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

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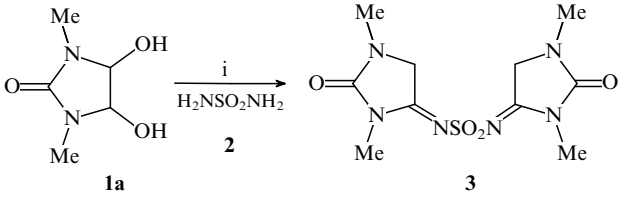
**For the first time the interactions of *N*-alkyl- and *N,N′*-dialkyl-4,5-dihydroxyimidazolidin-2-ones with sulfonamides have been studied and as a result *N*-alkyl- and *N,N′*-dialkyl-4(5)-aryl(alkyl)sulfonyliminoimidazolidin-2-ones and 4,4′-sulfonyldiiminobis(*N,N′*-dimethylimidazolidin-2-one) have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

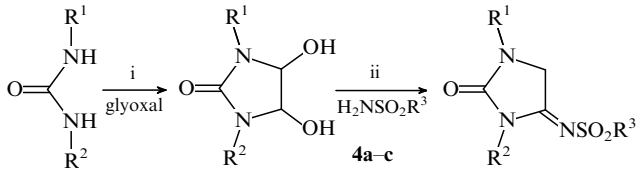
It is known that sulfonamide derivatives exhibit a wide range of pharmacological activity, including anticonvulsant,[1] antiulcer,[2] diuretic, antiinflammatory[3] activity and other properties. To find new potentially biologically active compounds the interaction of 4,5-dihydroxyimidazolidin-2-ones 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**

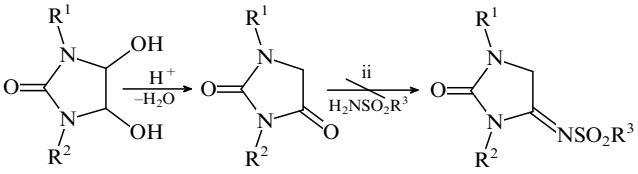
**a** $R^1 = R^2 = Me$, $R^3 = Ph$
**b** $R^1 = R^2 = Me$, $R^3 = C_6H_4Me\text{-}p$
**c** $R^1 = R^2 = Et$, $R^3 = Ph$
**d** $R^1 = R^2 = Et$, $R^3 = C_6H_4Me\text{-}p$
**e** $R^1 = H$, $R^2 = Me$, $R^3 = C_6H_4Me\text{-}p$
**f** $R^1 = H$, $R^2 = Et$, $R^3 = C_6H_4Me\text{-}p$
**g** $R^1 = R^2 = R^3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

**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.

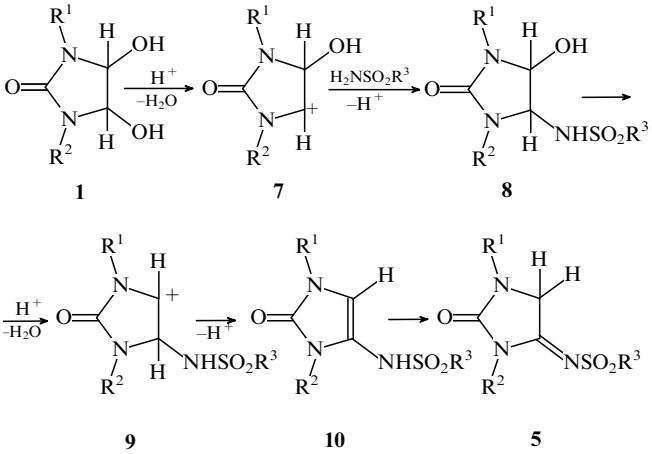
It is known that **1a–d** are converted into the corresponding 2,4-dioxoimidazolidines **6** in an acid medium[4] (Scheme 3).



**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-arylsulfonyl-iminoimidazolidin-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) $\nu$/cm$^{-1}$: 2924 (CH), 1742 (C=O), 1308, 1286, 1136, 1120 ($SO_2$); $^1H$ NMR ($CDCl_3$, ppm) $\delta$: 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) $\nu$/cm$^{-1}$: 2980, 2940, 2880 (CH), 1760 (C=O), 1640 (C=N), 1310, 1290, 1145 ($SO_2$); $^1H$ NMR ([$^2H_6$]acetone, ppm) $\delta$: 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) $\delta$: 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) $\nu$/cm$^{-1}$: 2930 (CH), 1765 (C=O), 1640 (C=N), 1290, 1270, 1145 ($SO_2$); $^1H$ NMR ([$^2H_6$] acetone, ppm) $\delta$: 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) $\delta$: 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) $\nu$/cm$^{-1}$: 3070, 2990, 2950 (CH), 1750 (C=O), 1615 (C=N), 1340, 1310, 1250, 1160 ($SO_2$); $^1H$ NMR ([$^2H_6$]acetone, ppm) $\delta$: 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) $\delta$: 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) $\nu$/cm$^{-1}$: 2980, 2960 (CH), 1760 (C=O), 1615 (C=N), 1350, 1290, 1150 ($SO_2$); $^1H$ NMR ([$^2H_6$] acetone, ppm) $\delta$: 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) $\delta$: 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) $\nu$/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) $\delta$: 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) $\delta$: 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) $\nu$/cm$^{-1}$: 3260 (NH), 2980, 2960 (CH), 1760 (C=O), 1610 (C=N), 1370, 1290, 1155 ($SO_2$); $^1H$ NMR ([$^2H_6$]acetone, ppm) $\delta$: 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) $\delta$: 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) $\nu$/cm$^{-1}$: 2980, 2935 (CH), 1770 (C=O), 1605 (C=N), 1340, 1290, 1140 ($SO_2$); $^1H$ NMR ($CDCl_3$, ppm) $\delta$: 3.00 (s, 3H, S–Me), 3.07 (s, 3H, N–Me), 3.08 (s, 3H, N–Me), 4.53 (s, 2H, $CH_2$).

## References


1 P. Aeberli, J. Gogerty and W. J. Houlihan, *J. Med. Chem.*, 1967, **10**, 636.
2 I. Yanagisawa, Y. Hirata and Y. Ishii, *J. Med. Chem.*, 1987, **30**, 1787.
3 P. Ahuja, J. Singh, M. B. Asthana, V. Sardana and N. Anand, *Indian J. Chem., Sect. B,* 1989, **28**, 1034.
4 H. Petersen, *Synthesis*, 1973, 243.
5 S. L. Vail, R. H. Barker and P. G. Mennitt, *J. Org. Chem.,* 1965, **30**, 2179.



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