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Dicyanoketene Acetals, a Novel Type of π-Acid Catalyst for Monothioacetalization of Acetals[1]

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Abstract: Dicyanoketene acetals such as dicyanoketene dimethyl acetal and ethylene acetal are introduced to be a novel type of π-acid catalyst for the monothioacetalization of acetals. Particularly, the catalytic activity of dicyanoketene ethylene acetal was found to be superior to that of tetracyanoethylene and chemoselective in the crossover reaction of the monothioacetalization of a ketone-, an aldehyde-acetal and an alcohol THP-ether providing a ketone monothioacetal favorably.

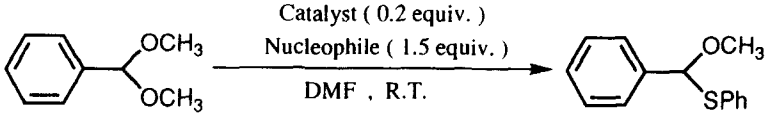
Monothioacetals are useful protected carbonyl compounds[2] and sometimes reactive intermediates[3] in organic synthesis. The most convenient method for preparation of monothioacetals is the transacetalization of acetals using such combination of reagents as RSH/BF_3-Et_2O,[4a] RSH/$MgBr_2$,[4b] Me_2BBr/RSH/iPr_2NEt,[4c] $Bu_{4-n}Sn(SPh)_n$/BF_3-Et_2O,[4d] or PhSH/Et_3Al.[4e] In these methods using strong acids, however, strict reaction conditions using a limited amount of thiols and conducting at low temperature were neccessary in order to avoid overreaction leading to dithioacetals. Furthermore, moisture sensitivity of the promotors appears to be another disadvantage on handling. Therefore, it is still of considerable interest to develop new efficient catalysts which can be easily prepared, handled, and used in simple operations.

2,3-Dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) which is one of the representative one electron oxidants was reported to catalyze alcoholysis of epoxides,[5a] tetrahydropyranylation of alcohols,[5b] C-glycosidation of glycals,[5c] and deprotection of acetals [5d] and orthoesters.[5e] In the context, we have recently reported that a catalytic amount of tetracyanoethylene (TCNE),[6] a representative π-acid and one-electron acceptor, accelerates substrate-specific rearrangement,[7a] acetonidation,[7a] and alcoholysis of epoxides [7b] and Mukaiyama aldol reaction of acetals.[7c] During investigation of the reaction mechanism of TCNE-catalyzed alcohlysis of epoxides,[7a] we have envisaged catalytic ability of dicyanoketene dimethylacetal ($(CN)_2C=C(OMe)_2$), which can be formed in methanolysis of TCNE,[8] in reactions of epoxides and acetals.

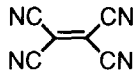
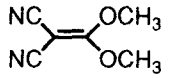
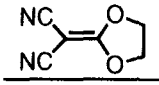
We wish to introduce herein a novel type of π-acid catalyst, dicyanoketene acetals such as dicyanoketene dimethyl acetal ($(CN)_2C=C(OMe)_2$) (DCKDMA)[8] and dicyanoketene ethylene acetal ($(CN)_2C=C(OCH_2)_2$) (DCKEA),[8] which effectively promote monothioacetalization of acetals under mild reaction conditions.

Treatment of benzaldehyde dimethylacetal (**1**) with thiophenol (PhSH) (1.5 equiv) in the presence of a 0.2 equiv. of DCKDMA in DMF at room temperature for 1 day afforded the corresponding monophenylthioacetal (**2**) in 76% yield. The same product (**2**) was obtained in good to high yield with DCKEA, another catalyst of the type, using PhSH as well as phenylthiotrimethylsilane (TMS-SPh) as the nucleophile. As shown in Table 1, TCNE worked but not so efficiently as the dicyanoketene acetals.

Table 1. Reactivity of Benzaldehyde Dimethyl Acetal with Sulfur Nucleophiles Catalyzed by TCNE-Related π-Acid.



1 **2**

Catalyst		Nucleophile	Time	Yield[a]
	(TCNE)	PhSH	42 h 42 h	62 % 48 %
	(DCKDMA)	PhSH	26 h	76 %
	(DCKEA)	PhSH	44 h 42 h	77 % 90 %

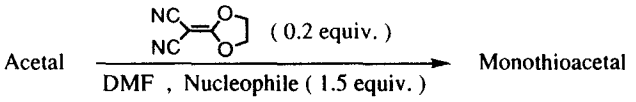
[a] Isolated yields.

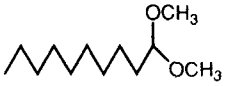
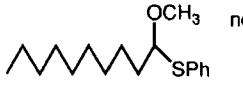
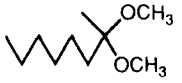
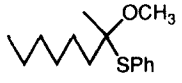
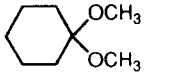
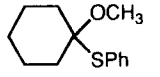
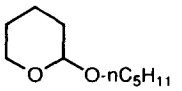
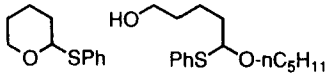
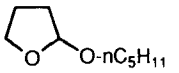
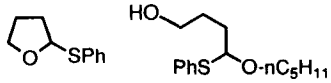
Because of ease of preparation and purification, we selected DCKEA as catalyst and screened reactions of several representative acetals. Results are displayed in Table 2. Typical acetals of aldehydes and ketones underwent smoothly monothioacetalization under the conditions at the ambient temperature to 60 °C for 1/2 to 2 days. Reaction of dimethyl acetals of aliphatic ketones proceeds more rapidly than that of an aliphatic aldehyde (entrys 1-3, 4-7). With mixed acetals, tetrahydropyranyl (THP)- and tetrahydrofuryl (THF)-ethers derived from *n*-pentanol underwent highly regioselective thiolysis of endo- or exo-cyclic C-O bond with PhSH and TMS-SPh as a nucleophile (entrys 11-13), although no reaction was observed with a methoxymethyl (MOM)-ether of *n*-dodecanol (entrys 8,9).

Mildness and high chemoselectivity of DCKEA as a catalyst for monothioacetalization were demonstrated in the crossover experiments in which competitive formation of the ketone monothioacetals followed by the aldehyde monothioacetal and intactness of the THP-ether were observed using a mixture of substrates of dimethylacetals of 2-octanone and *n*-decanal and *n*-pentyl-THP ether with one and two mole equiv. of TMS-SPh as a nucleophile. (Table 3)

It should be worth noting that the reduction-potential of DCKEA measured was very low (E_p^{red} <-2.0V vs. SCE in MeCN) compared with TCNE (E_p^{red} 0.15V vs. SCE in MeCN)[5d] and DDQ (E_p^{red} 0.59V vs. SCE in MeCN)[5d] and that any charge-transfer (CT) absorption band could not be detected in the UV spectroscopic measurement[9] of the mixture of DCKEA and dimethylacetal of *n*-decanal. These data strongly suggest that the

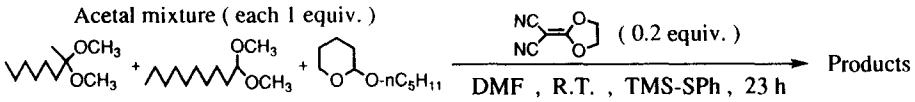
Table 2. Monothioacetalization of Dimethyl acetals or Acetal-Type Ethers Catalyzed by Dicyanoketene Ethylene Acetal.

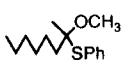
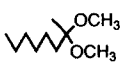
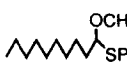
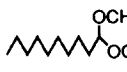
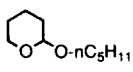


Entry	Acetal	Nucleophile	Temp.	Time	Product (Yield)[a]
1		PhSH	R.T.	44 h	 no reaction
2		PhSH	60 °C	42 h	80 %
3		TMS-SPh	R.T.	46 h	73 %
4		PhSH	R.T.	44 h	 66 %[b]
5		TMS-SPh	R.T.	13 h	93 %
6		PhSH	R.T.	49 h	 65 %[b]
7		TMS-SPh	R.T.	18 h	87 %
8	n-$C_{12}H_{25}$O-MOM	PhSH	R.T.	46 h	no reaction
9		TMS-SPh	R.T.	47 h	no reaction
10		PhSH	R.T.	49 h	 8 % (S.M. 70 %) —
11		PhSH	60 °C	42 h	89 % —
12		TMS-SPh	60 °C	6 h	4 % 61 %
13		PhSH	60 °C	24 h	 93 % —
14		TMS-SPh	60 °C	6 h	36 % 44 %

[a] Isolated yields. [b] A significant amount of the corresponding carbonyl compound was obtained as byproduct.

Table 3. Competitive Monothioacetalization of a Mixture of Acetals Catalyzed by Dicyanoketene Ethylene Acetal.



Equiv. of TMS-SPh	Yield (%)[a] of Product and Recovered Starting Material				
					
1.1	80	10	9	86	82
2.1	93	2	52	43	76

[a] Determined by ^{1}H NMR analysis directly on the crude reaction mixture.

activation of the C-O bond of acetal group for attack of sulfur nucleophiles is initiated by coordination of the acetal oxygen to the π-system of dicyanoketene acetals not by the single electron transfer (SET).

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References and Notes

1. This paper is dedicated to Professor Yoshifumi Maki on this occasion of his retirement from Gifu Pharmaceutical University in March 1994.
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9. The UV-visible absorption spectrum was taken for a mixture of DCKEA(8.0×10^{-3} mol dm^{-3}) and decanal dimethyl acetal (134×10^{-3} mol dm^{-3}).

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