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PREPARATION OF THIOMETHYLISOCYANIDES AND THEIR USE IN HETEROCYCLIC SYNTHESES.

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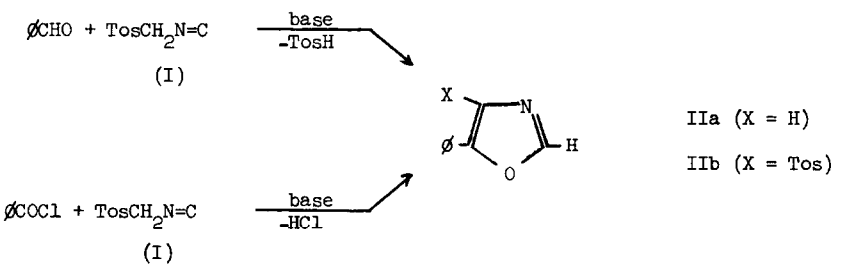
Sulfonylmethylisocyanides are valuable synthetic intermediates. At the moment especially tosylmethylisocyanide (TosMIC, p-$CH_3C_6H_4SO_2CH_2N{=}C$, I) is under investigation.[1] Its methylene group is convertible into a carbanion under a variety of experimental conditions, providing a reactive species with both a nucleophilic and an electrophilic centre (i.e. the carbanion and the isocyanide carbon, respectively). Employing this property, many different heterocycles have been synthesized[2] by addition of TosMIC (I) to unsaturated systems, e.g.[3]



IIa (X = H)

IIb (X = Tos)

For comparative purposes, thiomethylisocyanides, $RSCH_2N{=}C$ (IV), are of special interest. Their more strongly nucleophilic carbanions suggest that the synthesis of additional heterocycles should be possible by this method. Also, in products comparable with IIb, the substituent X = RS should be removable more readily by reductive desulfurisation.

Despite a recent negative report,[4] we were able to synthesize a series of thiomethylisocyanides[5] (IV) by dehydration of the appropriate formamides[6] III.

$$RSCH_2\overset{\overset{O}{\|}}{N}HCH \quad \xrightarrow[(CH_3OCH_2)_2,\ Et_3N]{POCl_3,\ 20^\circ \text{ to } 50^\circ C} \quad RSCH_2N=C \qquad (IV)$$

(III)

IVa R = p-tolyl; bp. 60°C/ ca. 0.001 mm; 53%

IVb R = benzyl ; bp. 64°C/ ca. 0.001 mm; mp. 27-28°C; 37%

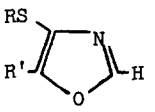
IVc R = n-butyl; bp. 55°C/ 0.8 mm; 32%

IVd R = t-butyl; bp. 41°C/ 0.5 mm; 40%

All compounds IV show a characteristic isocyanide band at 2140 (± 5) cm^{-1} (neat).

α-Lithio p-tolylthiomethylisocyanide (V) (from IVa and n-Buli in THF at -70°C) reacts with acetic anhydride at temperatures rising from -70° to 20°C (in 2 hr) to give 5-methyl-4-p-tolylthio-oxazole (VIa) in ca. 30% yield.

$$RS\text{-}\underset{\text{Li}}{\underset{|}{CH}}\text{-}N=C \ (V) \ + \ CH_3\overset{\overset{O}{\|}}{C}O\overset{\overset{O}{\|}}{C}CH_3 \quad \xrightarrow[-70^\circ \text{ to } 20^\circ C]{THF} \quad RS\text{-}CH(CH_3\text{-}\overset{\overset{O}{\|}}{C})\text{-}N=C \longrightarrow$$



R = p-tolyl VIa $R^1 = CH_3$

VIb $R^1 = o\text{-}C_6H_4COOH$

Similarly, 5-o-carboxyphenyl-4-p-tolylthio-oxazole (VIb) was obtained in 30% yield, mp. 149-150° C using phthalic anhydride instead of acetic anhydride.

The structures of all new compounds (IV and VI) are fully supported by elemental microanalyses and spectral data (IR, NMR and MS).

NOTES AND REFERENCES

1. a) See: A.M. van Leusen, H. Siderius, B.E. Hoogenboom and Daan van Leusen, Tetrahedron Letters 1972, in press, and previous papers; also ref. 5, and previous papers.
2. See ref. 1; O.H. Oldenziel and A.M. van Leusen, Synth. Comm., 1972, 281; U. Schöllkopf, R. Schröder and E. Blume, Liebigs Ann. Chem., in press; U. Schöllkopf and R. Schröder, Angew. Chem., 83, 358 (1971).
3. A.M. van Leusen, B.E. Hoogenboom and H. Siderius, Tetrahedron Letters 1972, 2369.
4. H. Böhme and G. Fuchs, Chem. Ber., 103, 2775 (1970).
5. The same type of compounds was synthesized independently by Schöllkopf et.al.(private communication). We acknowledge Prof. Schöllkopf's agreement to publish these results simultaneously, see U. Schöllkopf and E. Blume accompanying letter.
6. A.M. van Leusen, G.J.M. Boerma, R.B. Helmholdt, H. Siderius and J. Strating, Tetrahedron Letters 1972, 2367.