamide group in 1*H*-1-alkyl-8-X-2,2-dioxoisothiazolo[5,4,3-*d*,*e*]quinolines **2** undergoes substitution with cyanide anion giving after hydrolysis pyrrolo[4,3,2-*d*,*e*]quinolin-2(1*H*)-ones **3**.

Recently a considerable amount of attention has been focused on marine alkaloids having the 1,3,4,5-tetrahydropyrrolo[4,3,2-*d*,*e*]quinoline backbone **1** due to their potentialy valuable biological acivity. This class of compounds comprises vieutamine,[1] makaluvamines,[2] isobatzellines[3] and many others. Different methods of constructing the fused heterocyclic system were elaborated, starting either from an indole- or from quinoline-type substrate.



1 **2** **3**

Last year, we reported a new method for the synthesis of 1*H*-1-alkyl-8-X-2,2-dioxoisothiazolo[5,4,3-*d*,*e*]quinolines **2** structurally related to **1** by double intramolecular cyclization of *N*-alkyl-*N*-(2-X-5-nitrophenyl)pro-2-enyl sulfonamides.[4] Here, we would like to present the preliminary results on the conversion of **2** into **1**.

The desired transformation required replacing the SO_2 unit in **2** with a one carbon unit. It has previously been found that the $ArSO_2$ group in 4-arylsulfonylquinoline systems can be replaced by nucleophiles according to the S_NAr pattern.[5] We believed the same behaviour would be observes for the sulfonamide group in **2**. Cyanide anion was chosen as a one-carbon nucleophile. Thus, **2a** refluxed with tetraethylammonium cyanide (1.2 equiv.) in acetonitrile formed a very polar material which was not further investigated. After replacing MeCN with MeOH and acidification with concentrated aqueous HCl, on heating to reflux the crude mixture liberated gas and was transformed to 1-methylpyrrolo-[4,3,2-*d*,*e*]quinolin-2(1*H*)-one **3a**. Small amounts of 3-cyano-5-(*N*-methyl)aminoquinoline **8a** accompanied the formation of **3a**.

Other sultams **1** behaved similiarly giving **3** in 61–75% yield[6] (Scheme 1, Table 1).

The reaction presumably proceds via aminosulfinic acid tetraethylammonium salt intermediate **4** which after acidification loses SO_2 on heating. Similar behaviour was observed for aminosulfonic acid analogs.[7] Oxidation of **4** to sulfamic acid by air oxygen prior to loss of SO_3, also seems plausible. The liberated amine function in **5** thus formed undergoes intramolecular addition to the CN group to form imine **6** which immediately hydrolyses to **3** under the reaction conditions. Formation of **8** resulted from *cine*-substitution of sulfonamide group followed by the loss of SO_2.

Table 1.

2	X	R′	**3** (%)[a]	**8** (%)[a]
a	H	Me	75	11
b	H	*n*-Bu	72	4
c	H	Allyl	75	–
d	H	Bn	71	7
e	Cl	Me	67	7
f	MeO	Me	61	17

[a] Isolated yield.

Keywords: 2,2-dioxoisothiazolo[5,4,3-*d*,*e*]quinolines; pyrrolo[4,3,2-*d*,*e*]quinolin-2(1*H*)-ones; cyanide anion.

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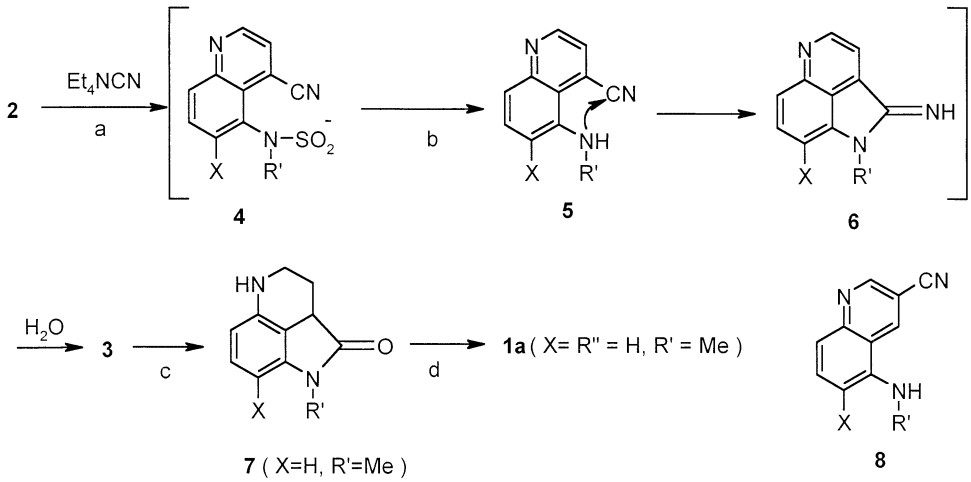

Scheme 1. *Reagents and conditions*: (a) MeCN, reflux; (b) HCl, MeOH, reflux; (c) $NaBH_4/NiCl_2$ (cat.), MeOH, rt, 69%; (d) DIBAL-H, CH_2Cl_2, 0°C, 73%.

Pyridooxindoles **3** seem to be convenient intermediates in the synthesis of pyrrolo[4,3,2-*d*,*e*]quinolines **1**. As an illustration **3a** was transformed to **7**[8] in $NaBH_4$/$NiCl_2$(cat.)/MeOH system according to the general method[9] followed by reduction of oxindole to indole with DIBAL-H/CH_2Cl_2[10] giving **1a**[8] in moderate yield.

The ^{1}H NMR spectrum of **7** exhibited complex sets of multiplets due to the presence of the proton at the bridge-head carbon. In contrast the ^{1}H NMR spectrum of **1a** appears simple: a three-proton AMX aromatic system, an indole proton at 6.56 ppm and expected signals in the aliphatic part of the spectrum.

Acknowledgements

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6. Structures of products were confirmed by MS (EI 70 eV), ^{1}H NMR ($CDCl_3$, *J* in Hz) and IR (KBr) data: Compound **3a**: $\delta=3.74$ (s, 3H), 6.92 (dd, $J=6.7$, 0.6, 1H), 7.66 (dd, $J=8.8$, 6.7, 1H), 7.75 (dd, $J=8.8$, 0.6, 1H), 7.85 (d, $J=4.4$, 1H), 9.22 (d, $J=4.4$, 1H); MS: 185 (12.5), 184 (100), 183 (39.0), 155 (16.9), 129 (7.7), 128 (18.4), 102 (5.2), 101 (7.0); IR: 1707.5 (CO); Compound **3b**: $\delta=0.98$ (t, $J=7.2$, 3H), 1.35–1.57 (m, 2H), 1.70–1.86 (m, 2H), 3.92 (t, $J=7.2$, 2H), 6.93 (d, $J=6.8$, 1H), 7.69 (dd, $J=8.8$, 6.8, 1H), 7.75 (dd, $J=8.8$, 0.5, 1H), 7.86 (d, $J=4.4$, 1H), 9.22 (d, $J=4.4$, 1H); MS: 227 (7.8), 226 (46.6), 209 (5.7), 184 (38.0), 183 (100), 170 (10.4), 156 (5.9), 153 (11.3), 128 (26.0); IR: 1713.4(CO); Compound **3c**: $\delta=4.55$ (dt, $J=5.6$, 1.6, 2H), 5.24–5.27 (m, 1H), 5.32 (ddt, $J=10.0$, 2.8, 1.4, 1H), 5.86–6.05 (m, 1H), 6.93 (d, $J=7.0$, 1H), 7.64 (dd, $J=8.7$, 7.0, 1H), 7.76 (d, $J=8.7$, 1H), 7.88 (d, $J=4.4$, 1H), 9.23 (d, $J=4.4$, 1H); MS: 211 (14.4), 210 (100), 209 (28.9), 193 (13.0), 184 (5.3), 183 (28.6), 182 (8.0), 181 (22.3), 156 (4.4), 155 (10.0), 128 (19.4); Compound **3d**: $\delta=5.11$ (s, 2H), 6.79 (d, $J=7.0$, 1H), 7.29–7.40 (m, 5H), 7.56 (dd, $J=8.7$, 7.0, 1H), 7.73 (d, $J=8.7$, 1H), 7.91 (d, $J=4.4$, 1H), 9.24 (d, $J=4.4$, 1H); MS: 261 (10.3), 260 (55.0), 259 (4.8), 92 (7.3), 91 (100); Compound **3e**: $\delta=3.71$ (s, 3H), 7.53 (d, $J=9.0$, 1H), 7.70 (d, $J=9.0$, 1H), 7.89 (d, $J=4.4$, 1H), 9.20 (d, $J=4.4$, 1H); MS: 220 (18.0), 219 (14.1), 218 (51.4), 217 (22.5), 192 (10.7), 167 (18.4), 153 (28.7), 149 (42.1); Compound **3f**: mp 153–155°C, lit.[11] mp 151–153°C; $\delta=3.65$ (s, 3H), 4.04 (s, 3H), 7.47 (d, $J=9.3$, 1H), 7.80 (d, $J=9.3$, 1H), 7.88 (d, $J=4.4$, 1H), 9.11 (d, $J=4.4$ 1H); MS: 215 (14.1), 214 (100), 200 (12.6), 199 (99.7), 171 (16.2), 144 (8.9); Compound **8a**: $\delta=3.04$ (s, 3H), 4.67 (broad s, 1H), 6.70 (d, $J=7.8$, 1H), 7.48 (dt, $J=8.4$, 0.9, 1H), 7.74 (dd, $J=8.4$, 7.8, 1H), 8.53 (dd, $J=2.0$, 0.9, 1H), 8.97 (d, $J=2.0$, 1H); MS: 184 (13.6), 183 (100), 182 (67.6), 181 (18.0), 168 (4.2), 156 (4.4), 155 (25.8), 154 (14.5), 153 (12.2), 141 (11.5), 114 (10.9); IR: 2224.3 (CN); Compound **8b**: $\delta=$ 1.03 (t, $J=7.2$, 3H), 1.44–1.66 (m, 2H), 1.70–1.86 (m, 2H), 3.24–3.34 (m, 2H), 4.48 (br s, 1H), 6.71 (d, $J=8.0$, 1H), 7.46 (d, $J=8.4$, 1H), 7.72 (app t, $J=8.2$, 1H), 8.54 (dd, $J=2.0$, 1.0, 1H), 8.96 (d, $J=2.0$, 1H): MS: 226 (6.6), 225 (39.9), 183 (16.8), 182 (100), 181 (18.6), 155 (21.7), 126 (8.5); IR: 2225.7 (CN); Compound **8d**: $\delta=4.50$ (d, $J=5.1$, 1H), 4.90 (broad s, 1H), 6.74 (d, $J=7.9$, 1H), 7.30–7.45 (m, 5H), 7.50 (dt, $J=8.4$, 0.9, 1H), 7.7 (dd, $J=8.4$, 7.9, 1H), 8.56 (dd, $J=2.0$, 0.8, 1H), 8.96 (d,

$J=2.0$, 1H); MS: 260 (19.3), 259 (100), 258 (3.6), 153 (5.4); IR: 2225.6 (CN); Compound **8e**: $\delta=3.12$ (s, 3H), 4.30 (broad s, 1H), 7.68 (dd, $J=9.0$, 0.8, 1H), 7.78 (d, $J=9.0$, 1H), 8.85 (dd, $J=2.0$, 0.8, 1H), 8.98 (d, $J=2.0$, 1H); MS: 219 (32.0), 218 (27.9), 217 (100), 216 (46.4), 202 (5.8), 189 (9.3), 182 (15.8), 181 (32.4), 180 (7.7), 177 (7.5), 175 (22.9), 153 (14.9); IR: 2229.8 (CN); Compound **8f**: $\delta=3.04$ (s, 3H), 4.00 (s, 3H), 4.20–4.50 (s, 1H), 7.57 (d, $J=9.1$, 1H), 7.75 (dd, $J=9.1$, 0.7, 1H), 8.81 (dd, $J=2.0$, 0.7, 1H), 8.84 (d, $J=2.0$, 1H); MS: 214 (11.8), 213 (80.0), 199 (12.4), 198 (100), 197 (5.6), 172 (8.22), 171 (80.0), 154 (7.3), 153 (22.4); IR: 2222.5 (CN).

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