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UTILIZATION OF SULFOXIDES CONTAINING PYRIDINE NUCLEI AS PHASE TRANSFER CATALYSTS: III.[1]

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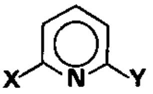
Abstract — Several sulfoxides bound to pyridine were prepared. These sulfoxides were found to promote nucleophilic substitution reactions of alkyl halides markedly in solid-liquid biphase system.

The phase transfer catalyzed reaction (PTC-Reaction) is a new useful procedure in organic syntheses,[2] and hence various catalysts for the reaction such as onium salts, i.e. ammonium or sulfonium salts, crown ethers and cryptates have been used. t-Amine,[3] t-amine oxides,[4] and α-phosphoryl sulfoxides[5] have also been found to function as catalysts which promote such reactions as alkylation and displacement reactions in liquid-liquid or solid-liquid biphase.

We have recently found methyl 2-pyridyl sulfoxide to be a good phase transfer catalyst for S_N2 type reaction of alkyl halides in a two-phase reaction system. In search of other possibly better catalysts of sulfoxide derivatives, several other sulfoxides bound to pyridine (**I**)-(**III**) and the corresponding sulfides and sulfones were synthesized, and their catalytic activities have been examined for some simple displacement reactions under solid-liquid two phase system. This paper describes that such simple sulfoxides as (**I**)-(**III**),[6] prepared according to the general method,[1] can be used as good phase transfer catalysts in S_N2 type reactions of alkyl halides with various nucleophiles.

In order to test the catalytic activity, the reaction was carried out between 1-octyl bromide and various nucleophiles in xylene in the presence of (**I**)-(**III**). When the amount of any of the sulfoxides was small, the rate of the reaction was considerably low. Therefore, a typical run of the substitution reaction was carried out with 4.0 mol equivalents of any one of the sulfoxides to the substrate unless otherwise specified. Without any catalyst, none of displacement reactions proceeded at all. The results thus obtained are summarized in Tables 1-3.



(Ia) $X{=}H,\ Y{=}SCH_3$

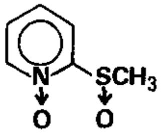
(Ib) $X{=}H,\ Y{=}\underset{\substack{\downarrow\\ O}}{S}CH_3$

(Ic) $X{=}H,\ Y{=}\overset{\substack{O\\ \uparrow}}{\underset{\substack{\downarrow\\ O}}{S}}CH_3$

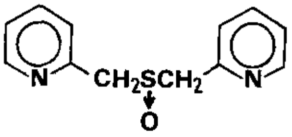
(Id) $X{=}H,\ Y{=}CH_2\underset{\substack{\downarrow\\ O}}{S}CH_3$

(Ie) $X{=}Y{=}\underset{\substack{\downarrow\\ O}}{S}CH_3$

(If) $X{=}Y{=}CH_2\underset{\substack{\downarrow\\ O}}{S}CH_3$



(II)



(III)

$$1{-}C_8H_{17}Br + MNu \xrightarrow[\text{Xylene}]{\text{Catalyst}} 1{-}C_8H_{17}Nu + MBr$$

Table 1. Solid-liquid two phase reactions catalyzed by some organo sulfur compounds.

Substrate	Nucleophile	Catalyst[a]	Temp.	Time(min.)	Yield(%)[b]	Product
$1\text{-}C_8H_{17}Br$	PhSK	(Ia)	r.t.	1440	8	$1\text{-}C_8H_{17}SPh$
$1\text{-}C_8H_{17}Br$	PhSK	(Ib)	r.t.	2	98	$1\text{-}C_8H_{17}SPh$
$1\text{-}C_8H_{17}Br$	PhSK	(Ic)	r.t.	360	65	$1\text{-}C_8H_{17}SPh$
$1\text{-}C_8H_{17}Br$	PhSK	(II)	r.t.	30	85	$1\text{-}C_8H_{17}SPh$

a) 4.0 mol equiv. b) by g.l.c. analysis

Table 2. Solid-liquid two phase reactions catalyzed by methyl 2-pyridyl sulfoxide (**Ib**).

Substrate	Nucleophile	(**Ib**)equiv.	Temp.(°C)	Time(h)	Yield(%)a)	Product
1-C_8H_{17}Br	PhSK	2.0	r.t.	1.0	98	1-C_8H_{17}SPh
1-C_8H_{17}Br	PhSK	1.0	r.t.	17.0	82	1-C_8H_{17}SPh
1-C_8H_{17}Br	PhSK	0.5	50	0.5	65	1-C_8H_{17}SPh
1-C_8H_{17}Br	PhSK	0.1	50	2.0	39	1-C_8H_{17}SPh
1-C_8H_{17}Br	PhSK	0.0	50	24.0	0	1-C_8H_{17}SPh

a) by g.l.c. analysis

Table 3. Solid-liquid two phase reactions catalyzed by some sulfoxides containing pyridine nuclei.

Substrate	Nucleophile	Catalysta)	Temp.(°C)	Time(h)	Yield(%)b)	Product
1-C_8H_{17}Br	NaCN	(**Ib**)	100	54	13	1-C_8H_{17}CN
1-C_8H_{17}Br	NaCN	(**Id**)	100	46	87	1-C_8H_{17}CN
1-C_8H_{17}Br	NaCN	(**Ie**)	100	--	--	-----
1-C_8H_{17}Br	NaCN	(**If**)	100	32	84	1-C_8H_{17}CN
1-C_8H_{17}Br	NaCN	(**III**)	100	50	64	1-C_8H_{17}CN
1-C_8H_{17}Br	KSCN	(**Ib**)	100	40	96	1-C_8H_{17}SCN
1-C_8H_{17}Br	KSCN	(**Id**)	100	27	96	1-C_8H_{17}SCN
1-C_8H_{17}Br	KSCN	(**Ie**)	100	40	20	1-C_8H_{17}SCN
1-C_8H_{17}Br	KSCN	(**If**)	100	40	23	1-C_8H_{17}SCN
1-C_8H_{17}Br	KSCN	(**III**)	100	17	75	1-C_8H_{17}SCN
1-C_8H_{17}Br	PhSK	(**Id**)	r.t.	0.5	91	1-C_8H_{17}SPh
1-C_8H_{17}Br	PhSK	(**Ie**)	r.t.	12	93	1-C_8H_{17}SPh
1-C_8H_{17}Br	PhSK	(**If**)	r.t.	12	88	1-C_8H_{17}SPh
1-C_8H_{17}Br	PhSK	(**III**)	r.t.	0.5	90	1-C_8H_{17}SPh
1-C_8H_{17}Br	PhOK	(**Ib**)	70	36	93	1-C_8H_{17}OPh
1-C_8H_{17}Br	PhOK	(**Id**)	70	36	93	1-C_8H_{17}OPh
1-C_8H_{17}Br	PhOK	(**Ie**)	70	40	33	1-C_8H_{17}OPh
1-C_8H_{17}Br	PhOK	(**If**)	70	40	88	1-C_8H_{17}OPh
1-C_8H_{17}Br	PhOK	(**III**)	70	14	93	1-C_8H_{17}OPh

a) 4.0 mol equiv. b) by g.l.c. analysis

Inspection of the data shown in Tables 1-3 reveals the following characteristic features concerning for the reactions. The rate of displacement reaction of 1-octyl bromide with potassium thiophenoxide and the yield of product depend remarkably on both the catalyst and the amount of the catalyst used. As shown in Table 1, among those sulfur compounds (Ia-c), sulfoxide (Ib) is the most effective catalyst. When the sulfoxide was used as catalyst, the reaction finished within 2 min. at room temperature, affording 1-octyl phenyl sulfide quantitatively. Whereas neither the sulfide (Ia) nor sulfone (Ic) functions as effectively as the sulfoxide (Ib). The catalytic activity of this sulfoxide (Ib) is considered to be due to the strong coordination of metal cation with both sulfinyl oxygen atom and nitrogen atom of pyrinine. Thus the counter anion is sufficiently liberated in the organic phase and hence becomes reactive. There is a possibility that pyridyl nitrogen attacks initially 1-octyl bromide to result in formation of 1-octylpyridinium salts which then react with nucleophile i.e. the Menshutkin reaction. However, the results in Table 1, demonstrate clearly that the Menshutkin reaction can be ruled out completely, since the sulfide (Ia) has a higher pK_a value,[7] i.e. a stronger nucleophile, and hence would be more reactive than sulfoxide (Ib) or sulfone (Ic). The complete inversion of configuration found in the reaction of optically active 2-octyl bromide with thiophenoxide in the presence of sulfoxide (Ib)[1] also ruled out the involvement of the Menshutkin reaction. One finds in Table 2, that even with 0.1 mol equivalent of (Ib), the reaction proceeded, though it required a prolonged heating. Several other sulfoxides (I),(II),(III) were also found to be good catalysts for the displacement reactions of 1-octyl bromide with several nucleophiles as shown in Table 3. None of these reactions also proceeded in the absence of any one of the sulfoxides. All these observations clearly indicate that the nucleophilic displacement reactions are promoted by such simple sulfoxides bound to pyridine such as (I),(II),(III). The main factor for the phase transfer catalytic activity of these sulfoxides in the nucleophilic substitution of alkyl halide is undoubtedly due to the specific affinity of the sulfoxides toward alkali metal ions, the gegen cations of nucleophiles. In the reactions of 1-octyl bromide with such nucleophiles as PhSK, KSCN, PhOK, the sulfoxides (Ib), (Id), and (III) seem to be good catalysts. In the reaction with NaCN as nucleophile, (Id) and (If) are the most effective, while the sulfoxide (**Ie**) is generally not a good catalyst for such a simple displacement reaction. Apparently, two sulfinyl groups attached directly to 2,6-positions of pyridine ring are too bulky for alkali metal cation to be inserted for chelation, unlike other sulfoxides. Another interesting observation is that when potassium phenoxide is used as nucleophile, the product obtained is only O-alkylated, but not C-alkylated product at all.[8] Thus with the use of these sulfoxides the O-alkylation product is obtained selectively.

Meanwhile all these sulfoxides bound to pyridine can be recovered very easily and quantitatively by simple treatment with any mineral acid. Therefore, these sulfoxides can be used as phase transfer catalysts of a new type.

References

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6. (**Ib**): bp 95-96°C(1.5 Torr.); ^{1}H-NMR($CDCl_3$) δ 2.83(s, 3H, CH_3), 7.20-7.50(m, 1H, γ-H), 7.74-8.16(m, 2H, β-H), 8.32-8.58(m, 1H, α-H); IR(NaCl) 1055 cm^{-1}($S\rightarrow O$).
   (**Id**): bp 135°C(3 Torr.); ^{1}H-NMR(CCl_4) δ 2.53(s, 3H, CH_3), 4.15(s, 2H, CH_2), 7.05-7.77(m, 2H, β,γ-H), 8.46-8.57(m, 1H, α-H); IR(NaCl) 1045 cm^{-1}($S\rightarrow O$).
   (**Ie**): mp 109-114°C; ^{1}H-NMR($CDCl_3$) δ 2.93(s, 6H, CH_3), 8.10-8.23(m, 3H, C_5H_4N); IR(KBr) 1050 cm^{-1}($S\rightarrow O$).
   (**If**): mp 135-142°C; ^{1}H-NMR($CDCl_3$) δ 2.66(s, 6H, CH_3), 4.20(s, 4H, CH_2), 7.30-7.91(m, 3H, C_5H_4N); IR(KBr) 1030 cm^{-1}($S\rightarrow O$).
   (**II**): mp 122-123°C; ^{1}H-NMR($CDCl_3$) δ 3.10(s, 3H, CH_3), 7.35-8.03(m, 3H, β,γ-H),

8.19-8.35(m, 1H, α-H); IR(KBr) 1025 cm^{-1}(S→O).

(III): mp 80-81°C; ^1H-NMR($CDCl_3$) δ 4.13 and 4.26(2H, J_{AB}=12 Hz, CH_2), 7.15-7.78(m, 6H, β,γ-H), 8.59- 8.69(m, 2H, α-H); IR(KBr) 1050 cm^{-1}(S→O).

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