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A NEW SYNTHESIS OF PRIMARY AMINES FROM DIARYLIDENESULFAMIDES

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ABSTRACT: *Addition of organometallic reagents to diarylidenesulfamides affords, after hydrolysis, primary amines illustrating the application of sulfamides as amino protecting groups.*

Many procedures have been devised for the synthesis of primary amines.[1] Usually these methods employ some nucleophilic ammonia equivalent, as for example, the phthalimides (Grabriel synthesis),[2] bis(sulfenyl) amides,[3] phosphoramides,[4] trifluoroamides[5] and sodium bis[trimethylsilyl]amide.[6] Use of these procedures is limited in the synthesis of secondary and tertiary carbinamines (RR'C(R")H-NH_2). The addition of an organometallic reagent to "masked" imines (RCH=NZ) is one alternative provided the protecting group, Z, can be easily removed (eq 1). Previously we described the application of N-alkylidenearenesulfenamides (Z=SAr) as "masked" imines of ammonia in the synthesis of secondary and tertiary carbinamines.[7] Related studies by Hart and co-workers have used N-trimethylsilyl imines (Z=$SiMe_3$) (eq 1).[8] Sulfenimines are not readily available[7] and N-silylimines are sometimes difficult to isolate, and attack at silicon has been reported.[8]

$$\underset{\text{Z=H, SR, SiMe}_3\text{, SO}_2\text{R}}{\text{RCH=N-Z}} + \text{R'M} \longrightarrow \text{RR'CH-NH-Z} \longrightarrow \text{RR'CHNH}_2 \quad (1)$$

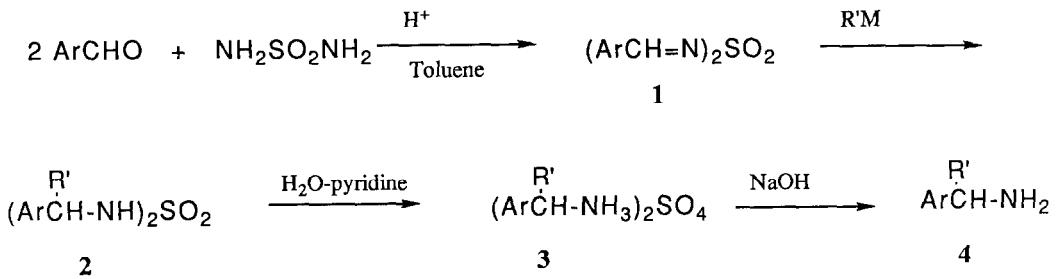
The C-N double bond in N-Arylidenesulfonamides (Z=SO_2R) is an efficient Michael acceptor for a variety of nucleophilic reagents.[9] A disadvantage in using these compounds is the difficulty in removing the sulfonyl protecting group. This usually requires strong acid or base conditions.[10] In this communication we describe the application of diarylidenesulfamides, 1, as "masked" imines of ammonia in a simple "one-pot" synthesis of primary amines.

The diarylidenesulfamides, 1, (typically 5 mmoles) are readily prepared by condensing two equivalents of the aldehyde with sulfamide (Aldrich) by refluxing overnight in benzene with 0.3 g of Amberlyst 15 ion-exchange

resin using a Dean-Stark trap (Scheme).[11] Sulfamylimines, 1, are isolated in greater than 85 percent yield in high purity simply by washing the crude reaction mixture with n-pentane.

The reaction of 1 with Grignard and lithium reagents is accomplished by two methods (Scheme). Method A: In one pot are combined 2 mmoles of the sulfamylimine, 1, 2.2-4 equivalents of the halide (R-X) and magnesium metal in 50 mL of dry ethyl ether or THF in an inert atmosphere. The reaction mixture is sonicated or heated at reflux until all the magnesium is dissolved (1-2 h). Method B: A 1.0 mmolar excess of the preformed lithium or Grignard reagent is added to 1 at 0 °C, allowed to come to room temperature and stirred for 1 h. At this time the reaction mixture (Method A or B) is quenched by addition of 10 mL of sat. NH_4Cl solution. The ether solution is dried, solvent removed under vacuum, 50 mL of 5% H_2O-pyridine added and the solution refluxed overnight. Solvent is removed under vacuum to give the crude amine hydrogen sulfate, 3, which is diluted with 50 mL of 5% HCl solution, washed once with ether followed, by addition 10 mL of 30% NaOH. Ether extraction affords the crude amine 4, in many cases analytically pure (GLC).

Scheme



The acid-catalyzed hydrolysis of diaryl sulfamides was thought to involve attack by water at the sulfonyl sulfur.[15] However, attempts to hydrolyze 2 (Ar=Ph, R'=Me) with conc. HCl resulted in benzylic cleavage to 1,3-diphenyl-1-butene[16] in 65% yield. This sulfamide, 2, also proved to be unreactive to $LiAlH_4$ and 30% NaOH. We believe that the pyridine induced hydrolysis of 2 involves elimination to give an intermediate sulfimide ($ArCH(R)-N{=}SO_2$) which adds water to give a sulfamic acid ($ArCH(R)-NHSO_3H$). Sulfamic acids are known to be hydrolyzed to 3.[15] The involvement of a sulfimide intermediate in the hydrolysis of 2 also is supported by the fact that the N-benzyl derivative of 2 (Ar=Ph, R'=Me, $H{=}CH_2Ph$)[17] is unreactive to the H_2O-pyridine conditions. Sulfimide intermediates have been proposed in the amination of aryl sulfamate esters.[18] Removal of the sulfamyl protecting group in the N-benzyl derivative of 2 (Ar=Ph, R'=Me, $H{=}CH_2Ph$) was accomplished in 60-70% yield using Na-naphthalene.[19]

Table: Synthesis of Amines by Reaction of R'M with Diarylidenesulfamides (1) in THF.

entry	1 Ar=	R'M	Conditions	(method)	Isolated Yield (%) $ArCH(R')NH_2$
1	Ph	MeMgI	sonication, Et_2O	(A)	65[a]
2		MeLi	Et_2O	(B)	95
3		CH_2=$CHCH_2MgBr$	sonication, Et_2O	(A)	83[b]
4		n-BuMgBr	sonication, Et_2O	(A)	80[a]
5		n-BuLi	Et_2O	(B)	90
6		PhMgBr	reflux	(B)	75[a]
7		PhLi	Et_2O	(B)	85
8	3,4-$(MeO)_2$Ph	MeMgI	reflux	(A)	94[c]
9		MeLi		(B)	86[c]
10		CH_2=$CHCH_2MgBr$	reflux	(A)	92[d]
11		Me_3CMgBr	reflux	(A)	91[e]
12	E-PhCH=CH-	MeMgI	reflux	(A)	90[f]
13		MeLi		(B)	94

a) Ref. 7a.
b) Ref. 8.
c) Potapov, V.M; Dem'yanovich, V. M; Skvortsova, T. V.; Melekhina, N. N.; Ser. 2: Khim. 1977, 18, 446.
d) Ref. 8.
e) Ref.13.
f) Schenck, T. G; Bosnich, B., J. Am. Chem. Soc., 1985, 107, 2058.

In summary, addition of organometallic reagents to diarylidenesulfamides, 1, is a useful route to substituted primary amines (Scheme). This methodology illustrates the application of sulfamides as an amino protecting group.

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References

1. For leading references see: Malpass, J. R.; Compr. Org. Chem., 1979, 2, 1.

2. Gibson, M. S.; Bradshws, R. W., Angew. Chem., Int. Ed. Engl., 1968 7, 919.

3. Mukaiyama, T.; Taguchi, T.; Nishi, M., Bull Chem. Soc. Jpn., 1971, 44, 2797.

4. Zwierzak, A.; Brylikowska-Piotrowicz, Angew. Chem., Int. Ed. Engl., 1977, 16, 107.

5. Hendrickson, J. B.; Bergeron, R.; Sternbach, D. D., Tetrahedron, 1975, 31, 2517. Nordlander, J. E.; Catalane; D. B., Eberlein, T. H.; Farkas, L. V., Howe, R. S.; Stevens, R. M.; Tripoulas, N. A.; Stansfield, R. E., Cox, J. L., Payne, M. J.; Viehbeck, A., Tetrahedron Lett., 1978, 4987.

6. Bestmann, H. J.; Wolfel, G., Angew. Chem., Int. Ed. Engl., 1984, 23, 53.

7. a) Davis, F. A.; Mancinelli, P. A., J. Org. Chem., 1977, 42, 389.

   b) For an improved synthesis of sulfenimines see: Morimoto, T.; Nezu, Y.; Achiwa, K.; Sekia, M., JCS Chem. Commun., 1985, 1584.

8. Hart, D. J.; Kanai, K.; Thomas, D. G.; Yang, T-K., J. Org. Chem., 1983, 48, 289.

9. Perlmutter, P.; Teo. C. C., Tetrahedron Lett., 1984, 5951;

10. For leading references see: Andersen, K. K., in Compr. Org. Chem., 1979, 3, 331; Greene, T. W., "Protective Groups in Organic Synthesis, John Wiley & Sons, New York, 1981, Chapter 7.

11. Sulfamides, 1 (Ar=Ph), 86%[12]; (Ar=3-MeO-4-MeOPh), 89% , mp 164-5 °C ;[13] (Ar= PhCH=CH-), 83%, mp 120-1 °C. Analytically pure samples were prepared by crystallization from i-propanol.

12. This compound was previously prepared by condensation of sulfamide with benzaldehyde in the presence of $SOCl_2$.[14]

13. All new compounds gave satisfactory elemental analyses or had high resolution mass spectra consistent with their structures. Amines 4, mp °C, NMR ($CDCl_3$): (Ar=3-MeO-4-MeOPh. R'=CMe_3): 256-258 (HCl) 0.9 (s, 9H, Me), 1.49 (s, 2H, NH_2), 3.65 (s, 1H, CHN), 3.87 (s, 6H, OMe), 6.82-6.94 (m,, 3H).

14. Knollmuller, M.; Reich, K. R., Monatsch fur Cheimie, 1975, 106, 1095.

15. Spillane, W. J.; Barry, J. A.; Scott, F.L., J.C.S. Perkin II, 1973, 481.

16. Bertoli, V.; Plesch, P. H., J. Chem. Soc. (B), 1968, 1500.

17. This compound was prepared in greater than 65% yield by treatment of 3 (R'=Me) with 2.2 eq of NaH in THF followed by reaction with 2.2 eq of benzyl bromide (mp 74-6 °C)[13]; NMR ($CDCl_3$) 1.49 (d, 2H, Me), 4.22 (ab quartet, 2H), 5.04 (ab quartet, 1H), 7.26 (d, 10 H).

18. DuBois, G. E., J. Org. Chem. 1980, 45, 5373.

19. Ji, S.; Gortler, L. B; Waring, A.; Wriede, P., J. Am. Chem. Soc. 1967, 89, 5311.

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