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A NEW SYNTHETIC METHOD OF UNSYMMETRICAL α-AMINOAZINES BY THE REACTION OF ALDEHYDE ARENESULFONYL HYDRAZONES WITH α-AMINO-α-ARYLACETONITRILES

Kazumasa TAKAHASHI,* Hideki KURITA, Katsuyuki OGURA, and Hirotada IIDA
Department of Synthetic Chemistry, Faculty of Engineering,
Chiba University, Yayoi-cho, Chiba 260

Treatment of α-amino-α-arylacetonitriles with aldehyde arenesulfonyl hydrazones affords unsymmetrical α-aminoazines in high yields, which formed by replacement of the arenesulfonyl group of the hydrazone by the acetonitrile carbanion. The formation-mechanism of azines is also discussed.

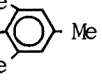
A few synthetic methods of unsymmetrical azines have been reported.[1] There is, however, no available information about an efficient synthesis of unsymmetrical azines. We now wish to report that the replacement of arenesulfonyl group of aldehyde arenesulfonyl hydrazones[3] (2) by carbanion derived from α-amino-α-arylacetonitriles[2] (1) gives unsymmetrical novel α-aminoazines (3) in high yields. In general, attack of nucleophiles [cyanide ion[4] and certain carbanions[5]] to arenesulfonyl hydrazones has been known to occur at carbon-nitrogen double bond of the hydrazones, so the replacement reported here is quite a new reaction and capable of extending a synthetic scope for utilization of the hydrazones.

Scheme 1.

$$\underset{\mathbf{1}}{Ar\text{-}CH(NR^1R^2)\text{-}CN} + \underset{\mathbf{2}}{R^3\text{-}CH{=}N\text{-}NH\text{-}SO_2Ar'} \xrightarrow[2.\ H_2O]{1.\ 2LDA,\ THF/HMPA} \underset{\mathbf{3}}{R^3\text{-}CH{=}N\text{-}N{=}C(Ar)NR^1R^2}$$

The typical synthesis of 3 was carried out under the following conditions [Methods A and B]. Method A [one-pot reaction]: To a mixture of α-morpholino-α-phenylacetonitrile (1d) (0.67 g, 3.3 mmol) and benzaldehyde tosylhydrazone (2a) (0.82 g, 3.0 mmol) dissolved in 20 ml of tetrahydrofuran (THF) and 2 ml of hexamethylphospholic triamide (HMPA) was added 7.0 mmol of lithium di-isopropylamide (LDA) dissolved in 8 ml of THF at -78 °C under a dry nitrogen atmosphere. The mixture was first stirred at -78 °C for 1 h, and then at room temperature for 1-2 d until the starting materials disappeared. The reaction mixture was poured into ice/water, and the aqueous layer was extracted with diethyl ether. Thus, α-morpholino-α,α'-diphenylazine (3e) was obtained in 81% yield as shown in Table 1. Likewise, the treatment of N,N-dimethylamino-acetonitrile (1a) with 2a gave α-(N,N-dimethylamino)-α,α'-diphenylazine (3a) in 51% yield. However, the treatment of 1a with benzaldehyde 2,4,6-trimethylbenzenesulfonyl hydrazone (2b) gave 3a in 95% yield. The 2,4,6-trimethylbenzenesulfonyl group is superior to tosyl group as a leaving group.[4] The treatment of 1a with p-bromobenzaldehyde tosylhydrazone (2c) gave α-(N,N-di-

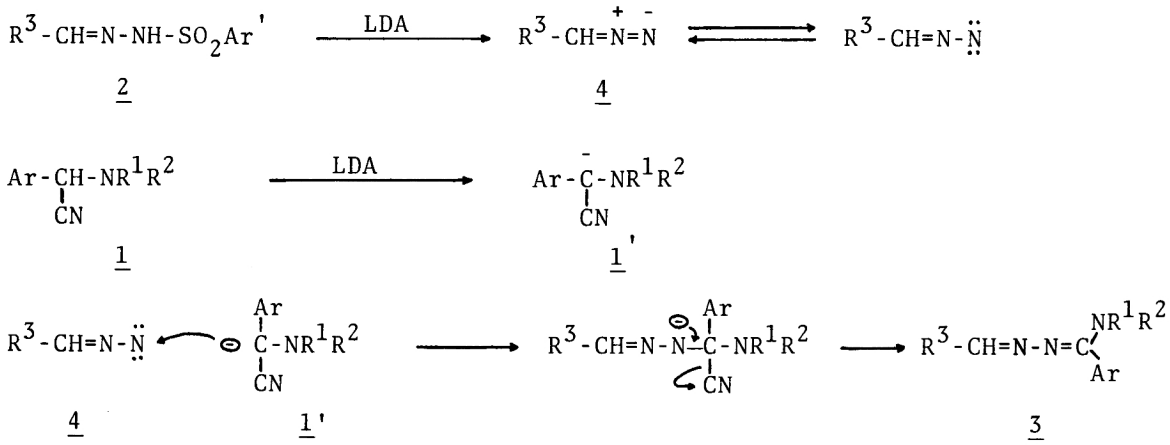
Table 1. Formation of azines (3) by the reaction of α-amino-α-arylacetonitriles (1) with hydrazones (2)

Run No	Nitriles (1)	Hydrazones (2)	Azines (3)	Method	Yield[a] (%)
1	$Me_2N(Ph)CHCN$ (1a)	PhCH=NNHTs (2a)	$Me_2N(Ph)C=NN=CHPh$ (3a)	A	51
2	1a	2a	3a	B	68
3	1a	PhCH=NNHSO$_2$  (2b)	3a	A	95
4	1a	p-BrC_6H_4CH=NNHTs (2c)	$Me_2N(Ph)C=NN=CH(p\text{-}BrC_6H_4)$ (3b)	A	75
5	$Me_2N(p\text{-}ClC_6H_4)CHCN$ (1b)	2a	$Me_2N(p\text{-}ClC_6H_4)C=NN=CHPh$ (3c)	B	82
6	$Me_2N(p\text{-}MeOC_6H_4)CHCN$ (1c)	2a	$Me_2N(p\text{-}MeOC_6H_4)C=NN=CHPh$ (3d)	B	82
7	 (1d)	2a	(3e)	A	81
8	1d	2a	3e	B	81
9	Me(Ph)N(Ph)CHCN (1e)	2a	Me(Ph)N(Ph)C=NN=CHPh (3f)	B	30
10	1d	Ph_2C=NNHTs (2d)	-	B	0
11	1d	PhCH=NN(Me)Ts (2e)	-	C[b]	-

a) Isolated yield. b) The reaction did not give any products resulting from replacement of tosyl group of 2e by carbanion derived from 1d, but afforded many kinds of by-products. Method C: A mixture of 1d and LDA was added to THF solution of 2e.

methylamino)-α-phenyl-α'-(p-bromophenyl)-azine (3b) in 75% yield. Method B: The carbanion of 1a (0.94 g, 5.9 mmol) was prepared separately in a mixture of THF (10 ml) and LDA (6.5 mmol), and then added to a solution of preformed N-lithio derivative of 2a (1.5 g, 5.5 mmol) dissolved in 10 ml of THF and 3 ml of HMPA. The subsequent procedure is similar to that of Method A. Thus, 3a was obtained in 68% yield. Likewise, the treatment of α-(N,N-dimethylamino)-α-(p-chlorophenyl)-, α-(N,N-dimethylamino)-α-(p-methoxyphenyl)-, α-morpholino-α-phenyl- and α-(N-methylanilino)-α-phenyl-acetonitriles (*i.e.*, 1b, 1c, 1d,and 1e) with 2a gave α-(p-chlorophenyl)- and α-(p-methoxyphenyl)-α-(N,N-dimethylamino)-α'-phenylazines (3c in 82% and 3d in 82% yields), and α-morpholino- and α-(N-methylanilino)-α,α'-diphenylazines (3e in 81% and 3f in 30% yields), respectively. In the case of 1e, the steric hindrance of a bulky N-methylanilino group and the stabilization of carbanion by neighboring phenyl group appear to be responsible for the decreased reactivity. Method A [one-pot reaction] is simple and will be recommended in the present work. On the other hand, the reaction of 1d with benzophenone tosylhydrazone (2d) did not proceed but gave a substantial amount of unreacted 1d and 2d. The structures of azines (3) were confirmed by IR, mass, ^{1}H-NMR and ^{13}C-NMR spectroscopy, and microanalysis.[6]

The formation-mechanism of azines (3) is considered to be as follows: Firstly, the decomposition of aldehyde arenesulfonyl hydrazones (2) in the presence of bases



Scheme 2. Formation-mechanism of azines (3).

is suggested to give diazo compound (4). This type of decomposition has been reported to give symmetrical olefines and azines.[7] The formation of symmetrical azines is suggested to be brought about by the reaction of 4 with the carbene formed by the loss of nitrogen from 4. In the present reaction, the formation of 4 is also assumed, but the formation of unsymmetrical α-aminoazines (3) is presumed to caused by the reaction of 4 with the carbanion (1') derived from 1 as depicted in Scheme 2. In the case of 2e, the corresponding azine could not be prepared for lack of the removable hydrogen atom by LDA. The reaction of 1d with 2d did not give the corresponding azine (3f), either. It appears to be due to the high stability of 2d: The decomposition of 2d did not take place under conditions used in the reaction.

References

1) a) J. E. Baldwin and T. C. Bottaro, J. Chem. Soc., Chem. Commun., 1982, 624; b) M. Regitz and D. Stadler, Chem. Ber., 101, 2351 (1968).
2) Physical properties and synthetic procedure of α-aryl-α-aminoacetonitriles (1) are described in the literature [K. Takahashi, M. Matsuzaki, K. Ogura, and H. Iida, J. Org. Chem.] to be published in June, 1983.
3) The tosylhydrazones (2) used in this work were synthesized according to the procedure reported in the literature [M. P. Cava, R. L. Litle, and D. R. Napier, J. Am. Chem. Soc., 80, 2257 (1958)]. Physical properties of 2 agreed with those reported in the literature (see ref. 7).
4) J. Jiricny, D. M. Orere, and C. B. Reese, J. Chem. Soc., Perkin Trans. 1, 1980, 1487.
5) E. Vedejs, J. M. Dolphin, and W. T. Stolle, J. Am. Chem. Soc., 101, 249 (1979).
6) All α-aminoazines (3) are new compounds. They gave satisfactory results in microanalyses (C ± 0.19, H ± 0.05, N ± 0.12). Their physical properties are as follows:
3a: mp 65-66 °C; MS: m/e 251(M^+); ^{1}H-NMR ($CDCl_3$/TMS) δ: 2.91(s, 6H, N-Me_2), 7.00-7.66(m, 10H, ArH), 8.39(s, 1H, N=CH).

3b: mp 105-106 °C; MS: m/e 331(M^+ + 1), 329(M^+ - 1); ^{1}H-NMR ($CDCl_3$/TMS) δ: 2.98 (s, 6H, N-Me$_2$), 7.05-7.61(m, 9H, ArH), 8.27(s, 1H, N=CH).

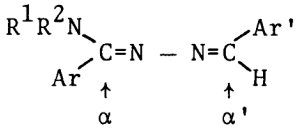
3c: mp 138-139 °C; MS: m/e 285(M^+); ^{1}H-NMR ($CDCl_3$/TMS) δ: 2.96(s, 6H, N-Me$_2$), 7.05-7.61(m, 9H, ArH), 8.34(s, 1H, N=CH).

3d: mp 98-99 °C; MS: m/e 281(M^+); ^{1}H-NMR ($CDCl_3$/TMS) δ: 2.91(s, 6H, N-Me$_2$), 3.73 (s, 3H, OMe), 6.90(d, 2H, J=8 Hz, ArH), 7.34(d, 2H, J=8 Hz, ArH), 7.06-7.07 (m, 5H, ArH), 8.38(s, 1H, N=CH).

3e: mp 144-145 °C; MS: m/e 293(M^+); ^{1}H-NMR ($CDCl_3$/TMS) δ: 3.25-3.58(t-like, 4H), 3.58-3.88(t-like, 4H), 7.05-7.60(m, 10H, ArH), 8.35(s, 1H, N=CH).

3f: mp 101-102 °C; MS: m/e 313(M^+); ^{1}H-NMR ($CDCl_3$/TMS) δ: 3.58(s, 3H, N-Me), 6.80-7.70(m, 15H, ArH), 8.47(s, 1H, N=CH).

^{13}C-NMR data shown below are only for α- and α'-carbons of C=N bonds ($CDCl_3$/TMS, δ units).



	3a	3b	3c	3d	3e	3f
α:	167.551(s)	167.754(s)	166.285(s)	167.264(s)	166.573(s)	165.162(s)
α':	152.036(d)	150.447(d)	152.522(d)	151.975(d)	153.768(d)	154.134(d)

7) W. R. Bamford and T. S. Stevens, J. Chem. Soc., 1952, 4735.

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