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A NEW SYNTHESIS OF SYMMETRICAL AND UNSYMMETRICAL α-DIKETONES THROUGH α-ISOCYANO-α-TOSYL KETONES[1]

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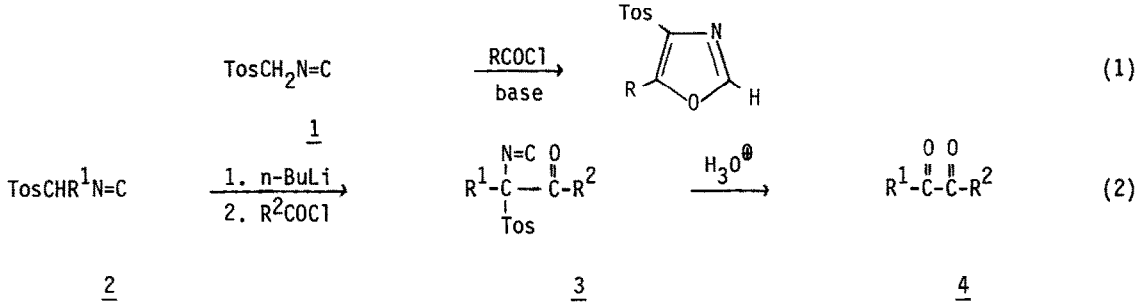
In the foregoing letter a novel ketone synthesis is reported.[1b] This new method is based on the umpolung of carbonyl reactivity[2] by using tosylmethyl isocyanide (TosMIC) as a masked formaldehyde reagent. We here wish to report the application of this principle to a new synthesis of α-diketones. Both symmetrical and, more importantly, unsymmetrical α-diketones are readily accessible by this method.



TosMIC (1) has previously been shown to react with acid chlorides (or anhydrides) and base to give oxazoles (eq 1).[3] We now find, according to expectations, that mono alkyl- and aryl-substituted TosMIC-derivatives (2) can be acylated effectively to non-cyclized compounds 3 (eq 2). As is shown in the foregoing paper,[1b] a geminal arrangement of a tosyl and an isocyano group (as in 3) gives access to a carbonyl function. Thus compounds 3 are potential precursors to α-diketones. Ample experimentation has proven the validity of this concept.

TABLE I. α-Diketones (4) Synthesized from TosMIC-derivatives (2) According to Eq 2. (New compounds marked with †).

R^1-C(=O)-C(=O)-R^2	Overall Yield (% from 2)	R^1-C(=O)-C(=O)-R^2	Overall Yield (% from 2)
MeCOCOPh (4a)	56 [a]	PhCOCO-2-thienyl (4i)	71
MeCOCOC$_6$H$_4$OMe-4 (4b)	57	† PhCH$_2$COCOBu-t (4j)	52 [g]
† EtCOCOAd-1 (4c)	75 [b]	† PhCH$_2$COCOAd-1 (4k)	15 [h]
PhCOCOMe (4d)	73 [c]	PhCH$_2$COCOPh (4l)	51 [i]
PhCOCOCH$_2$Ph [d] (4e)	54	PhCH$_2$COCOC$_6$H$_4$NO$_2$-4 (4m)	65
PhCOCOPh (4f)	68 [e]	† PhCH$_2$COCOC$_6$H$_4$NMe$_2$-4 (4n)	53 [j]
PhCOCOC$_6$H$_4$NO$_2$-4 (4g)	51 [f]	PhCH$_2$COCOC$_6$H$_2$Me$_3$-2,4,6 (4o)	22 [k]
PhCOCOC$_6$H$_2$Me$_3$-2,4,6 (4h)	29	† PhCH$_2$COCO-2-thienyl (4p)	67 [l]

[a] Yield calcd on TosMIC (1) instead of 2, i.e. including phase-transfer methylation[4] of 1. [b] Oil, short path distilled from bath at 120-130°C (13 mm), $\nu_{C=O}$ 1700, 1730 cm^{-1}; quinoxaline deriv[8] in 46%, mp 106-107°C. [c] In 87% yield from 3d; compd 4d is identical with 4a. [d] Characterized as quinoxaline deriv. [e] In 89% yield from 3f. [f] In 63% yield from 3g. [g] Prepared in 73% yield from 3j by heating for 5 min in EtOH: conc HCl = 4 : 1; oil, short path distilled from bath at 80-100°C (13 mm),[8] $\nu_{C=O}$ 1710, 1720 cm^{-1}; quinoxaline deriv,[8] mp 90-91°C. [h] Oil, characterized as quinoxaline deriv,[8] mp 164°C. [i] As quinoxaline deriv; 4l in 50% yield from 3l; compd 4l identical with 4e. [j] Mp 118-123°C,[8] $\nu_{C=O}$ 1715, 1650 cm^{-1}. [k] Stirring with acid (see text) was continued for 18 h. [l] Yield as quinoxaline deriv,[8] mp 118-119°C.

In a typical experiment, 2-phenyl-1-tosylethyl isocyanide[4] (2, R^1 = $PhCH_2$, 5 mmol) in THF (15 ml) was lithiated with n-BuLi (1 equiv) at -70°C, and then acylated with 4-nitrobenzoyl chloride (1.2 equiv) at a temperature from -80°C to 20°C. Subsequently, this reaction mixture (containing crude 3) was stirred rapidly for 2.5 h with 38% aqueous HCl (2.5 ml) to give 3-phenyl-1-(4 nitrophenyl)propane-1,2-dione [4m, mp 113 - 121°C, mainly enol form; quinoxaline derivative, mp 157 - 162°C][5] in 65% overall yield. All α-diketones listed in Table I (known compounds with the exception of 4c, j, k and n) were prepared similarly, without isolating the intermediates. In a number of cases, however, the acylated isocyanides 3 (new compounds) were isolated and characterized (Table II), and converted separately to α-diketones.

TABLE II. α-Isocyano-α-Tosyl Ketones 3 [a]

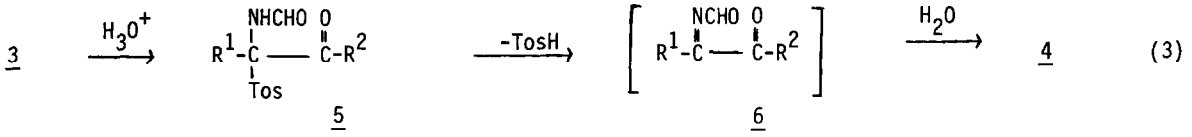
	R^1	R^2	Yield (%)	Mp(°C) (with decomp)
3d	Ph	Me	72	111-113
3f	Ph	Ph	72	119-122
3g	Ph	4-$O_2NC_6H_4$	57	117-130
3j	$PhCH_2$	t-Bu	54	125-128
3l	$PhCH_2$	Ph	58	98-104
3m	$PhCH_2$	4-$O_2NC_6H_4$	77	150

[a] Compds 3 are not fully stable at room temperature; nevertheless satisfactory elemental microanalysis (C,H,N,S) were obtained for 3d, j, l, m.

The next intermediates in this reaction are the formamides 5, formed by acid catalyzed hydration[6] of 3 (eq 3). In some cases compounds 5 have been detected spectroscopically, and a few of them have been isolated and characterized.[7] For the further steps we assume elimination of p-toluenesulfinic acid from 5, followed by hydrolysis of the hypothetical imine 6. Occasionally,

we have effected the conversion of 5 to 4 with NaOH or Na_2CO_3 also.

Further work on these reactions is in progress.



(3)

References and Notes

1. (a) Chemistry of Sulfonylmethyl Isocyanides 17; for part 16, see:
   (b) O. Possel and A.M. van Leusen, Tetrahedron Lett., foregoing letter.
2. See 1b, ref. 5.
3. A.M. van Leusen, B.E. Hoogenboom, and H. Siderius, Tetrahedron Lett., 1972, 2369.
4. Prepared in 80% yield by phase-transfer benzylation of commercially available TosMIC (1); compounds 2 with R^1 = Me and Et were prepared similarly in 95 and 90% yield, respectively: A.M. van Leusen, R.J. Bouma, and O. Possel, Tetrahedron Lett., 1975, 3478. For compd 2, R^1 = Ph, see: A.M. van Leusen, J. Wildeman, and O.H. Oldenziel, J. Org. Chem., 42, 1153 (1977).
5. Reported melting points 129 - 131° and 167°C, respectively: V. Petrov, O. Stephenson, and B. Sturgeon, J. Chem. Soc., 1953, 4066.
6. See 1b, ref. 8.
7. E.g. compd 5d (R^1 = Ph, R^2 = Me), mp 121.5 - 122.5°C (decomp); ν_{NH} 3350, $\nu_{C=O}$ 1700 br, ν_{SO_2} 1310, 1140 cm^{-1}.[8]
8. Satisfactory elemental microanalysis were obtained.