

SYNTHESIS OF TOSYL-SUBSTITUTED IMIDAZOLES FROM  
TOSYLMETHYLISOCYANIDE AND IMIDOYL CHLORIDES

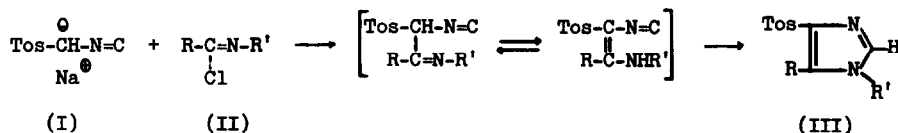
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Tosylmethylisocyanide (TosMIC) is of considerable utility in the synthesis of various heterocycles. In the preceding paper the preparation of a number of oxazoles was discussed.<sup>1</sup> These results now are extended to a new synthetic approach to imidazoles. Imidoyl chlorides (II), which are readily available<sup>2</sup>, are converted in high yield into 4-tosylimidazoles (III), by the use of the sodium derivative of TosMIC (I).

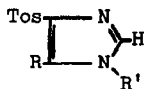


The reaction is most conveniently performed as follows. A 1:1 mixture of TosMIC and an imidoyl chloride (II) in dry dimethoxyethane or THF<sup>3</sup> is added dropwise to a stirred suspension of 1 equiv. of NaH in dry DMSO<sup>3</sup> (at 20° under N<sub>2</sub>). After stirring for one hour, the product is obtained upon dilution with water and is crystallized from 80% methanol. The spectral data and elemental analyses support structure III for the products listed in the Table.

Imidoyl chlorides in general are highly reactive towards nucleophiles.<sup>4,5</sup> Even so, there are dramatic differences in the rates of hydrolysis within this group, depending on the nature of the substituents R and R'. It is, therefore, not surprising that using IIIf (R=t-butyl, R'=cyclohexyl), which is known to have an extremely fast rate of hydrolysis<sup>4</sup>, no imidazole IIIIf was obtained. Instead, IIIf was converted into the corresponding amide (t-BuCONHc-Hex, IV),

most likely by reaction with traces of water present in the solvents, despite considerable precautions to work under dry conditions. The formation of amide IV from II<sub>f</sub> could be explained alternatively by a process in which the oxygen of DMSO is involved. This possibility, however, was excluded, as will be discussed in the full paper on this subject.

T A B L E



|                  | R                                               | R'                                              | m.p. °C     | % yield | IR (cm <sup>-1</sup> ) |
|------------------|-------------------------------------------------|-------------------------------------------------|-------------|---------|------------------------|
| IIIa             | C <sub>6</sub> H <sub>5</sub>                   | C <sub>6</sub> H <sub>5</sub>                   | 188.5-189.0 | 60      | 3110, 1600             |
| IIIb             | C <sub>6</sub> H <sub>5</sub>                   | p-O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> | 231.5-232.0 | 85      | 3120, 1620             |
| IIIc             | p-O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> | C <sub>6</sub> H <sub>5</sub>                   | 240.0-240.5 | 88      | 3110, 1610             |
| IIId             | C <sub>6</sub> H <sub>5</sub>                   | c-C <sub>6</sub> H <sub>11</sub>                | 215.0-215.5 | 80      | 3120, 1600             |
| IIIe             | p-O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> | c-C <sub>6</sub> H <sub>11</sub>                | 264.5-265.5 | 75      | 3110, 1610             |
| III <sub>f</sub> | t-C <sub>4</sub> H <sub>9</sub>                 | c-C <sub>6</sub> H <sub>11</sub>                | -           | --      | - -                    |

#### Acknowledgement.

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#### REFERENCES

1. This letter is considered Part 3 of Chemistry of Sulfonylmethylisocyanides. For part 1 and 2, see the immediately preceding papers.
2. F. Cramer and U. Baer, Chem. Ber. **93**, 1231 (1960).
3. The solvents are distilled from Na (dimethoxyethane) and LiAlH<sub>4</sub> (THF). Anhydrous DMSO (MCB) was stored over mol. sieves (Linde 4A).
4. I. Ugi, F. Beck and U. Fetzer, Chem. Ber. **95**, 126 (1962).
5. R.J. Morath and G.W. Stacy in The Chemistry of the Carbon-Nitrogen Double Bond, S. Patai (ed.) Interscience London 1970, p. 327.