A Simple and Efficient Method for the Oxidation of Aryl Substituted Semicarbazide with $NaNO_2/NaHSO_4{\cdot}H_2O/SiO_2$ under Mild Conditions

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In this paper, eighteen aryl substituted semicarbazide underwent efficient oxidation to aryl azo compounds using $NaNO_2/NaHSO_4{\cdot}H_2O/SiO_2$ under mild conditions with excellent yields.

INTRODUCTION

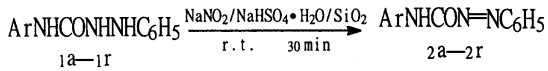
Azo compounds have caused great interest in organic synthesis. They are widely used as dyes and analytical reagents.[1] Optical-switching and image storage can be made by azobenzene liquid crystal film.[2,3] Recently, many noteworthy studies have shown that some azo compounds possess excellent optical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

Substituted semicarbazide or carbazide can make many reactions,[6,7] such as oxidation, reduction, substitution, cyclization, condensation and addition. The oxidation of aryl substituted semicarbazide into aryl azo compounds is an important transformation in organic synthesis. We have been paying particular and continuous attention to this field. In our laboratory, $FeCl_3{\cdot}6H_2O$,[8] DMF-NO_x,[9] $KClO_3/H_2SO_4/FeSO_4$,[10] Galvinoxy[11] and NBS/pyridine[12] have been used as effective oxidants and gotten relatively better results. But most of the methods are deficient because of tedious operation,[11,12] expensive catalysts,[11] the use of a large amount of solvent,[11,12] or strong acid or basic media.[8,10] These limit their application in organic synthesis. Therefore, there is much room for improvement of the existing methods.

RESULTS AND DISCUSSION

In continuation of our studies on the synthesis of azo compounds, we decided to develop a new reagent or reagent system to overcome the above limitations. The combination of $NaNO_2$ and $NaHSO_4{\cdot}H_2O$ in the presence of SiO_2 has been used as an effective oxidizing agent for the dehydrogenation of 4-substituted-1,2,4-triazole-3,5-diones successfully.[13] The $[NO^+{\cdot}crown{\cdot}H(NO_3)_2^-]$ complex is also reported as an effective oxidizing agent for its dehydrogenation.[14] We rationalized that $NaNO_2/NaHSO_4{\cdot}H_2O$ might be suitable for the oxidation of aryl substituted semicarbazide. After our experiments, it was demonstrated that this is an effective reagent. All reactions were performed smoothly at room temperature (Scheme I) and completed within 30 min with excellent yields.

Scheme I



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

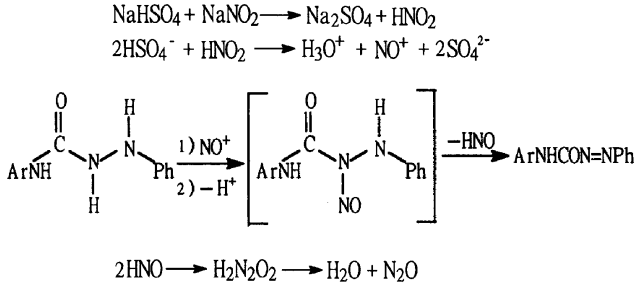
Table 1. Oxidation of **1a** (1 mmol) in the Presence of SiO_2 (0.3 g, 60-100 mesh) with Different Molar Ratios of $NaNO_2$[a]:$NaHSO_4{\cdot}H_2O$[a]

Entry	$NaNO_2$:$NaHSO_4{\cdot}H_2O$	Reaction time	Yield (%)
1	1:1	30 min	40
2	1.5:1.5	30 min	55
3	2:2	30 min	65
4	2.5:2.5	30 min	80
5	3:3	30 min	98
6	3:3	3 h	95
7	3:3	30 min	40[b]
8	3:0	24 h	a little

[a] crushed to a fine powder [b] without SiO_2

In the oxidation study, we selected **1a** as a model, a relatively unreactive substrate. The optimum molar ratio was searched by reaction using **1a** (1 mmol) and SiO_2 (0.3 g, 60-100 mesh) with various molar ratios of $NaNO_2$:$NaHSO_4 \cdot H_2O$. The results are summarized in Table 1. If $NaNO_2$ was used for the oxidation alone, the reaction did not occur after stirring 24 h. The oxidation of **1a** was efficiently achieved with this oxidation system. The presence of SiO_2 is crucial. Although the reaction occurs without SiO_2, the reaction period would be much longer. Therefore, we thought that the presence of SiO_2 will act as a media and will provide a heterogeneous effective surface area for the generation of HNO_2. No additional products were identified from this reaction. The possible mechanism is shown in Scheme II.

Scheme II



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

EXPERIMENTAL SECTION

Melting points were determined on a Kolfler micro melting points apparatus and measured in °C without correction. Elemental analyses were performed on a Perkin-Elmer 240C analytical instrument. Infrared spectra were recorded on a SP3-300 spectra photometer using KBr pellets. ^{1}H NMR 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.).

General Procedure for the Preparation of Aryl Azo Compounds

A mixture of aryl substituted semicarbazide (1 mmol), $NaNO_2$ (0.207 g, 3 mmol) and $NaHSO_4 \cdot H_2O$ (0.324 g, 3 mmol) and SiO_2 (0.3 g, 60-100 msh) in acetone (15 mL) was vigorously stirred at room temperature. After completion of the reaction (TLC), the reaction mixture was filtered. Then cool water (30 mL) was poured into the filtrate slowly. After 30 min, the resulting precipitate was collected, washed with water, recrystallized from EtOH-H_2O (3:1) mixture and dried under vacuum.

2a: red tabular; Yield 98%; mp 109-111 °C; IR (KBr) ν_{max}: 3232, 3060, 1680, 1600, 1500, 1420 (cm^{-1}); ^{1}H NMR ($CDCl_3$) δ (ppm): 7.03-7.80 (m, 10H, Ar-H), 8.90 (s, 1H, NH); MS (*m/z*): 225 (M^+), 120 (B), 105, 92, 91, 77; Anal. Calcd. for $C_{13}H_{11}N_3O$: C, 69.31; H, 4.93; N, 18.66. Found: C, 69.07; H, 5.11; N, 18.89.

2b: orange tabular; Yield 94%; mp 103-104 °C; IR (KBr) ν_{max}: 3240, 3060, 2995, 1682, 1580, 1480, 1402 (cm^{-1}); ^{1}H NMR ($CDCl_3$) 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, 70.14; H, 5.38; N, 17.85.

2c: orange tabular; Yield 95%; mp 70-72 °C; IR (KBr) ν_{max}: 3260, 3030, 2970, 2850, 1685, 1598, 1470, 1425 (cm^{-1}); ^{1}H NMR ($CDCl_3$) 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.

2d: orange tabular; Yield 94%; mp 103-105 °C; IR (KBr) ν_{max}: 3320, 3050, 2990, 2850, 1685, 1600, 1580, 1442 (cm^{-1}); ^{1}H NMR ($CDCl_3$) 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.

2e: orange needle; Yield 96%; mp 125-126 °C; IR (KBr) ν_{max}: 3320, 3050, 2995, 2880, 1675, 1580, 1490, 1433 (cm^{-1}); ^{1}H NMR ($CDCl_3$) δ (ppm): 1.27 (t, 3H, CH_3), 3.90 (q, 2H, CH_2), 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.

2f: brown tabular; Yield 92%; mp 122-124 °C; IR (KBr) ν_{max}: 3220, 3020, 2965, 2900, 1695, 1580, 1495, 1430 (cm^{-1}); ^{1}H NMR ($CDCl_3$) 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.

2g: yellow tabular; Yield 91%; mp 120-122 °C; IR (KBr) ν_{max}: 3225, 3040, 2960, 2850, 1680, 1580, 1490, 1450 (cm^{-1}); ^{1}H NMR ($CDCl_3$) 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.

2h: orange tabular; Yield 97%; mp 118-120 ℃; IR (KBr) ν_{max}: 3300, 3010, 2950, 2840, 1685, 1580, 1485, 1435 (cm^{-1}); ^1H NMR ($CDCl_3$) 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.

2i: orange tabular; Yield 96%; mp 126-128 ℃; IR (KBr) ν_{max}: 3250, 3060, 2965, 2900, 1690, 1590, 1445, 920 (cm^{-1}); ^1H NMR ($CDCl_3$) 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, 71.01; H, 5.76; N, 16.88.

2j: orange needle; Yield 96%; mp 134-136 ℃; IR (KBr) ν_{max}: 3260, 3040, 1685, 1590, 1478, 1440, 923 (cm^{-1}); ^1H NMR ($CDCl_3$) 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, 74.42; H, 4.53; N, 15.50.

2k: yellow needle; Yield 95%; mp 106-108 ℃; IR (KBr) ν_{max}: 3340, 3020, 1710, 1600, 1500, 1420 (cm^{-1}); ^1H NMR ($CDCl_3$) δ (ppm): 7.09-8.03 (m, 9H, Ar-H), 8.45 (s, 1H, NH); MS (*m/z*): 243 (M^+), 138, 110 (B), 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.

2l: orange tabular; Yield 92%; mp 82-84 ℃; IR (KBr) ν_{max}: 3340, 3020, 1710, 1600, 1500, 1420 (cm^{-1}); ^1H NMR ($CDCl_3$) 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.

2m: red tabular; Yield 98%; mp 84-86 ℃; IR (KBr) ν_{max}: 3260, 3030, 1680, 1600, 1480, 1430 (cm^{-1}); ^1H NMR ($CDCl_3$) 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.

2n: red tabular; Yield 95%; mp 139-141 ℃; IR (KBr) ν_{max}: 3320, 3050, 1680, 1600, 1585, 1440 (cm^{-1}); ^1H NMR ($CDCl_3$) δ (ppm): 7.20-8.05 (m, 9H, Ar-H), 8.60 (s, 1H, NH); MS (*m/z*): 259 (M^+), 154, 126 (B), 105, 90, 77; Anal. Calcd. for $C_{13}H_{10}N_3OCl$: C, 60.13; H, 3.88; N, 16.18. Found: C, 60.42; H, 3.99; N, 15.91.

2o: red tabular; Yield 93%; mp 70-72 ℃; IR (KBr) ν_{max}: 3280, 3040, 1680, 1580, 1500, 1435 (cm^{-1}); ^1H NMR ($CDCl_3$) 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.

2p: orange needle; Yield 98%; mp 94-96 ℃; IR (KBr) ν_{max}: 3320, 3030, 1700, 1580, 1500, 1430 (cm^{-1}); ^1H NMR ($CDCl_3$) 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.

2q: red tabular; Yield 96%; mp 138-140 ℃; IR (KBr) ν_{max}: 3325, 3040, 1680, 1580, 1490, 1450 (cm^{-1}); ^1H NMR ($CDCl_3$) 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 (B), 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.

2r: orange tabular; Yield 97%; mp 133-135 ℃; IR (KBr) ν_{max}: 3300, 3020, 1680, 1580, 1485, 1440 (cm^{-1}); ^1H NMR ($CDCl_3$) δ (ppm): 7.26-8.00 (m, 9H, Ar-H), 8.57 (s, 1H, NH); MS (*m/z*): 351 (M^+), 246, 218 (B), 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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Key Words

Aryl substituted semicarbazide;
$NaNO_2/NaHSO_4{\cdot}H_2O/SiO_2$; Mild conditions.

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