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REACTIONS OF NITRILE OXIDES WITH 2-LITHIO-1,3-DITHIANES
SYNTHESIS OF α-DIKETONES

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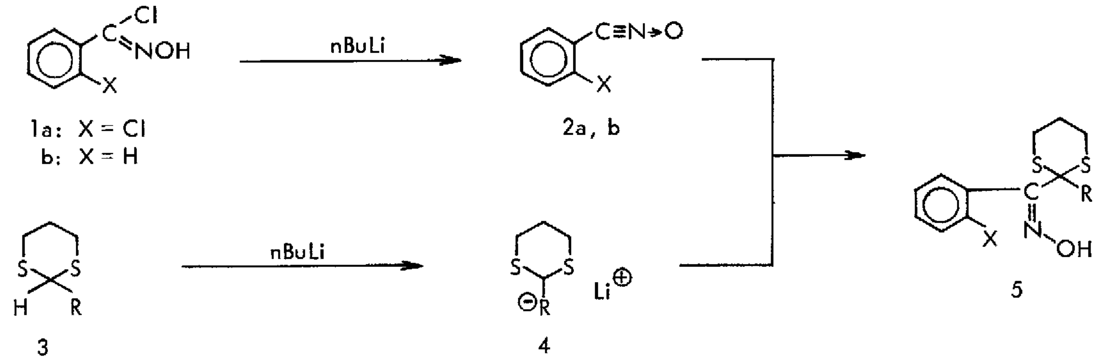
Summary: Nitrile oxides (2) were treated with 2-lithio-1,3-dithianes (4) to give in good yields masked ketoximes (5), new synthetic tools for α-diketones.

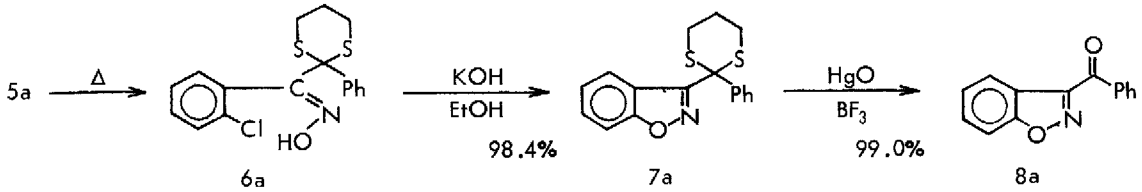
Nitrile oxides, typical 1,3-dipoles, undergo a wide range of cycloaddition reactions to unsaturated compounds leading to heterocyclic systems.[1] They also react with nucleophiles such as amines, thiols, carboxylates, chloride ion and azide to yield 1,3-addition products,[2] but only a few studies have been reported for the reactions of nitrile oxides with carbanions.[3] This type of reaction is interesting since it involves the formation of the carbon-carbon bond to provide the functionalized compounds.

We wish to report herein the reactions of nitrile oxides with 2-lithio-1,3-dithianes, synthetic equivalents of the acylanion,[4] and also a new synthesis of α-diketones from the 1,3-adducts. o-Chlorobenzohydroxamoyl chloride (1a, 10 mmol), a precursor of o-chlorobenzonitrile oxide (2a),[5] was added to a solution of 2-lithio-2-phenyl-1,3-dithiane (4, R = Ph) in THF, prepared from 2-phenyl-1,3-dithiane (12 mmol) and n-butyllithium (22 mmol) in the presence of TMEDA (30 mmol)[6] at -78° under N_2. The reaction mixture was left overnight at -78°, quenched and worked up to give the crystalline ketoxime (5a) in 69.7% yield;[7] $C_{17}H_{16}ClNOS_2$, M^+ 349, ir (Nu) 3170 (OH), nmr (DMSO-d^6) δ 1.87 (m, 2H), 2.68 (m, 4H), 7.53 (m, 9H), 11.37 (s, OH). These data are consistent with the structure 5a. The product (5a) was thermally unstable and readily became converted on heating with ethanol into the isomer (6a) in a quantitative yield; mp 247° (decomp.), ir (Nu) 3170 (OH), nmr (DMSO-d^6) δ 1.76 (m, 2H), 2.76 (m, 4H), 7.37 (m, 9H), 11.50 (s, OH). The structures with Z- and E-configurations were tentatively assigned to (5a) and (6a), respectively, on the basis of the following facts: 1) the isomer (6a) underwent cyclization to give 3-substituted 1,2-benzisoxazole (7a), the formation of which appears to be a proof that the isomer (6a) is of the E-configuration,[8] and 2) in several cases of the reactions of nitrile oxides with nucleophiles, evidence shows that a similar stereospecificity leading to the Z-form exists.[2,9] Similar reactions of nitrile

Fig. 1



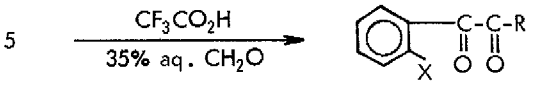
No.	X	R	5 (%)	No.	X	R	5 (%)
a	Cl	Ph	69.7	m	H	Ph	72.3
b	Cl	p-ClPh	72.2	n	H	p-ClPh	91.4
c	Cl	p-MeOPh	59.4	o	H	p-MeOPh	69.5
d	Cl	p-HOPh	46.4	p	H	p-HOPh	78.7
e	Cl	p-Me_2NPh	66.4	q	H	p-Me_2NPh	80.4
f	Cl	3,5-Me_2-4-HOPh	66.0	r	H	α-naphthyl	65.7
g	Cl	α-naphthyl	55.0	s	H	α-furyl	39.4
h	Cl	β-pyridyl	39.9	t	H	β-pyridyl	52.5
i	Cl	α-thienyl	56.2	u	H	α-thienyl	46.6
j	Cl	Me	81.3	v	H	Me	89.1
k	Cl	Me_2CH	46.8	w	H	Me_2CH	71.6
l	Cl	benzyl	60.4	x	H	benzyl	60.0



oxides (2) with a variety of 2-lithio-1,3-dithianes (4) provide the corresponding ketoximes (5).[10] This method is fairly simple and gives better yields of the ketoximes. We feel, therefore, that it sufficiently has a general applicability.

In connection with the development of the new ketoxime synthesis, the 1,3-addition products (5) constitute an important class of compounds; of particular current interest is the conversion into both symmetrical and more importantly unsymmetrical α-diketones.[4,11] Since the ketoximes (5) could not be hydrolyzed with generally used demasking agents,[4] we finally adopted a CF_3CO_2H-aq. CH_2O

Fig. 2



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No.	X	R	9 (%)	No.	X	R	9 (%)
a	Cl	Ph	77.7	h	H	p-Me_2NPh	98.4
b	Cl	p-ClPh	64.5	i	H	p-HOPh	86.4
c	Cl	p-MeOPh	72.8	j	H	α-naphthyl	65.3
d	Cl	p-Me_2NPh	95.5	k	H	α-thienyl	64.8
e	H	Ph	68.6	l	H	Me	--
f	H	p-ClPh	70.7	m	H	Me_2CH	--
g	H	p-MeOPh	89.5	n	H	benzyl	--

treatment. In a typical procedure for the hydrolysis, the ketoxime (5 m, 10 mmol) was stirred with CF_3CO_2H (5 ml) and 35% aq. CH_2O (1 ml) in $CHCl_3$ (10 ml) for 3 days at room temperature under N_2 to give benzil (9e) in a 68.6% yield. Similar hydrolysis of the ketoximes (5, R = aryl) gave the corresponding α-diketones (9) in reasonable yields. With ketoximes (5, R = alkyl), however, α-diketones were not obtained and only decomposition of 5 took place.

The 1,3-addition products (5, X = Cl) will be employed for the synthesis of hitherto unknown 3-acyl-1,2-benzisoxazoles (8) and some results will be published shortly (Fig. 1). The scope and limitation of the new reaction described in this paper are under investigation.

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5. Treatment of 1a with n-butyllithium in THF give nitrile oxide (2a) in good yield, so the reaction of 1a with 4 (R = Ph) may proceed through this

intermediate (2a).

6. These dithianes are readily prepared from the corresponding aldehydes and propan-1,3-dithiol following the procedure in reference 4.
7. Ketoxime (5a) was also obtained in 59.9% yield by the similar reaction using the isolated nitrile oxide (2a) and 4 (R = Ph).
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