Tetrahedron Letters No. 2, pp 143 - 146, 1976. Pergamon Press. Printed in Great Britain.

PREPARATION OF N-TOSYLMETHYLIMINO COMPOUNDS AND THEIR USE IN THE SYNTHESIS OF OXAZOLES, IMIDAZOLES AND PYRROLES

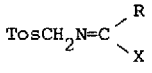
H A Houwing, J Wildeman and A M. van Leusen*

Department of Organic Chemistry, The University,

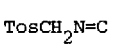
Zernikelaan, Groningen, The Netherlands

(Received in UK 14 November 1975; accepted for publication 27 November 1975)

We herein wish to describe the preparation and synthetic applications of a series of N-tosylmethylimino compounds of type 1

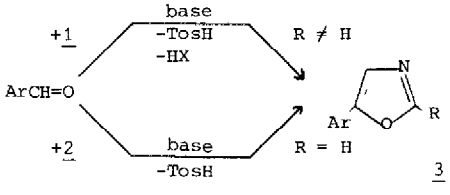


1 X = SMe, OMe, Cl, R see Table II



2

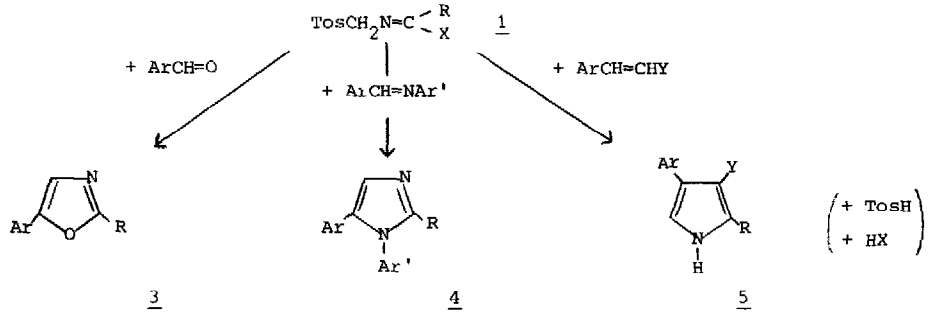
Recently, it was shown in our laboratory that tosylmethyl isocyanide (TosMIC, 2) can be used successfully to cycloadd a CH-N=CH fragment to unsaturated substrates [1] This process, involving an addition-cyclisation of TosMIC-anion ($TosCH\overset{\ominus}{N}-C$) and concomitant loss of $Tos^{\ominus}$, for example converts aldehydes to oxazoles [2] Thus, the isocyano carbon of 2 ends up in the, by necessity, unsubstituted 2-position of oxazole 3 (R = H) By using imines of type 1, instead of TosMIC (2), 2-substituted oxazoles 3 (R ≠ H) are expected in a related process



3

We here illustrate the synthetic potentialities of N-tosylmethylimino derivates (1) in the synthesis of a number of oxazoles 3, imidazoles 4 and pyrroles 5 in a single operation at room temperature from aldehydes, aldimines and Michael acceptors, respectively (Scheme and Table I) So far, especially the results obtained with methyl N-tosylmethylthiobenzimidate (1c) seem promising In particular, 1c gives good yields of 2-phenyl substituted pyrroles with Michael acceptors as appears from the examples 5b,e,f

SCHEME and TABLE[3] I



Product[a]	R	X	Ar	Ar'/Y	yield (%)	mp (°C)	base/solvent
	from $TosCH_2N=CRX$		and aldehyde				
3a	Me	OMe (1a)	Ph	-	49	57-59 (rep[4] 58-60)	NaH/DME-DMSO
b	Me	OMe (1a)	p-ClPh	-	63	74-75 5	NaH/DME-DMSO
c	Ph	SMe (1c)	$p\text{-}O_2NPh$	-	50	194 5-195 5 (rep[5] 189 5-190 5)	t-BuOK/DME
			and aldimine				
4a	Ph	SMe (1c)	Ph	Ph	23	251-252 5 (subl) (rep[6] 248-250)	NaH/DME-DMSO
b	Ph	SMe (1c)	p-ClPh	p-ClPh	51	203.5-204	NaH/DME-DMSO
c	SMe	SMe (1d)	p-ClPh	p-ClPh	64	148-149 5	t-BuOK/t-BuOH-DME
			and Michael acceptor				
5a	Me	SMe (1b)	Ph	COPh	91[b]	235-236 (sl dec) (rep[7] 231)	NaH/DME-DMSO
b	Ph	SMe (1c)	Ph	COPh	73	199 5-200 5	NaH/DME-DMSO
c	SMe	SMe (1d)	Ph	COPh	65	171-173 (sl dec)	NaH/DME
d	OMe	OMe (1g)	Ph	COPh	42	dec at ca. 100	t-BuOK/THF
e	Ph	SMe (1c)	Ph	COOMe	58	164 5-165 5	NaH/DME-DMSO
f	Ph	SMe (1c)	Ph	C≡N	63	266-267 (sl dec)	NaH/DME-DMSO

a No heterocyclic products were obtained in reactions of p-chlorobenzaldehyde with 1e or 1c, 1-methylindole-3-carbaldehyde with 1a, N-p-nitrobenzylideneemethylamine with 1c, cinnamonitrile with 1a and 3-penten-2-one with 1a, reaction of 1e with p-nitrobenzoylchloride (t-BuOK/DME) yields 2-chloro-5-p-nitrophenyl-4-tosyloxazole (20%), mp 187-189° (dimorphous)

b. The same product was obtained in 75% by using 1a instead of 1b.

To rationalize the formation of the products 3, 4 and 5 it seems logical to assume as the first step the generation of a 2-azaallyl anion ($TosCH\text{-}N\text{-}CRX^{\ominus}$, 6) by proton abstraction from the activated methylene.[8,9] Reaction of 6 with the unsaturated substrate (i e aldehyde, aldimine or Michael acceptor) could be either a [3+2] 1,3-anionic cycloaddition,[10] or a [3+2] 1,3-dipolar cycloaddition (after loss of $Tos^{\ominus}$ or $X^{\ominus}$) [11]

We have employed the following reactions in the synthesis of the previously unknown N-tosylmethylimino derivates 1, which are fairly stable crystalline solids They can well be kept at -20° (under N_2) The known N-tosylmethylacetamide (7), obtained by a Mannich condensation of TosH, CH_2O and CH_3CONH_2,[12] was O-methylated smoothly with methyl fluorosulfonate (Magic Methyl)[13] to give methyl N-tosylmethylacetimidate (1a, Scheme and Table II) The analogous reaction of N-tosylmethylbenzamide[12] (8) was unsuccessful

Both 7 and 8 were readily converted with P_4S_{10} in DME[14] to the corresponding thioamides 9 (mp 142-143°, 81%) and 10 (mp 142 5-144°, 97%),[15] respectively Reaction with methyl fluorosulfonate gave in good yields the S-methylated thioimidates 1b and 1c A Mannich condensation carried out with methyl dithiocarbamate provided methyl N-tosylmethyldithiocarbamate[16] (11, mp 150-152°, 72%), from which 1d was obtained in 93% by methylation analogous to 1b,c

SCHEME and TABLE[3] II

$TosCH_2N{=}C(Me)(OMe)$ (1a) $\xleftarrow{MeOSO_2F}$ $TosCH_2NHCR$ (O) $\xrightarrow[DME]{P_4S_{10}}$ $TosCH_2NHCR$ (S) $\xrightarrow[CH_2Cl_2]{MeOSO_2F}$ $TosCH_2N{=}C(R)(SMe)$

R = Me

7 R = Me; 8 R = Ph

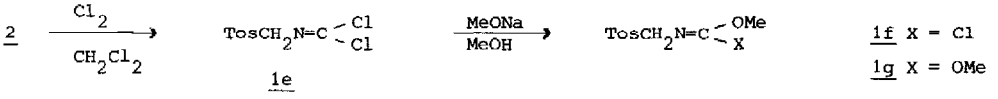
9 R = Me; 10 R = Ph; 11 R = SMe

1b R = Me; 1c R = Ph; 1d R = SMe[17]

Compd	R	X	yield (%)	mp (°C)
1a	Me	OMe	80	90-93 (dec)[a]
1b	Me	SMe	73	103-104 5
1c	Ph	SMe	74	95-97
1d	SMe	SMe	93	122-123
1e	Cl	Cl	68	70-73 5 (rep[19] 70-73.5)
1f	MeO	Cl	72	131 5-133
1g	MeO	MeO	65	108-110 (sl dec)

a isolated as HSO_3F salt

Addition of chlorine to TosMIC (2) yields N-tosylmethyldichloroformimide[18] (1e) from which either one or both chlorines can be displaced with MeONa in MeOH to give 1f and 1g, respectively (Table II)



Further synthetic applications of N-tosylmethylimino derivatives (1) are currently under investigation

Notes and References

1. A.M. van Leusen, R J. Bouma and O Possel, Tetrahedron Lett., 1975, 3487, and references cited therein
2. A M van Leusen, B E Hoogenboom and H Siderius, Tetrahedron Lett , 1972, 2369.
3 The structures of all compounds are supported by IR, PMR and Mass spectra, correct microanalyses were obtained for all new compounds except for 4b and 5d (1a HSO_3F was not determined)
4. F Wolfheim, Ber , 47, 1440 (1914)
5. R Huisgen, G. Binsch and L Ghosez, Chem Ber , 97, 2628 (1964), also the IR spectrum of 3c is in agreement with IR data reported by Huisgen et al.
6 F Asinger, A. Saus, A Offermanns, P Krings and H. Andree, Liebigs Ann. Chem , 744, 51 (1971).
7 L Knorr and A Lange, Ber , 35, 3005 (1902)
8. Previously oxazoles have been prepared in a two-step process involving 2-azaallyl anions J.W Cornforth and H T Huang, J. Chem Soc , 1948, 1969, and previous papers
9 Recently an imidazole synthesis from N-alkyl-C-phenylnitrones, formulated as a [3+2] 1,3-anionic cycloaddition, was published N G Clark and E Cawkill, Tetrahedron Lett , 1975, 2717
10 Review T. Kauffmann, Angew Chem , 86, 715 (1974), or Int Ed., 13, 627 (1974)
11 R Huisgen, H Stangl, H.J. Sturm, R Raab and K. Bunge, Chem Ber , 105, 1258 (1972), K. Bunge, R. Huisgen and R. Raab, ibid, 105, 1296 (1972)
12. T Olijnsma, J B F.N. Engberts and J Strating, Recl Trav. Chim Pays-Bas, 86, 463 (1967).
13 P Beak and J-K Lee, J Org. Chem , 40, 147 (1975), and references cited therein.
14. Review K A Petrov and L N Andreev, Russ. Chem Revs , 38, 25 (1969)
15 Compd 10 was prepared previously in 20%, mp 140 5-142° by a direct Mannich condensation using thiobenzamide, H Meijer, R M Tel, J Strating and J.B F N Engberts, Recl Trav. Chim Pays-Bas, 92, 72 (1973)
16 Compd 11 was prepared analogous to ethyl N-tosylmethyldithiocarbamate, J B F N. Engberts, T. Olijnsma and J Strating, ibid, 85, 1211 (1966)
17 Recently, reactions of 2-azaallyl anions derived from dialkyl N-alkyliminodithiocarbonates were reported, D Hoppe, Angew Chem , 87, 450 (1975), or Int. Ed , 14, 426 (1975), and previous paper
18 D van Leusen, unpublished results
19. T Olijnsma, and J.B.F N. Engberts, Synth Comm , 3, 1 (1973)