SHORT PAPER

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A simple and efficient method for the *N*-nitrosation of secondary amines with $NaNO_2$–Ac_2O under mild conditions

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Secondary amines can be easily converted into their corresponding nitroso derivations using $NaNO_2$–Ac_2O as a nitrosating agent in dichloromethane at room temperature with high yields.

Keywords: *N*-nitrosation, secondary amines, $NaNO_2$–Ac_2O

N-Nitrosation of secondary amines is very important in organic synthesis. Some nitroso compounds are widely produced in industry. Various nitrosating agents have been reported, such as, the most general, nitrous acid, generated from sodium nitrite and mineral acid in water or in mixed alcohol-water solvents,[1] nitrosyl salts,[2] alkyl nitrites,[3] dinitrogen tetroxide,[4] oxyhyponitrite,[5] Fremy's salt,[6] *N*-haloamides and sodium nitrite under phase-transfer conditions,[7] bis(triphenylphosphine) ammonium nitrite,[8] solid acids (*i.e.* oxalic acid dihydrate,[9] inorganic acidic salts[10] and hydrolysable chloride salts[11]) and sodium nitrite, $[NO^{+}\cdot \text{Crown}\cdot \text{H}(NO_3)_2^{-}]$,[12] and silica chloride/$NaNO_2$.[13]

We wished to develop a new nitrosating agent. In the course of our study on the oxidation of aryl substituted semicarbazides to aryl azo compounds with $NaNO_2$–Ac_2O,[14] we found the generation of NO^+ in this oxidation system. It is well known that the nitrosating key is the generation of NO^+ in the nitrosating reaction. Therefore, we evaluated $NaNO_2$–Ac_2O as the nitrosation agent for secondary amines. In our experiment, we selected Ph_2NH as a model. The optimum molar ratio was sought by using Ph_2NH (1 mmol) with different molar ratios of $NaNO_2$: Ac_2O. The optimum molar ratio ($NaNO_2$: Ac_2O) (3: 3) is required for the most excellent yields. The results are summarised in Table 1.

All reactions were performed smoothly in dichloromethane at room temperature (Scheme 1) and completed with excellent yields. The results are summarised in Table 2.

To conclude, we recommend this simple, efficient method for the *N*-nitrosation of secondary amines under mild conditions with excellent yields. In all cases, reactions can be monitored by TLC. We believe that the present methodology is an important addition to existing methodology.

Table 1 *N*-Nitrosation of Ph_2NH with different molar ratio of $NaNO_2$–Ac_2O

Entry	Ph_2NH :	$NaNO_2$:	Ac_2O	Time/h	Yield/%
1	1	1	1	1.5	45
2	1	1.5	1.5	1.5	55
3	1	2	2	1.5	90
4	1	2.5	2.5	1.5	95
5	1	3	3	1.5	98
6	1	3.5	3.5	1.5	96

$$R_1R_2NH \xrightarrow[CH_2Cl_2,\ \text{r.t.}]{NaNO_2-Ac_2O} R_1R_2N{-}N{=}O$$

Scheme 1

Table 2 *N*-Nitrosation of secondary amines using $NaNO_2$–Ac_2O as the nitrosating agent

Entry	R_1	R_2	Time/h	Yield/%
1	Me	Me	1	91
2	Et	Et	1	94
3	*iso*-Pr	*iso*-Pr	1.5	93
4	Butyl	Butyl	1.5	94
5			1	96
6	Ph	Ph	1.5	98
7	Ph	$COCH_3$	2	86
8	Ph	Me	1	89

Experimental

Melting points and boiling points were measured using uncorrected temperature gauges. Yields refer to isolated pure products. The nitrosation products were characterised by comparison of their melting or boiling points, Anal. Calcd and spectral (IR, ^1H NMR).

A mixture of secondary amine (1 mmol), acetic anhydride (0.306 g, 3 mmol) and $NaNO_2$ (0.207 g, 3 mmol) in dichloromethane (10 ml) was vigorously stirred at room temperature. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was filtered, the undesired precipitates were removed and washed with dichloromethane (2×8 ml). The solvent was evaporated from the combined dichloromethane solutions and the *N*-nitroso compounds were obtained. If further purification is needed, column chromatography on silica gel [eluent: acetone/petroleum ether (10:90)] gives pure *N*-nitroso compounds.

Data on products: *N-Nitrosodimethylamine*: Yellow liquid, b.p. 154°C/774mm (Lit.[15] 153°C /774mm); IR (KBr)ν:2970, 1440, 1305, 1048; ^1H NMR ($CDCl_3$) δ:2.93 (s, 3H, CH_3), 3.69 (s, 3H, CH_3); Anal. Calcd for $C_2H_6N_2O$:C, 32.41;H, 8.16; N, 37.83. Found: C, 32.36; H, 8.23; N, 37.88.

N-Nitrosodiethylamine: Yellow oil, b.p. 175–177°C (Lit.[15] 177°C); IR (KBr)ν: 2973, 1451, 1223, 1058; ^1H NMR ($CDCl_3$)δ : 1.12 (t, 3H, CH_3), 1.44 (t, 3H, CH_3), 3.61 (q, 2H, CH_2), 4.13 (q, 2H, CH_2); Anal. Calcd for $C_4H_{10}N_2O$: C, 47.02; H, 9.87; N, 27.43. Found: C, 47.12; H, 9.80; N, 27.46.

N-Nitrosodiisopropylamine: White crystal, m.p. 47–48°C (Lit.[15] 48°C); IR (KBr)ν: 2962, 1466, 1382, 1120; ^1H NMR ($CDCl_3$)δ : 1.13(d, 6H, $2CH_3$), 1.51(d, 6H, $2CH_3$), 2.8-3.4 (m, 2H, 2CH); Anal.

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Calcd for $C_6H_{14}N_2O$: C, 55.33; H, 10.84; N, 21.53. Found: C, 55.18; H,10.89; N, 21.48.

N-Nitrosodibutylamine: Yellow liquid, b.p. 103–104°C /8 mm (Lit.[16] 104–105°C /8mm); IR (KBr)ν: 2978, 1449, 1382, 1070; ^{1}H NMR ($CDCl_3$)δ: 0.92 (t, 6H, $2CH_3$), 1.12–2.13 (m, 8H, $4CH_2$), 3.58 (t, 2H, CH_2), 4.09 (t, 2H, CH_2); Anal. Calcd for $C_8H_{18}N_2O$: C, 60.70; H, 11.47; N, 17.71. Found: C, 60.10; H, 11.58; N, 17.68.

N-Nitrosopyrrolidine: Yellow oil, b.p. 213°C (Lit.[15] 214°C); IR (KBr)ν: 2983, 1445, 1305, 1202; ^{1}H NMR ($CDCl_3$) δ: 2.10 (m, 4H, $2CH_2$), 3.51 (t, 2H, CH_2), 4.23 (t, 2H, CH_2); Anal. Calcd for $C_4H_8N_2O$: C, 47.96; H, 8.06; N, 27.99. Found: C, 47.86; H, 7.98; N, 28.12.

N-Nitrosodiphenylamine: Yellow crystal, m.p. 65–66°C (Lit.[15] 66.5°C); IR (KBr)ν: 3070, 1470, 1040, 748, 690; ^{1}H NMR ($CDCl_3$) δ: 7.02–7.56 (m, 10H, $2C_6H_5$); Anal. Calcd for $C_{12}H_{10}N_2O$: C, 72.69; H, 5.09; N, 14.14. Found: C, 72.72; H, 5.02; N, 14.21.

N-Nitrosoacetanilide: Yellow needles, m.p. 51–52°C (Lit.[15] 51°C); IR (KBr)ν: 3050, 2980, 1790, 1455, 760, 701; ^{1}H NMR ($CDCl_3$)δ: 2.06 (s, 3H, CH_3), 7.01–7.65 (m, 5H, C_6H_5); Anal. Calcd for $C_8H_8N_2O_2$: C, 58.51; H, 4.92; N, 17.07. Found: C, 58.45; H, 5.02; N, 17.14.

N-Methyl-N-nitrosoaniline:Yellow oil, b.p. 129°C /19 mm (Lit.[15] 128–128.4°C /19mm); IR (KBr)ν: 3070, 2973, 1595, 1450, 1091, 758, 704; ^{1}H NMR ($CDCl_3$) δ: 3.40 (s, 3H, CH_3), 7.18–7.55 (m, 5H, C_6H_5); Anal. Calcd for $C_7H_8N_2O$: C, 61.73; H, 5.92; N, 20.59. Found: C, 61.43; H, 6.01; N, 20.54.

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