New products from the reactions of 4,5-dihydroxyimidazolidin-2-ones with sulfonamides

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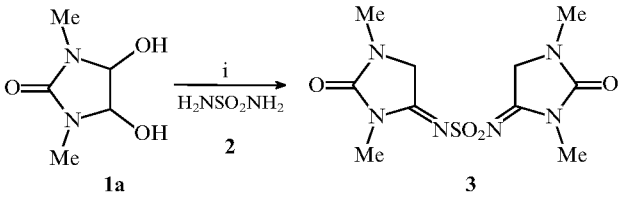
For the first time the interactions of *N*-alkyl- and *N,N′*-dialkyl-4,5-dihydroxyimidazolidin-2-ones with sulfonamides have been studied and as a result *N*-alkyl- and *N,N′*-dialkyl-4(5)-aryl(alkyl)sulfonyliminoimidazolidin-2-ones and 4,4′-sulfonyldiiminobis(*N,N′*-dimethylimidazolidin-2-one) have been synthesized.

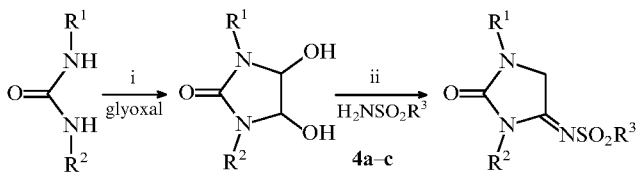
It is known that sulfonamide derivatives exhibit a wide range of pharmacological activity, including anticonvulsant,[1] antiulcer,[2] diuretic, antiinflammatory[3] activity and other properties. To find new potentially biologically active compounds the interaction of 4,5-dihydroxyimidazolidin-2-ones with sulfonamides has been studied. The previously unreported compounds 4(5)-aryl(alkyl)sulfonyliminoimidazo-lidin-2-ones and 4,4′-sulfonyldiiminobis(*N,N′*-dimethylimidazolidin-2-one) were obtained.

Similar compounds have been prepared by the reaction of sulfonamides and ureas with lactam acetals.[3] 4,5-Dihydroxyimidazolidin-2-ones are known to react with ureas to give 2,4,6,8-tetraazabicyclo[3.3.0]octane-3,7-diones.[4] We have established that the interaction of *N,N′*-dimethyl-4,5-dihydroxyimidazolidin-2-one **1a**, prepared according to the literature,[5] with sulfonamide **2** leads to the formation of 4,4′-sulfonyldiiminobis(*N,N′*-dimethylimidazolidin-2-one) **3** (Scheme 1).



Scheme 1 *Reagents and conditions:* i, H_2O, dil. HCl, 80–90 °C, 1 h.

The reaction found was extended to several 4,5-dihydroxyimidazolidin-2-ones **1** and sulfonamides **4**. The reactions of **1a–d** with aryl- and alkylsulfonamides **4a–c** proceeded in analogous fashion to give 4(5)-aryl(alkyl)sulfonylimino-imidazolidin-2-ones **5a–g** (Scheme 2). In turn **1b–d** were prepared under similar conditions to those employed with **1a**.[5]



1a–d

R^1, R^2 = H, Me, Et

a $R^1 = R^2 = Me$
b $R^1 = R^2 = Et$
c $R^1 = H$, $R^2 = Me$
d $R^1 = H$, $R^2 = Et$

4a–c

a $R^3 = Ph$
b $R^3 = C_6H_4Me\text{-}p$
c $R^3 = Me$

5a–g

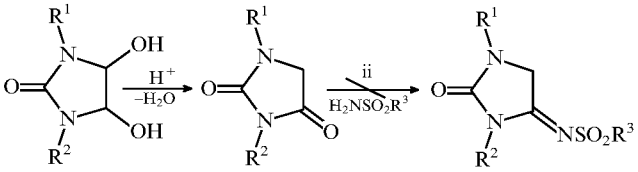
a $R^1 = R^2 = Me$, $R^3 = Ph$
b $R^1 = R^2 = Me$, $R^3 = C_6H_4Me\text{-}p$
c $R^1 = R^2 = Et$, $R^3 = Ph$
d $R^1 = R^2 = Et$, $R^3 = C_6H_4Me\text{-}p$
e $R^1 = H$, $R^2 = Me$, $R^3 = C_6H_4Me\text{-}p$
f $R^1 = H$, $R^2 = Et$, $R^3 = C_6H_4Me\text{-}p$
g $R^1 = R^2 = R^3 = Me$

Scheme 2 *Reagents and conditions*: i, H_2O, pH 4–7, 45–50 °C, 2–7 h; ii, MeOH, conc. HCl, 70 °C, 0.5 h.

The unsymmetrical products **1c,d** were further reacted with sulfonamide without isolation.

The mechanism of formation of **3** and **5** is of special interest as such reactions have not been described in the literature.

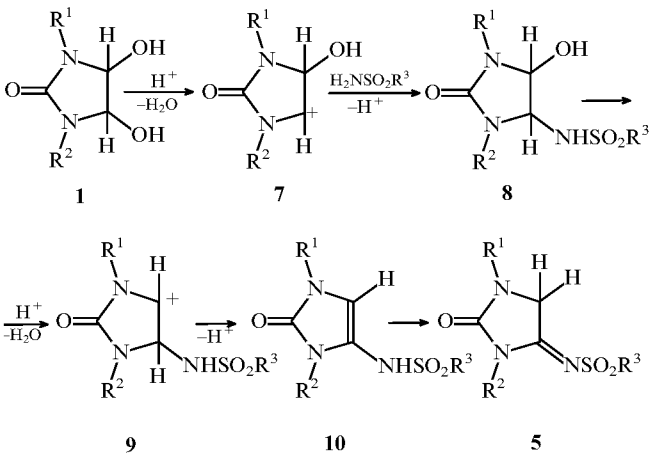
It is known that **1a–d** are converted into the corresponding 2,4-dioxoimidazolidines **6** in an acid medium[4] (Scheme 3).



Scheme 3 *Reagents and conditions:* ii, MeOH, conc. HCl, 70 °C, 2 h.

In fact, compounds **1a–d** are converted into the corresponding products **6** under the present reaction conditions in the absence of sulfonamide. However, sulfonamides react very quickly with **1** and thus **6** is not formed. This is confirmed by TLC data. It has been also shown that **5** is not obtained *via* **6** (Scheme 3).

On the basis of the data obtained we propose the following mechanism for the reactions of **1** with **2** and **4** (Scheme 4).



Scheme 4

The carbocation **7** formed as result of dehydration of **1** is not deprotonated in an enol/keto system but rather it is condensed with the sulfonamide to give **8** which undergoes rapid dehydration to give the carbocation **9**. If **9** were further attacked by the amino group of sulfonamide then the sulfoanalogues of 2,4,6,8-tetraazabicyclo[3.3.0]octane-3,7-dione[4] or 4,5-disulfonamidoimidazolidin-2-ones would be formed. However, in this case **9** is deprotonated to give imine **5** (the dimer of which is **3**).

The structures of **3** and **5** were confirmed by elemental

analyses and ^1H, ^{13}C NMR-, IR- and mass-spectra.†

Separately, we obtained data for *N*-alkyl-5-arylsulfonyliminoimidazolidin-2-ones which enabled us to confirm the structures of the products **5e**,**f** (Scheme 2).

The signals of CH_2 ring protons in **5e** and **5f** ^1H NMR spectra are split into doublets with a coupling constant 1.2 Hz by three-bond HN–CH_2 spin–spin coupling. This splitting was not observed in a double resonance experiment with irradiation of the broad NH signal. This data confirms the above structures of compounds **5e** and **5f** (Scheme 2).

† NMR spectra were registrated on a Bruker AM 300 spectrometer at 300.13 MHz (^1H) and 75.47 MHz (^{13}C). Chemical shifts were measured relative to solvents: acetone 2.05 ppm (^1H), 30.0 ppm (^{13}C); chloroform 7.27 ppm (^1H), 77.0 ppm (^{13}C).
All new compounds gave satisfactory elemental analysis data.

3: yield 45%; mp 269–271 °C, R_f 0.27 ($Me_2CO/CHCl_3$ 1:3); *m*/*z* 316 (M^+); IR (KBr) ν/cm^{-1}: 2924 (CH), 1742 (C=O), 1308, 1286, 1136, 1120 (SO_2); ^1H NMR ($CDCl_3$, ppm) δ: 2.88 (s, 6H, NCH_3), 2.95 (s, 6H, NCH_3), 4.50 (s, 4H, CH_2).

5a: yield 82%; mp 125–127 °C, R_f 0.70 ($Me_2CO/CHCl_3$ 1:3); *m*/*z* 267 (M^+); IR (KBr) ν/cm^{-1}: 2980, 2940, 2880 (CH), 1760 (C=O), 1640 (C=N), 1310, 1290, 1145 (SO_2); ^1H NMR ([$^2H_6$]acetone, ppm) δ: 3.00 (s, 6H, Me), 4.65 (s, 2H, CH_2), 7.6 (m, 3H, *m*+*p*-Ph), 7.95 (m, 2H, *o*-Ph); ^{13}C NMR ([$^2H_6$] acetone) δ: 27.3 (NMe), 30.1 (NMe), 52.3 (CH_2), 127.5 (CH–Ph), 129.9 (CH–Ph), 133.4 (CH–Ph), 143.5 (C–Ph), 167.2 (C=O).

5b: yield 83%; mp 196–198 °C, R_f 0.75 ($Me_2CO/CHCl_3$ 1:3), *m*/*z* 281 (M^+); IR (KBr) ν/cm^{-1}: 2930 (CH), 1765 (C=O), 1640 (C=N), 1290, 1270, 1145 (SO_2); ^1H NMR ([$^2H_6$] acetone, ppm) δ: 2.40 (s, 3H, Me–Ph), 2.96 (s, 3H, NMe), 2.97 (s, 3H, NMe), 4.62 (s, 2H, CH_2), 7.37 (m, 2H, *m*-Ph), 7.80 (m, 2H, *o*-Ph); ^{13}C NMR ([$^2H_6$]acetone) δ: 21.6 (CH_3–Ph), 27.2 (NMe), 30.0 (NMe), 52.3 (CH_2), 127.2 (CH–Ph), 127.7 (CH–Ph), 130.4 (CH–Ph), 144.2 (C–Ph).

5c: yield 81%; mp 61–63 °C, R_f 0.80 ($Me_2CO/CHCl_3$ 1:3), *m*/*z* 295 (M^+); IR (KBr) ν/cm^{-1}: 3070, 2990, 2950 (CH), 1750 (C=O), 1615 (C=N), 1340, 1310, 1250, 1160 (SO_2); ^1H NMR ([$^2H_6$]acetone, ppm) δ: 1.06 (t, 3H, Me), 1.20 (t, 3H, Me), 3.45 (q, 2H, CH_2), 3.57 (q, 2H, CH_2), 4.67 (s, 2H, CH_2), 7.60 (m, 3H, *m*+*p*-Ph), 7.95 (d, 2H, *o*-Ph); ^{13}C NMR ([$^2H_6$] acetone) δ: 12.9 (Me), 13.3 (Me), 36.3 (CH_2), 38.4 (CH_2), 49.9 (CH_2), 127.4 (CH–Ph), 129.9 (CH–Ph), 133.4 (CH–Ph), 143.4 (C–Ph), 155.2 (C=N), 166.7 (C=O).

5d: yield 93%; mp 98–99 °C, R_f 0.84 ($Me_2CO/CHCl_3$ 1:3), *m*/*z* 309 (M^+); IR (KBr) ν/cm^{-1}: 2980, 2960 (CH), 1760 (C=O), 1615 (C=N), 1350, 1290, 1150 (SO_2); ^1H NMR ([$^2H_6$] acetone, ppm) δ: 1.07 (t, 3H, Me), 1.21 (t, 3H, Me), 2.41 (s, 3H, Me-Ph), 3.45 (q, 2H, CH_2), 3.57 (q, 2H, CH_2), 4.65 (s, 2H, CH_2), 7.38 (d, 2H, *m*-Ph), 7.82 (d, 2H, *o*-Ph); ^{13}C NMR ([$^2H_6$] acetone) δ: 12.9 (Me), 13.3 (Me), 21.6 (Me–Ph), 36.2 (CH_2), 38.4 (CH_2), 49.7 (CH_2), 127.5 (CH–Ph), 130.4 (CH–Ph), 140.7 (C–Ph), 144.1 (C–Ph), 155.2 (C=N), 166.4 (C=O).

5e: yield 16%; mp 179–182 °C, R_f 0.46 ($Me_2CO/CHCl_3$ 1:3), *m*/*z* 267 (M^+); IR (KBr) ν/cm^{-1}: 3290 (NH), 2980, 2960, 2840 (CH), 1760 (C=O), 1615 (C=N), 1355, 1290, 1155 (SO_2); ^1H NMR ([$^2H_6$] acetone, ppm) δ: 2.40 (s, 3H, Me–Ph), 2.97 (s, 6H, NMe), 4.63 (d, 2H, CH_2), 7.38 (d, 2H, *m*-Ph), 7.4 (s, 1H, NH), 7.82 (m, 2H, *o*-Ph); ^{13}C NMR ([$^2H_6$]acetone) δ: 21.6 (Me–Ph), 26.8 (NMe), 46.9 (CH_2), 127.6 (CH–Ph), 130.4 (CH–Ph) 140.7 (C–Ph), 144.2 (C–Ph), 157.2 (C=N), 168.7 (C=O).

5f: yield 15%; mp 193–195 °C, R_f 0.57 ($Me_2CO/CHCl_3$ 1:3), *m*/*z* 281 (M^+); IR (KBr) ν/cm^{-1}: 3260 (NH), 2980, 2960 (CH), 1760 (C=O), 1610 (C=N), 1370, 1290, 1155 (SO_2); ^1H NMR ([$^2H_6$]acetone, ppm) δ: 1.10 (t, 3H, Me), 2.40 (s, 3H, Me–Ph), 3.57 (q, 2H, CH_2), 4.63 (d, 2H, CH_2), 7.38 (d, 2H, Ph), 7.4 (s, 1H, NH), 7.82 (d, 2H, Ph); ^{13}C NMR ([$^2H_6$]acetone) δ: 12.9 (Me), 21.5 (Me–Ph), 35.9 (CH_2), 46.8 (CH_2), 127.5 (CH–Ph), 130.4 (CH–Ph).

5g: yield 50%; mp 139–141 °C, R_f 0.55 ($Me_2CO/CHCl_3$ 1:3), *m*/*z* 205 (M^+), IR (KBr) ν/cm^{-1}: 2980, 2935 (CH), 1770 (C=O), 1605 (C=N), 1340, 1290, 1140 (SO_2); ^1H NMR ($CDCl_3$, ppm) δ: 3.00 (s, 3H, S–Me), 3.07 (s, 3H, N–Me), 3.08 (s, 3H, N–Me), 4.53 (s, 2H, CH_2).

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