***SHORT PAPER***

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# An efficient method for the oxidation of aryl substituted semicarbazides to aryl azo compounds with $NaNO_2$-$Ac_2O$†

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In this paper 18 aryl substituted semicarbazides undergo rapid oxidation to the corresponding aryl azo compounds using $NaNO_2$-acetic anhydride as a novel oxidizing agent under mild conditions for the first time.

**Keywords:** oxidation, aryl azo compounds, $NaNO_2$-acetic anhydride, mild condition

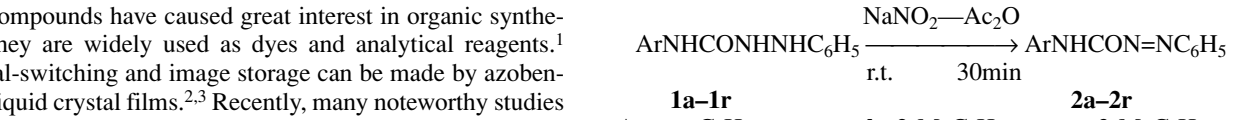
Azo compounds have caused great interest in organic synthesis. They are widely used as dyes and analytical reagents.[1] Optical-switching and image storage can be made by azobenzene liquid crystal films.[2,3] Recently, many noteworthy studies have shown that some azo compounds possess excellent optical memory and photoelectric properties.[4,5]

The oxidation of aryl substituted semicarbazides to aryl azo compounds is an important transformation in organic synthesis. We have been paying particular and continuous attention to this field. In our laboratory, $FeCl_3{\cdot}6H_2O$,[6] 4-hydroxy-2,2,6,6-tetramethyl-1-piperidinyloxy,[7] DMF-$NO_x$,[8] $KClO_3/H_2SO_4/FeSO_4$,[9] NBS/pyridine[10] and galvinoxyl[11] have been used as effective oxidants with good results. But most of the methods are deficient in some aspects. For example, tedious operation,[7,10,11] expensive catalysts,[7,11] the use of a large amount of solvent,[7,10,11] strong acidic or basic media,[6,9] and an accurate control of the molar ratio of oxidants[8]. These limit their application in organic synthesis. $Fe(NO_3)_3{\cdot}9H_2O$[12] was also used as efficient reagent for the oxidation of aryl substituted semicarbazides, which are fast and simple.

To continue our research project on the synthesis of azo compounds, we decided to develop a new reagent or reagent system to overcome the above limitations. $NaNO_2$–$Ac_2O$ is known oxidation system for the rapid and selective oxidation of a variety of alcohols to their corresponding carbonyl compounds.[13] We rationalised that this method might be suitable for the oxidation of aryl substituted semicarbazide to azo compounds. After our experiments, it was demonstrated that this is an effective reagents. All reactions were performed smoothly at room temperature (Scheme 1) and completed within 30min with excellent yields. The results are summarised in Table 1.

In the oxidation study, we selected **1a** as a model, a relatively unreactive substrate. The optimum molar ratio was searched by using **1a** (1mmol) with different molar ratio of $NaNO_2$:$Ac_2O$. The results are summarised in Table 2. If $NaNO_2$ was used for the oxidation of **1a** alone, the reaction could occur after stirring 24h. The optimum molar ratio $NaNO_2$:$Ac_2O$ (3:3) is required for complete oxidation of **1a**.

Overall, we recommend this simple, clean and economical procedure for the oxidation of aryl substituted semicarbazide with excellent yields under mild conditions. In all cases, clean




**1a–1r** **2a–2r**

Ar: **a:** $C_6H_5$ **b:** 2-$MeC_6H_4$ **c:** 3-$MeC_6H_4$
**d:** 4-$MeC_6H_4$ **e:** 4-$EtOC_6H_4$ **f:** 2,3-$Me_2C_6H_3$
**g:** 2,5-$Me_2C_6H_3$ **h:** 2,6-$Me_2C_6H_3$ **i:** 3,4-$Me_2C_6H_3$
**j:** α-$C_{10}H_7$ **k:** 4-$FC_6H_4$ **l:** 2-$ClC_6H_4$
**m:** 3-$ClC_6H_4$ **n:** 4-$ClC_6H_4$ **o:** 2-$BrC_6H_4$
**p:** 3-$BrC_6H_4$ **q:** 4-$BrC_6H_4$ **r:** 4-$IC_6H_4$

**Scheme 1**

**Table 1** The oxidation of aryl substituted semicarbazides using the oxidation system of $NaNO_2$–$Ac_2O$

| Product | Ar | Yield/% | M.p./°C | Lit. mp./°C |
|---|---|---|---|---|
| **2a** | $C_6H_5$ | 97 | 109–111 | 110–112[11] |
| **2b** | 2-$MeC_6H_4$ | 92 | 103–104 | 103–105[11] |
| **2c** | 3-$MeC_6H_4$ | 97 | 70–72 | 69–71[11] |
| **2d** | 4-$MeC_6H_4$ | 96 | 103–105 | 104–106[11] |
| **2e** | 4-$EtOC_6H_4$ | 93 | 125–126 | 127–129[11] |
| **2f** | 2,3-$Me_2C_6H_3$ | 98 | 122–124 | 122–124[11] |
| **2g** | 2,5-$Me_2C_6H_3$ | 93 | 120–122 | 121–123[11] |
| **2h** | 2,6-$Me_2C_6H_3$ | 97 | 118–120 | 118–120[11] |
| **2i** | 3,4-$Me_2C_6H_3$ | 92 | 126–128 | 126–128[11] |
| **2j** | α-$C_{10}H_7$ | 94 | 134–136 | 132–134[11] |
| **2k** | 4-$FC_6H_4$ | 95 | 106–108 | 105–107[9] |
| **2l** | 2-$ClC_6H_4$ | 96 | 82–84 | 80–82[9] |
| **2m** | 3-$ClC_6H_4$ | 98 | 84–86 | 86–87[9] |
| **2n** | 4-$ClC_6H_4$ | 96 | 139–141 | 139–140[9] |
| **2o** | 2-$BrC_6H_4$ | 95 | 70–72 | 69–71[9] |
| **2p** | 3-$BrC_6H_4$ | 98 | 94–96 | 93–95[9] |
| **2q** | 4-$BrC_6H_4$ | 96 | 138–140 | 137–138[9] |
| **2r** | 4-$IC_6H_4$ | 98 | 133–135 | 132–134[9] |

**Table 2** Oxidation of **1a** (1mmol) with different molar ratio of $NaNO_2$:$Ac_2O$

| Entry | **1a**:$NaNO_2$:$Ac_2O$ | Reaction time | Yield/% |
|---|---|---|---|
| 1 | 1:1:1 | 30min | 40 |
| 2 | 1:1.5:1.5 | 30min | 50 |
| 3 | 1:2:2 | 30min | 65 |
| 4 | 1:2.5:2.5 | 30min | 80 |
| 5 | 1:3:3 | 30min | 97 |
| 6 | 1:4:4 | 30min | 95 |
| 7 | 1:3:3 | 3h | 95 |
| 8 | 1:3:0 | 24h | little |

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

transformation could be detected by TLC. We believe that the present methodology is an important addition to existing methodology.

## Experimental

Melting points were determined on Kolfler micro melting point apparatus and measured in °C without correction. Element analyses were performed on a Perkin-Elmer 240C analytical instrument. Infrared spectra were recorded on a SP3-300 spectra photometer using KBr pellets. $^1$HNMR spectra were measured in $CDCl_3$ using TMS as internal standard with a JEOL-90Q NMR spectrometer. Mass spectra were recorded on a KRATOS-AEI- MS50 (U.K.).

A mixture of aryl substituted semicarbazide (1mmol), acetic anhydride (0.306g, 3mmol) and $NaNO_2$ (0.207g, 3mmol) in acetone (15 ml) was vigorously stirred at room temperature. After completion of the reaction (TLC), the reaction mixture was filtered. Then cool water (30ml) was poured into the filtrate slowly. After 30min, the resulting precipitate were filtered, washed with water and dried under vacuum. No further purification was needed.

Under these experimental conditions no unusual safety problems were encountered on mixing of $NaNO_2$ and acetic anhydride in acetone solution or during the subsequent use of the mixture.

## Data of products

*Compound* **2a:** Red tabular crystals; IR (KBr) $\nu_{max}$: 3232, 3060, 1680, 1600, 1500, 1420 (cm$^{-1}$); $^1$HNMR ($CDCl_3$) δ(ppm): 7.03–7.80 (m, 10H,Ar-H), 8.90 (s, 1H, NH); MS (*m*/*z*): 225 ($M^+$), 120(100), 105, 92, 91, 77; Anal. Calcd. for $C_{13}H_{11}N_3O$: C, 69.31; H, 4.93; N, 18.66. Found: C, 69.13; H, 4.80; N, 19.13.

*Compound* **2b:** Orange tabular crystals; IR (KBr) $\nu_{max}$: 3240, 3060, 2995, 1682, 1580, 1480, 1402 (cm$^{-1}$); $^1$HNMR ($CDCl_3$) δ(ppm): 2.27 (s, 3H, $CH_3$), 7.06–7.98 (m, 9H,Ar-H), 8.90 (s, 1H, NH); Anal. Calcd. for $C_{14}H_{13}N_3O$: C, 70.29; H, 5.44; N, 17.57. Found: C, 70.18; H, 5.42; N, 17.91.

*Compound* **2c:** Orange tabular crystals; IR (KBr) $\nu_{max}$: 3260, 3030, 2970, 2850, 1685, 1598, 1470, 1425 (cm$^{-1}$); $^1$HNMR ($CDCl_3$) δ(ppm): 2.26 (s, 3H, $CH_3$), 6.80–8.02 (m, 9H,Ar-H), 8.25 (s, 1H, NH); Anal. Calcd. for $C_{14}H_{13}N_3O$: C, 70.29; H, 5.44; N, 17.57. Found: C, 70.11; H, 5.62; N, 17.81.

*Compound* **2d:** Orange tabular crystals; IR (KBr) $\nu_{max}$: 3320, 3050, 2990, 2850, 1685, 1600, 1580, 1442 (cm$^{-1}$); $^1$HNMR ($CDCl_3$) δ(ppm): 2.27 (s, 3H, $CH_3$), 7.10–8.05 (m, 9H,Ar-H), 8.26 (s, 1H, NH); Anal. Calcd. for $C_{14}H_{13}N_3O$: C, 70.29; H, 5.44; N, 17.57. Found: C, 70.15; H, 5.31; N, 17.84.

*Compound* **2e:** Orange needles; IR (KBr) $\nu_{max}$: 3320, 3050, 2995, 2880, 1675, 1580, 1490, 1433 (cm$^{-1}$); $^1$HNMR ($CDCl_3$) δ(ppm): 1.27 (t, 3H, $CH_3$), 3.90 (q, 2H, CH2), 6.81–8.00 (m, 9H,Ar-H), 8.25 (s, 1H, NH); Anal. Calcd. for $C_{15}H_{11}N_3O$: C, 66.91; H, 5.58; N, 15.61. Found: C, 67.01; H, 5.30; N, 15.42.

*Compound* **2f:** Brown tabular crystals; IR (KBr) $\nu_{max}$: 3220, 3020, 2965, 2900, 1695, 1580, 1495, 1430 (cm$^{-1}$); $^1$HNMR ($CDCl_3$) δ(ppm): 2.20 (s, 6H, $2CH_3$), 7.02–8.02 (m, 8H,Ar-H), 8.21 (s, 1H, NH); Anal. Calcd. for $C_{15}H_{15}N_3O$: C, 71.15; H, 5.93; N, 16.60. Found: C, 70.94; H, 5.65; N, 16.79.

*Compound* **2g:** Yellow tabular crystals; IR (KBr) $\nu_{max}$: 3225, 3040, 2960, 2850, 1680, 1580, 1490, 1450 (cm$^{-1}$); $^1$HNMR ($CDCl_3$) δ(ppm): 2.25 (s, 6H, $2CH_3$), 7.80–8.02 (m, 8H,Ar-H), 8.20 (s, 1H, NH); Anal. Calcd. for $C_{15}H_{15}N_3O$: C, 71.15; H, 5.93; N, 16.60. Found: C, 71.10; H, 5.75; N, 16.80.

*Compound* **2h:** Orange tabular crystals; IR (KBr) $\nu_{max}$: 3300, 3010, 2950, 2840, 1685, 1580, 1485, 1435 (cm$^{-1}$); $^1$HNMR ($CDCl_3$) δ(ppm): 2.24 (s, 6H, $2CH_3$), 7.42–8.02 (m, 8H,Ar-H), 8.77 (s, 1H, NH); Anal. Calcd. for $C_{15}H_{15}N_3O$: C, 71.15; H, 5.93; N, 16.60. Found: C, 71.05; H, 5.73; N, 16.50.

*Compound* **2i:** Orange tabular crystals; IR (KBr) $\nu_{max}$: 3250, 3060, 2965, 2900, 1690, 1590, 1445, 920 (cm$^{-1}$); $^1$HNMR ($CDCl_3$) δ(ppm): 2.20 (s, 6H, $2CH_3$), 7.05–8.02 (m, 8H,Ar-H), 8.22 (s, 1H, NH); Anal. Calcd. for $C_{15}H_{15}N_3O$: C, 71.15; H, 5.93; N, 16.60. Found: C, 71.08; H, 5.28; N, 16.81.

*Compound* **2j:** Orange needles; IR (KBr) $\nu_{max}$: 3260, 3040, 1685, 1590, 1478, 1440, 923 (cm$^{-1}$); $^1$HNMR ($CDCl_3$) δ(ppm): 7.04–8.24 (m, 12H,Ar-H), 8.83 (s, 1H, NH); Anal. Calcd. for $C_{17}H_{13}N_3O$: C, 74.18; H, 4.73; N, 15.27. Found: C, 74.36; H, 4.23; N, 15.46.

*Compound* **2k:** Yellow needles; IR (KBr) $\nu_{max}$: 3340, 3020, 1710, 1600, 1500, 1420 (cm$^{-1}$); $^1$HNMR ($CDCl_3$) δ(ppm): 7.09–8.03 (m, 9H,Ar-H), 8.45 (s, 1H, NH); MS (*m*/*z*): 243 ($M^+$), 138(100), 110, 105, 90, 77; Anal. Calcd. for $C_{13}H_{10}N_3OF$: C, 64.19; H, 4.14; N, 17.28. Found: C, 64.28; H, 4.18; N, 17.20.

*Compound* **2l:** Orange tabular crystals; IR (KBr) $\nu_{max}$: 3340, 3020, 1710, 1600, 1500, 1420 (cm$^{-1}$); $^1$HNMR ($CDCl_3$) δ(ppm): 7.09–8.03 (m, 9H,Ar-H), 8.45 (s, 1H, NH); Anal. Calcd. for $C_{13}H_{10}N_3OCl$: C, 60.13; H, 3.88; N, 16.18. Found: C, 60.21; H, 3.90; N, 16.15.

*Compound* **2m:** Red tabular crystals; IR (KBr) $\nu_{max}$: 3260, 3030, 1680, 1600, 1480, 1430 (cm$^{-1}$); $^1$HNMR ($CDCl_3$) δ(ppm): 7.10–8.60 (m, 9H,Ar-H), 9.06 (s, 1H, NH); Anal. Calcd. for $C_{13}H_{10}N_3OCl$: C, 60.13; H, 3.88; N, 16.18. Found: C, 60.34; H, 3.92; N, 16.10.

*Compound* **2n:** Red tabular crystals; IR (KBr) $\nu_{max}$: 3320, 3050, 1680, 1600, 1585, 1440 (cm$^{-1}$); $^1$HNMR ($CDCl_3$) δ(ppm): 7.20–8.05 (m, 9H,Ar-H), 8.60 (s, 1H, NH); MS (*m*/*z*): 259($M^+$), 154, 126(100), 105, 90, 77; Anal. Calcd. for $C_{13}H_{10}N_3OCl$: C, 60.13; H, 3.88; N, 16.18. Found: C, 60.59; H, 3.90; N, 15.95.

*Compound* **2o:** Red tabular crystals; IR (KBr) $\nu_{max}$: 3280, 3040, 1680, 1580, 1500, 1435 (cm$^{-1}$); $^1$HNMR ($CDCl_3$) δ(ppm): 7.10–8.60 (m, 9H,Ar-H), 9.04 (s, 1H, NH); Anal. Calcd. for $C_{13}H_{10}N_3OBr$: C, 51.49; H, 3.33; N, 13.86. Found: C, 51.79; H, 3.36; N, 13.94.

*Compound* **2p:** Orange needles; IR (KBr) $\nu_{max}$: 3320, 3030, 1700, 1580, 1500, 1430 (cm$^{-1}$); $^1$HNMR ($CDCl_3$) δ(ppm): 7.08–8.57 (m, 9H,Ar-H), 9.05 (s, 1H, NH); Anal. Calcd. for $C_{13}H_{10}N_3OBr$: C, 51.49; H, 3.33; N, 13.86. Found: C, 51.60; H, 3.41; N, 13.71.

*Compound* **2q:** Red tabular crystals; IR (KBr) $\nu_{max}$: 3325, 3040, 1680, 1580, 1490, 1450 (cm$^{-1}$); $^1$HNMR ($CDCl_3$) δ(ppm): 7.08–8.57 (m, 9H,Ar-H), 9.05 (s, 1H, NH); MS (*m*/*z*): 305 (M+2), 303 ($M^+$), 200, 198, 172, 170(100), 105, 90, 77; Anal. Calcd. for $C_{13}H_{10}N_3OBr$: C, 51.49; H, 3.33; N, 13.86. Found: C, 51.63; H, 3.44; N, 13.87.

*Compound* **2r:** Orange tabular crystals; IR (KBr) $\nu_{max}$: 3300, 3020, 1680, 1580, 1485, 1440 (cm$^{-1}$); $^1$HNMR ($CDCl_3$) δ(ppm): 7.26–8.00 (m, 9H,Ar-H), 8.57 (s, 1H, NH); MS (*m*/*z*): 351 ($M^+$), 246(100), 218, 105, 90, 77; Anal. Calcd. for $C_{13}H_{10}N_3OBr$: C, 51.49; H, 3.33; N, 13.86. Found: C, 51.63; H, 3.44; N, 13.87.

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