SHORT PAPER

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A facile route to amino-azines†

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Amino-azines have been prepared from *S*-methylisothioamide hydroiodides and hydrazones in high yields.

Aminoazines are interesting intermediates in the preparation of 1,2,4-triazoles[1,2] and imidazoles.[3] 1-Amino-1,4-diphenyl-2,3-diazabutadiene (**3**) was first made in 1914 by Stollé,[4] from the reaction of the corresponding chloro-azine with ammonia. 3,5-Diphenyltriazole and diphenyltetrazine were formed as by-products. In 1971, Taylor and co-workers repeated this reaction and obtained the amino-azine (**3**) in 38% yield. 1,4-Diamino-1,4-diphenyl-2,3-diazabutadiene, 3,5-diphenyltriazole, and diphenyltetrazine were also obtained as by-products.[1]

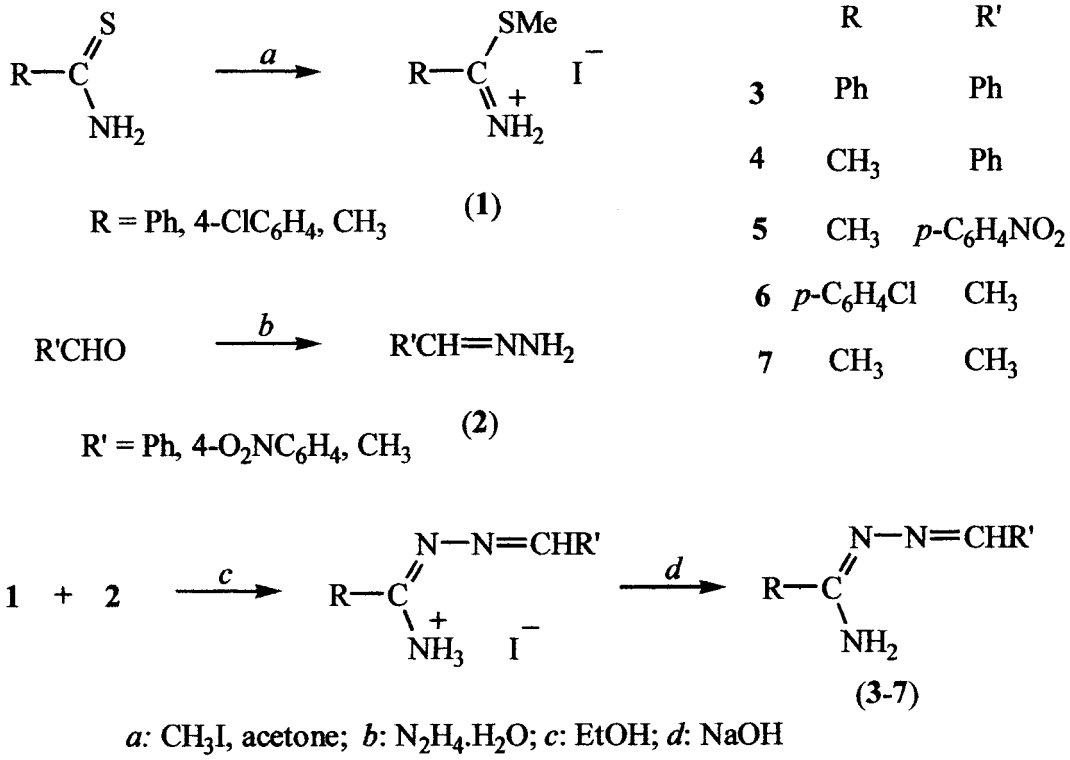
Another route to amino-azine (**3**) was reported by van der Burg,[5] who claimed that the reaction of amidrazones with benzaldehyde would give their N^1-benzylidene derivatives, which are amino-azines. However, conflicting reports have appeared in the literature concerning the products formed in such reactions.

Taylor[6] and Case[7] came to the same conclusion as van der Berg, and stated that the reaction of amidrazones with monocarbonyl compounds would give their aryl or alkylidene derivatives. On the other hand, Case reported the formation of 1,2,4-triazolines rather than amino-azines.[8-10] Zelenin claimed the formation of both amino-azines and triazolines.[11]

Since amino-azines can be considered as amidrazone derivatives, an alternative synthetic route to compounds (**3**) would involve condensation of ethyl benzimidate with benzaldehyde hydrazone. This reaction is based on the well-known reaction of imidates with hydrazines, which is frequently used for the preparation of amidrazones.[12, 13] However, in this reaction, amino-azine (**3**) was obtained in 70% yield, but again some diamino-azine were formed as by-product.[14] Amino-azines were also prepared from the reaction of imidate hydrochlorides and hydrazones.[3]

The formation of diamino-azine and a trace of benzaldazine, observed by TLC analysis, could be evidence for the reaction termed disproportionation, a frequent and unexplained complication in azine chemistry.[15] However, in these methods the products were contaminated with diamino-azine and the amino-azine could not readily be purified by crystallization.

In the present work, in view of the variety of established routes to amidrazones[13,16] and in order to prevent disproportionation reactions, compounds (**3**–**7**) were prepared as hydroiodide salts, from the reaction of isothioamide hydroiodides (**1**) and hydrazones (**2**) in high yield according to Scheme 1.



	R	R'
3	Ph	Ph
4	CH_3	Ph
5	CH_3	*p*-$C_6H_4NO_2$
6	*p*-C_6H_4Cl	CH_3
7	CH_3	CH_3

Scheme 1 Synthesis of compounds **3–7**

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† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Experimental

Melting points were taken on a Electrothermal 910 V melting point apparatus. IR spectra were recorded with a Shimadzu IR-408 spectrometer (KBr). ^{1}H NMR spectra were determined in chloroform-*d* and/or DMSO-d_6 solution on a F7 NMR Bruker AC-80 (80 MHz); chemical shifts are reported in δ ppm.

Aromatic hydrazones were prepared from corresponding aldehydes and hydrazine hydrate.[17-19] *S*-Methylisothioamide hydroiodides were prepared from thioamides and methyl iodide in "analar" acetone.[20] Petroleum ether refers to the fraction b.p. 40–60 °C.

General procedure for preparation of amino-azine hydroiodides: A stirred solution of *S*-methyl isothiobenzamide hydroiodide (20 mmole) in dry ethanol (10 cm^3) was treated for an appropriate time with hydrazine hydrate (20 mmole) in ethanol (5 ml) under nitrogen. The evolved methanethiol was absorbed in 0.1 M aqueous potassium permanganate containing an equimolar amount of sodium hydroxide. After a while TLC indicated the absence of both starting materials. The volume of the solution was reduced by evaporation *in vacuo* to *ca* 7–10 ml and diethyl ether (*ca* 3–5 ml) was added.The resulting mixture was kept at –20 ºC for 3 h and the solid products separated as hydriodide salts.

General procedure for preparation of amino-azines: Sodium hydroxide (24 mmol) in distilled water (3 ml) was added to a hot solution of the hydroiodide salt (6 mmole) in ethanol (5 ml). After evaporation of the solvent the resulting oil or solids were crystallized from an appropriate solvent to give compounds (**3**–**7**).

1-Amino-1,4-diphenyl-2,3-diazabutadiene (**3**): Obtained from benzaldehyde hydrazone and *S*-methylisothiobenzamide hydroiodide; m.p. 227-229 ºC; yield, 89%; upon neutralization with sodium hydroxide the free base obtained as yellow prisms, yield 90%; recrystallized from ethanol / light petroleum; m.p. 133-135 ºC (lit.[4] 134 ºC), ^{1}H NMR ($CDCl_3$): δ 8.55 (s, 1H, CH), 7.2-8.0 (m, 10H, Ar-H), 5.75 (br s, 2H, NH_2) (D_2O-labile). Anal: calcd. for $C_{14}H_{13}N_3$, C, 75.3, H, 5.86, N, 18.8; found, C, 75.1; H, 5.8; N, 19.0%.

1-Amino-1-methyl-4-phenyl-2,3-diazabutadiene **(4):** Obtained from benzaldehyde hydrazone and *S*-methylisothioacetamide hydroiodide; m.p. 164–166ºC; yield 75%; upon neutralization with sodium hydroxide the free base was obtained as white prisms; yield 90%; recrystallized from ethyl acetate / light petroleum; mp 81–82 ºC (lit.[11] 82–84ºC), ^{1}H NMR ($CDCl_3$): δ 8.4 (s,1H, CH), 7.1–7.85 (m, 5H, Ar-H), 2.0 (s, 3H, CH_3), 5.85 (br s, 2H, NH_2) (D_2O-labile). Anal: calcd. for $C_9H_{11}N_3$: C, 67.0; H, 6.87; N, 26.1; found: C, 66.9; H, 6.9; N, 26.0%.

1-Amino-1-methyl-4-nitrophenyl-2,3-diazabutadiene (**5**)**:** Obtained from 4-nitrobenzaldehyde hydrazone and *S*-methylisothioacetamide hydroiodide , m.p. 225 ºC; yield, 75%; upon neutralization with sodium hydroxide the free base was obtained as a yellow solid, yield 95%; recrystallized from ethanol; m.p. 186 ºC (lit.[3] 190 ºC); ^{1}H NMR (DMSO-d_6): δ 8.45 (s, 1H, CH), 7.85-8.35 (m, 4H, Ar-H), 2.1 (s, 3H, CH_3), 5.5 (br s, 2H, NH_2) (D_2O-labile). Anal: calcd. for $C_9H_{10}N_4O_2$: C, 52.42; H, 4.88; N, 27.1; found: C, 52.26; H, 5.09; N, 27.23%.

1-Amino-1-(4-chlorophenyl)-4-phenyl-2,3-diazabutadiene **(6):** Obtained from benzaldehyde hydrazone and *S*-methyl-4-chloroisothiobenzamide hydroiodide, m.p. 208-212 ºC (decomp.); yield, 76%; upon neutralization with sodium hydroxide the free base was obtained as yellow crystals, yield 96%; recrystallized from ethanol; m.p. 158-160ºC; ^{1}H NMR (DMSO-d_6): δ 8.5 (s, 1H, CH), 7.25–8.17 (m, 9H, Ar-H), 7.1 (br s, 2H, NH_2) (D_2O-labile); Anal: calcd. for $C_{14}H_{12}ClN_3$: C, 65.2; H, 4.7; Cl, 13.7; N, 16.3; found: C, 65.5; H, 4.4; Cl, 13.7; N,16.1%.

1-Amino-1,4-dimethyl-2,3-diazabutadiene (**7**): Obtained from acetaldehyde hydrazone and *S*-methylisothioacetamide hydroiodide; m.p. 128–130 ºC, 60%;upon neutralization with sodium hydroxide the free base obtained as white solid yield, 51%; recrystallized from diethyl ether / light petroleum, m.p. 74–76 ºC (lit.[11] 76–78 ºC); ^{1}H NMR ($CDCl_3$) δ 7.76 (q, 1H, CH-CH_3), 5.5 (br s, 2H, NH_2), (D_2O-labile), 1.97 (d, 3H, CH_3-CH), 1.95 (s, 3H, CH_3-C) Anal: calc. for $C_4H_9N_3$, C, 48.5; H, 9.15; N, 42.4; found: C, 48.2; H, 9.4; N, 42.2%.

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