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NOVEL CONVERSION OF AROMATIC THIOAMIDES AND ALDEHYDES INTO NITRILES WITH ELEMENTAL SULFUR AND SODIUM NITRITE IN LIQUID AMMONIA

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Various aromatic nitriles were obtained from aromatic thioamides, aldehydes, and the related compounds with elemental sulfur and sodium nitrite in liquid ammonia in good yields. A new type of the Willgerodt-Kindler reaction is suggested in this study.

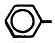
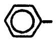
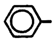
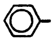
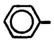
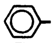
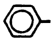
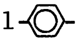
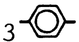
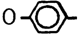
The Willgerodt-Kindler reaction[1)] has been widely studied for the synthesis of amides and thioamides in this century. Although many interests of chemists have been centered on the mechanism, there have been some unresolved problems.[2)] Recently we have reported some new types of reactions with elemental sulfur in liquid ammonia and amines in synthetic organic chemistry.[3)] Further studies on the reaction with elemental sulfur led us to finding of a new type of the Willgerodt-Kindler reaction involving elemental sulfur and sodium nitrite in liquid ammonia which was found to be readily applicable to the conversion of aromatic thioamides and aldehydes into the corresponding nitriles (Scheme 1).

$$\text{R-CS-NH}_2 \xrightarrow{S_8/\text{NaNO}_2/\text{NH}_3} \text{R-CN} \xleftarrow{S_8/\text{NaNO}_2/\text{NH}_3} \text{R-CHO} \qquad \text{Scheme 1.}$$

In this communication, we wish to report preliminarily a new type of the Willgerodt-Kindler reaction and its application.

Typical procedure is as follows. 10 ml of liquid ammonia was charged into titanium autoclave containing 1 mmol of thiobenzamide and sodium nitrite and 4 mg atom of elemental sulfur. The solution was allowed to react at 100 °C for 1 h with stirring by magnetic stirrer. After evaporation of ammonia, resulted products were extracted with 10 ml of methanol and then provided for GLPC to determine the yield of benzonitrile obtained using nitrobenzene or p-chlorobenzaldehyde as an internal standard. Conversion of aromatic aldehydes into nitriles with elemental sulfur and sodium nitrite in liquid ammonia was also carried out in a similar manner to the reaction of thiobenzamide. The products obtained were identified by the comparison of the NMR, IR, and MS with those of authentic samples. These results are summarized in Tables 1 and 2.

Table 1. Reaction of Thioamides with Elemental Sulfur and Sodium Nitrite in Liquid Ammonia

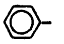
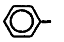
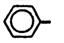
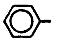
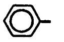
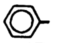
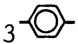
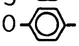
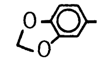
Run[a)]	Substrate: $R\text{-}CS\text{-}NH_2$ R	S_8/mg atom	$NaNO_2$/mmol	Yield of nitrile/%[b)] R-CN
1		0	1	44
2		4	1	92
3		2	0	26
4		2	1	87
5		2	1[c)]	20
6		4	1[d)]	44
7		4	1[e)]	60
8	Cl- 	4	1	31
9	CH_3- 	4	1	84
10	CH_3O- 	4	1	89
11	Ph_2N-	4	1	32
12	$Ph\text{-}CH_2$-	4	1	21 (Ph-CN/36%)

a) In all cases 1 mmol of substrate and 10 ml of ammonia were used. All reactions were carried out at 100 °C for 1 h. b) The yields were determined by GLPC based on the substrate. c) Ammonium nitrate was used. d) Sodium methoxide was served. e) Sodium amide was employed.

Various aromatic nitriles were obtained in good yields from the corresponding thioamides. Elemental sulfur and sodium nitrite increased the yield of nitrile as shown in runs 1, 2, and 3(Table 1). Although other bases (sodium amide and methoxide) instead of sodium nitrite were also employed, comparable effect was not observed(runs 5, 6, and 7). These facts suggest that both elemental sulfur and sodium nitrite in liquid ammonia are necessary to the dehydrosulfurization of aromatic thioamide. Other successful examples were also shown in the results of runs 8 to 12 . Surprisingly, benzonitrile(36%) was obtained in the reaction of thiophenylacetoamide(run 12) along with normal product, phenylacetonitrile(21%). The formation of benzonitrile is interpreted by further reaction of the resulted phenylacetonitrile with elemental sulfur and sodium nitrite in liquid ammonia to afford thiobenzamide, which is dehydrosulfurized.[4)] This characteristic reaction encouraged us to study the direct conversion of aromatic aldehydes to the corresponding aromatic nitriles by our present procedure involving a new type of the Willgerodt-Kindler reaction.

Desired aromatic nitriles were obtained in moderate to good yields as shown in Table 2. Sodium nitrite also accerelated this reaction as shown in run 2. The results in run 7 to 10 show that present procedure is generally applicable to convert aromatic aldehydes to the corresponding nitriles. In this reaction, only nitrite anion was found to accelerate exclusively the formation of aromatic nitrile from aldehyde(runs 4, 5, and 6). Further application of this system was also shown in the reaction of benzyl chloride with elemental sulfur and sodium nitrite in liquid ammonia affording benzonitrile in yield of

Table 2. Reaction of Benzaldehydes with Elemental Sulfur and Sodium Nitrite in Liquid Ammonia

Run[a)]	Aldehyde: R-CHO R	S_8/mg atom	$NaNO_2$/mmol	Yield of nitrile/%[b)] R-CN
1		0	1	-
2		4	0	24[c)]
3		4	1	74
4		4	1[d)]	18
5		4	1[e)]	20
6		4	1[f)]	30
7	CH_3-	4	1	83
8	CH_3O-	4	1	83
9	Cl-	4	1	45
10		4	1	59

a) Substrate: 1 mmol, React.temp : 100 °C, Time: 4 h, b) The yield of nitrile were determined by GLPC based on the substrate. c) As by-product, thiobenzamide was obtained in yield of 12%. d) Ammonium nitrate was used. e) Sodium methoxide was served. f) Sodium amide was employed.

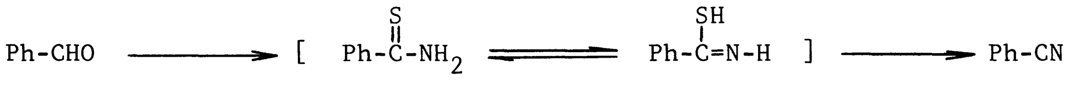
55%(Eq. 1).[5)] The interesting application was found in the reactions of two nitroalkanes(1,2-dinitro-1,2-diphenylethane and α-nitrobenzyl phenyl sulfone), which contained nitro group to supply nitrite anion, with only elemental sulfur in liquid ammonia giving the corresponding benzonitrile in fair yields as follows(Eqs. 2 and 3).[5)]

$$\text{Ph-CH}_2\text{-Cl} \xrightarrow[100\ ^\circ\text{C},\ 4\ \text{h}]{S_8/\text{NaNO}_2/\text{NH}_3} \text{Ph-CN(55\%)} \qquad (1)$$

$$\text{Ph-CH(NO}_2\text{)-CH(NO}_2\text{)-Ph} \xrightarrow[100\ ^\circ\text{C},4\ \text{h}]{S_8/\text{NH}_3} \text{Ph-CN(52\%)} + \text{Ph-CHO(36\%)} \qquad (2)$$

$$\text{Ph-CH(NO}_2\text{)-SO}_2\text{-Ph} \xrightarrow[100\ ^\circ\text{C},4\ \text{h}]{S_8/\text{NH}_3} \text{Ph-CN(70\%)} + \text{Ph-SO}_2\text{SNH}_4\text{(98\%)}^{6)} \qquad (3)$$

Dehydrosulfurization of thioamides into nitriles has been investigated by many workers using various systems of reagents.[7)] Whereas conversion of aldehydes into nitriles has been achieved by dehydration of the corresponding aldoxim,[8)] oxidation of the Schiff bases,[9)] and reaction with sulfilimines[10)] and $Me_3SiN_3/ZnCl_2$.[11)]



$$\text{Ph-CHO} \longrightarrow [\ \text{Ph-}\overset{\overset{\text{S}}{\|}}{\text{C}}\text{-NH}_2 \rightleftharpoons \text{Ph-}\overset{\overset{\text{SH}}{|}}{\text{C}}\text{=N-H}\ ] \longrightarrow \text{Ph-CN}$$

Scheme 2.

To our knowledges, there have been no report on the elemental sulfur catalyzed reaction, except our current investigation on the formation of heterocyclic compounds.[12)] Although at the present stage the role of sodium nitrite is not neccesarily clear, a plausible pathway from benzaldehyde to benzonitrile may be illustrated as shown in Scheme 2 involving the formation of thioamide by the Willgerodt-Kindler reaction followed by dehydrosulfurization to give benzonitrile. Thus, this procedure provides a new type of the Willgerodt-Kindler reaction. Further studies on its synthetic application and mechanism are now in progress.

References

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3) For examples:R.Sato, K.Araya, Y.Takikawa, S.Takizawa, and S.Oae, Phosphorus and Sulfur, 5,245(1978); R.Sato, T.Sato, K.Segawa, Y.Takikawa, S.Takizawa, and S.Oae, ibid., 7,217(1979); R.Sato, T.Goto, Y.Takikawa, and S.Takizawa, Synthesis, 1980,615; R.Sato, T.Etchu, Y.Takikawa, S.Takizawa, and M.Saito, ibid., 1981,44; R.Sato, S.Chiba, Y.Takikawa, S.Takizawa, and M.Saito, Chem. Lett., 1983, 535; R.Sato, N.Saito, and M.Saito, ibid., 1983, 1603 ; R.Sato, N.Saito, Y.Takikawa, S.Takizawa, and M.Saito, Synthesis, 1983, 1045.
4) Actually, benzonitrile was obtained in yield of 80% from phenylacetonitrile at 100 °C for 4 h.
5) These reactions were carried out in a similar manner to the reaction of the benzaldehyde.
6) For the formation of thiosulfonic acid, see Ref. 3.
7) For examples: T.Saraie, T.Ishiguro, K.Kawashima, and K.Morita, Tetrahedron Lett.,1973,2121;T. Sodeyama, M. Kodomari, and K.Itabashi, Chem.Lett., 1973, 577;H.Fujita, R.Endo, and K.Murayama, Bull. Chem. Soc. Jpn., 45,1582(1972); H. Sing and C. S. Gandhi, Synth. Commun., 9, 569(1979); E. J. Kupchik and H. E. Hanke, J. Organomet. Chem., 97, 39(1975); M. I. Lim, W. Y. Ren, and R.S.Klein, J. Org. Chem., 47, 4594(1982).
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