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THE UNEXPECTED SYNTHESIS OF 2-THIOXO-1-IMIDAZOLIDINECARBOXAMIDES FROM 2-OXO-1-IMIDAZOLIDINETHIOCARBONYL CHLORIDE

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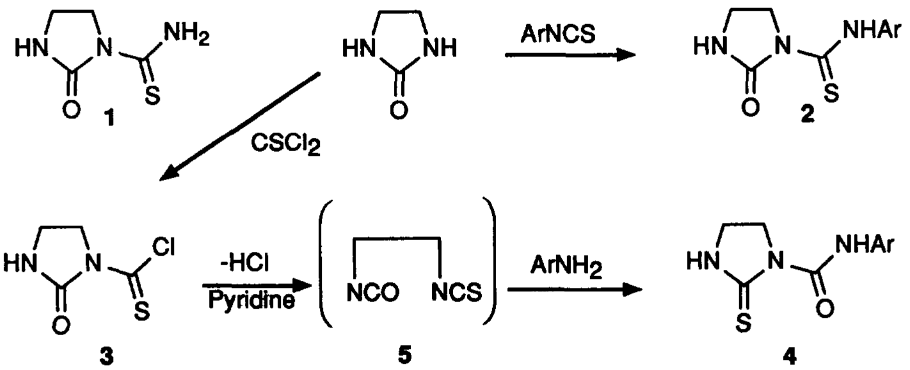
Abstract: *The reaction of 2-oxo-1-imidazolidinethiocarbonyl chloride with aromatic amines gives N-aryl-2-thioxo-1-imidazolidinecarboxamides. This finding is consistent with an ethylene isocyanate isothiocyanate intermediate.*

During our recent involvement in a project based on the immunoregulator NIF **1**,[1] we had need to prepare several N-aryl-2-oxo-1-imidazolidinethiocarboxamides **2**. The majority of these compounds were available by reacting 2-oxoimidazolidine with aryl isothiocyanates;[2] however, in cases where the necessary aryl isothiocyanates were unavailable, an alternate synthesis was required. A method utilizing 2-oxo-1-imidazolidinethiocarbonyl chloride **3** seemed reasonable, since the preparation of **3** from thiophosgene and 2-oxoimidazolidine, and the reaction of **3** with amines has been reported to give N-substituted-2-oxo-1-imidazolidinethiocarboxamides.[2,3] In our hands this procedure did not give products **2**, but instead the isomeric N-aryl-2-thioxo-1-imidazolidinecarboxamides **4** (Scheme I).

Scheme I.

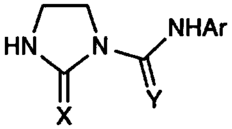


Our initial attempt to react **3** with aniline in pyridine gave only **4a**, which had an IR spectrum that was identical to an authentic sample of **4a** prepared from 2-thioxoimidazolidine and phenyl isocyanate.[4] A sample of **2a** prepared from 2-oxoimidazolidine and phenyl isothiocyanate (Table I) had an IR $\nu_{C=O}$50 cm^{-1} higher than **4a** (Table I). Three other examples of **4** were prepared from **3** and are listed in Table I.

We believe that the structural integrity of **3** is retained until it is treated with base whereupon elimination of HCl gives intermediate **5**. Evidence for **3** is found in the mass spectrum, M$^+$ = 164 and M$^+$- HCl = 128, and the IR $\nu_{C=O}$ absorption at 1740 cm^{-1}. Also, the IR of crude **5**, isolated from the reaction of **3** with sodium tert. butoxide in THF, showed what appear to be N=C=S and N=C=O absorptions at 2110 and 2200 cm^{-1}. The reaction of aromatic amines with **5** takes place at the more reactive isocyanate[5] followed by intramolecular ring closure to **4**.

The preparation of **4a** is exemplary of this general method for synthesizing **4**. Aniline (186 mg, 20 mmoles) was added in one portion to a stirred solution of 3[3] (330 mg, 20 mmoles) in 10 ml pyridine. Stirring at ambient temperature was continued 16 hrs. Analysis of the reaction mixture by tlc (SiO_2, eluted with isopropanol:chloroform, 1:19) showed no **2a** ($R_f = 0.48$), only **4a** ($R_f = 0.42$). The reaction mixture was cooled to 5° C and 20 ml of water was added dropwise. The resulting precipitate was collected, dried, and recrystallized from dioxane/hexane giving 250 mg (57%) of **4a**, mp 200-201°C (lit.[4] mp 202-203°C).

TABLE I: Comparison of N-Phenyl-2-oxo-1-imidazolidinethiocarboxamides with the reaction products of 2-Oxo-1-imidazolidinethiocarbonyl Chloride and Aromatic Amines



cmpd	X	Y	Ar	mp, °C	IR($\nu_{C=O}$, cm^{-1})[a]	% yield	formula[b]
2a	O	S	Ph	177-179	1720	55	$C_{10}H_{11}N_3OS$
4a	S	O	Ph	200-201[c]	1670	57	
4b	S	O	2-pyridinyl	230-232	1670	27	$C_9H_{10}N_4OS$
4c	S	O	2-thiazolyl	235-236	1690	22	$C_7H_8N_4OS_2$
4d	S	O	2-benzothiazolyl	256-258	1675	38	$C_{11}H_{10}N_4OS_2$

[a] The infrared spectra were run as KBr pellets. [b] All new compounds gave satisfactory C, H, N, analyses (±0.4 %). [c] Lit.[4] mp 202-203°C.

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