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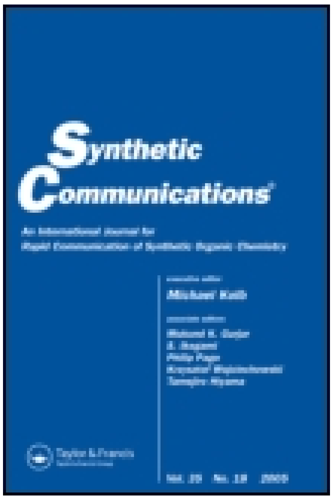

Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Facile Transfer Hydrogenation of Azo Compounds to Hydrazo Compounds and Anilines by Using Raney Nickel and Hydrazinium Monoformate

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Published online: 16 Aug 2006.

To cite this article: H. S. Prasad , Shankare Gowda & D. Channe Gowda (2004) Facile Transfer Hydrogenation of Azo Compounds to Hydrazo Compounds and Anilines by Using Raney Nickel and Hydrazinium Monoformate, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 34:1, 1-10, DOI: 10.1081/SCC-120027231

To link to this article: http://dx.doi.org/10.1081/SCC-120027231

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SYNTHETIC COMMUNICATIONS®
Vol. 34, No. 1, pp. 1–10, 2004

Facile Transfer Hydrogenation of Azo Compounds to Hydrazo Compounds and Anilines by Using Raney Nickel and Hydrazinium Monoformate

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ABSTRACT

Azo compounds are conveniently reduced to either partially reduced hydrazo compounds or completely reduced anilines by employing Raney nickel in presence of hydrazinium monoformate depending upon reaction conditions. The other reducible moieties like –COOH and halogens are tolerated. The reduction process is selective, rapid and high yielding.

Key Words: Azo compounds; Hydrazo compounds; Anilines; Raney nickel; Hydrazinium monoformate; Catalytic transfer hydrogenation.

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DOI: 10.1081/SCC-120027231
0039-7911 (Print); 1532-2432 (Online)
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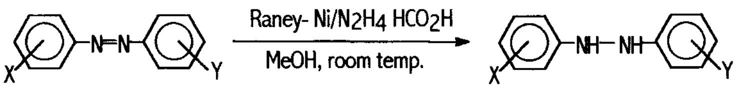
Reduction of aromatic azo and azoxy compounds has received a good deal of attention, both preparatively and analytically. Reductive cleavage of azo and azoxy benzenes has become a useful tool in structural determination of azo dyes.[1] There are some methods available in the literature for the conversion of azo compounds to hydrazo compounds[2–6] and amines.[1,2,7,8] But the earlier mentioned methods require longer reaction time and expensive catalysts such as Pd/C[2] and 5%Pd on asbestos.[9] If the azo compounds contain reducible or hydrogenolysable groups like halogen or nitrile, then the systems like 10% Pd-C/$HCOONH_4$[10] and 10% Pd-C/triethylammonium formate[11] reduce the nitriles to methyl groups and reductively remove the halogen from the aromatic ring. Moreover, poor yields were reported during the reduction of azo compounds to anilines.

Raney nickel is routinely used as a catalyst in the field of catalytic hydrogenation [12] as well as in the field of heterogeneous catalytic transfer hydrogenation.[13–18] It is used for the selective reduction of nitro compounds,[15] dinitro substituted diphenylsulfones,[18] *O*- and *N*-benzyl containing nitro compounds,[13] for the conversion of nitro olefins into carbonyl derivatives,[19] and for the synthesis of halo amines from halo nitro compounds.[16] In all these cases, hydrogen donors like formic acid, cyclohexene,[9] ammonium formate,[20] triethylammonium formate,[21] hydrazine[22] and hydrazine derivatives like methyl hydrazine,[22] unsymmetrical dimethyl hydrazine[22] and phenyl hydrazine in presence of various metals are commonly used. Recently, we reported that hydrazinium monoformate, a new hydrogen donor with magnesium as catalyst for deblocking protecting groups in peptide synthesis[23] and also successfully employed for the reduction of nitro compounds and nitrile moieties to the corresponding amines and methyl amines by using Raney nickel/hydrazinium monoformate.[24]

In this communication, we wish to report a rapid, selective and simple transfer hydrogenation of symmetrically and unsymmetrically substituted azo compounds to the corresponding hydrazo compounds and anilines by using Raney nickel and hydrazinium monoformate when carried out at room temperature (Sch. 1) and at reflux temperature (Sch. 2) respectively. The other functional groups like –OH, –COOH and halogens are tolerated.



X or Y = -H, halogen, -OH, $-OCH_3$, -COOH, $-CH_3$

Scheme 1.

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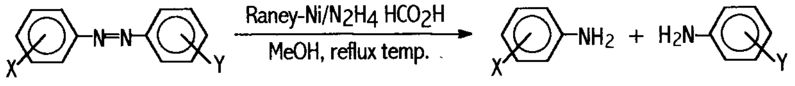

X or Y = -H, halogen, -OH, -OCH 3, -COOH, -CH3

Scheme 2.

The reduction of azo compounds to hydrazo compounds in the presence of Raney nickel and hydrazinium monoformate at room temperature was completed within 5 to 15 min. The course of reaction was monitored by thin layer chromatography (or colour disappearance of the starting material) and concomitant formation of the product. All the reduced products of azo compounds (few examples are listed in Table 1) by this system were obtained in good yields. The products were characterized by comparison of their melting points, TLC and IR spectra with authentic samples. The disappearance of a strong absorption band between 1630–1575 cm^{-1} due to –N=N– stretching and the appearance of strong absorption band between 2290–2440 cm^{-1} due to the –NH–NH– group, clearly showed that azo compounds have been reduced to hydrazo compounds. When a control experiment was carried out using azo compound with hydrazinium monoformate, in absence of Raney nickel, the reaction did not proceed at all.

The azo compounds were reductively cleaved to the corresponding substituted anilines in the presence of Raney nickel and hydrazinium monoformate at reflux temperature. The course of reaction was monitored by thin layer chromatography and IR spectra. The work-up and isolation of the products were easy. Thus, all the reduced products (few examples are listed in Table 2) by this system were obtained in good yields. The products were characterized by comparison of their melting points, TLC and IR spectra with authentic samples. The disappearance of a strong absorption band between 1630–1575 cm^{-1} due to the –N=N– stretching and the appearance of a strong absorption band between 3500–3300 cm^{-1} due to the –NH$_2$ group clearly showed that the azo compounds had been cleaved into their substituted anilines. Furthermore there was no absorption between 2290–2440 cm^{-1}, which clearly indicated the absence of the –NH–NH– group. A control experiment was carried out using azo compounds with hydrazinium monoformate in the absence of Raney nickel, but it did not yield the desired product. The appearance of one spot in TLC in the case of symmetrical azo compounds and two spots, in the case of unsymmetrical azo compounds clearly indicated that no hydrazo compounds were formed during the reductive cleavage of the azo compounds.

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Table 1. Catalytic transfer hydrogenation of azo compounds to hydrazo compounds by using Raney nickel and hydrazinium monoformate at room temperature.

				Melting point (°C)	
Substrate	Product	Duration (min)	Yield (%)[a]	Found	Lit.[25]
Azobenzene	Hydrazobenzene	5	85	125–126	127
4,4′-Dimethyl azobenzene	4,4′-Dimethyl hydrazobenzene	3	86	133–135	134
3,3′-Dimethyl azobenzene	3,3′-Dimethyl hydrazobenzene[b]	5	85	Oil	38
4,4′-Diethoxy azobenzene	4,4′-Diethoxy hydrazobenzene	8	87	83–85	86
3,3′-Diethoxy azobenzene	3,3′-Diethoxy hydrazobenzene	10	90	121–122	119
2,2′-Dimethoxy azobenzene	2,2′-Dimethoxy hydrazobenzene	10	88	99–101	102
2,2′-Azodiphenol	2,2′-Hydrazodiphenol	12	84	149–151	148
2,2′-Azonaphthalene	2,2′-Hydrazonaphthalene	15	85	140–142	141
4,4′-Azodibiphenyl	4,4′-Hydrazodibiphenyl	15	82	168–170	169
3,3′-Dichloroazobenzene	3,3′-Dichlorohydrazobenzene[b]	5	88	89–91	—
Methylorange	N, N′-Dihydromethylorange[b]	5	50[c]	Oil	—
Methylred	N, N′-Dihydromethylred[b]	3	56[c]	Oil	—
Azobenzene 4-carboxylic acid	N, N′-Dihydroazobenzene 4-carboxylic acid[b]	12	60[c]	176–178	—

[a] Isolated yields are based on single experiment and the yields were not optimized.

[b] Satisfactory elementary analysis is obtained for these compounds.

[c] The low yield is due to water soluble nature of these compounds, but TLC analysis shows more than 90% reduction.

Furthermore, the hydrazinium monoformate/Raney nickel system is more effective than either cyclohexene/5% Pd on asbestos,[9] hydrazine/10% Pd-C[2] or $HCOONH_4$/10% Pd-C,[1] Most of the reactions were completed in less than 15 min. at reflux temperature. But the earlier mentioned methods require longer reaction time e.g., 16 to 48 h and high temperature.

Thus the azo compounds were easily reduced to either hydrazo compounds or anilines in a shorter duration, depending upon reaction temperatures, with Raney nickel, instead of using expensive catalyst such as palladium without affecting other reducible substituents. The yields were virtually quantitative and the products were analytically pure. This procedure will therefore be of general use, especially in cases where rapid, mild and selective reduction is required.

EXPERIMENTAL

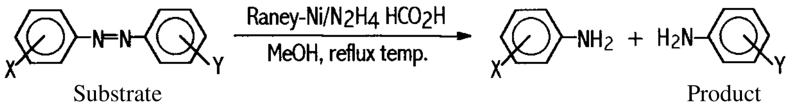
Materials

Some of the azo compounds were purchased from Aldrich Chemical Company (USA). The rest of the azo compounds were prepared according to standard procedures reported earlier.[5] Raney nickel, formic acid and hydrazine were purchased from SISCO Research Laboratories Pvt. Ltd., Bombay (India). All of the solvents used were analytical grade or were purified according to standard procedures. Thin layer chromatography was carried out on silica gel plates obtained from Whatman Inc. The melting points were determined by using a Thomas–Hoover melting point apparatus and are uncorrected. IR spectra were recorded on a Shimadzu FTIR-8300 spectrometer. For preparative TLC plates were prepared from Kieselgel 60 GF_{254}, Merck, Darmstadt and for column chromatography 60–120 mesh silica gel was used (obtained from SISCO Research Laboratories) with a suitable eluting system 50 : 50 chloroform : benzene, 60 : 40 chloroform : benzene, 80 : 20 chloroform : benzene, 90 : 10 chloroform : benzene, 80 : 20 chloroform : methanol, 85 : 15 chloroform : methanol, 9 : 10 chloroform : methanol, 95 : 5 chloroform : methanol.

Typical Procedure

(a) Procedure for the preparation of hydrazinium monoformate: Equal moles of 85% formic acid and 99–100% hydrazine were neutralized slowly, cooling in an ice bath with stirring to obtain hydrazinium monoformate. The obtained hydrazinium monoformate is used as such for reactions.

Table 2. Rapid cleavage of azo compounds to anilines using Raney nickel and hydrazinium monoformate at reflux temperature.



Substrate		Product		Time	Yield	Melting point (°C)	
X	Y	X	Y	(min)	(%)	Found	Lit.
-H	-H	-H	-H	3	95	112^c	114[26]
$2\text{-}CH_3$	$2'\text{-}CH_3$	$2\text{-}CH_3$	$2\text{-}CH_3$	6	94	142^b	144[26]
$3\text{-}CH_3$	$3'\text{-}CH_3$	$3\text{-}CH_3$	$3\text{-}CH_3$	5	95	126^b	125[26]
2-Br	2′-Br	2-Br	2-Br	7	93	115^b	116[26]
$3\text{-}OC_2H_5$	$3'\text{-}OC_2H_5$	$3\text{-}OC_2H_5$	$3\text{-}OC_2H_5$	7	94	82^c	80[26]
-H	4′-COOH	-H	4-COOH	10	95, 80	$113,^c$ 188	114,[26] 186[26]
$4\text{-}N(CH_3)_2$	-H	$4\text{-}N(CH_3)_2$	-H	8	95, 95	52, 113^c	53,[27] 114[26]
$4\text{-}N(CH_3)_2$	$4'\text{-}SO_3Na$	$4\text{-}N(CH_3)_2$	$4\text{-}SO_3Na$	13	92, 55^d	52, n.d.	53,[27]

4-$N(CH_3)_2$	2′-COOH	4-$N(CH_3)_2$	2-COOH	15	91, 88	53, 146	53,[27] 145[26]
4-NH_2, 3-CH_3	2′-CH_3	4-NH_2, 3-CH_3	2-CH_3	12	92, 93	65, 144[b]	64,[26] 144[26]
3-$COCH_3$	3′-$COCH_3$	3-$COCH_3$	3-$COCH_3$	9	90	99	101[26]
4-Cl	4′-Cl	4-Cl	4-Cl	8	91	71	70[26]
4-NH_2	-H	4-NH_2	-H	5	93, 95	140, 113	141,[26] 114[26]
2-OH	2′-OH	2-OH	2-OH	7	89	172	174[26]
1,1′-Azonaphthalene		1-Aminonaphthalene		15	85	188	190[26]
4,4′-Diazobiphenyl		4-Aminobiphenyl[e]		15	85	53	—
2,2′-Azofluorene		2-Aminofluorene		15	80	162	160[28]

Note: In the case of unsymmetrical azo compounds, the first mentioned data refers to the left hand side fragment azo compound and the next mentioned data refers to the right hand side fragment of the reductively cleaved azo compound.

[a] Isolated yields are based on single experiment and the yields were not optimized.

[b] Melting point of benzoyl derivative.

[c] Melting point of acetyl derivative.

[d] The low yield is due to its water soluble nature, TLC analysis indicates 95–98% cleavage.

[e] Satisfactory elemental analysis is obtained for this compound.

n.d. Not determined.

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(b) Procedure for the reduction of azo compounds to hydrazo compounds: A suspension of an appropriate azo compound (10 mmole), Raney nickel (30 mmole) in methanol or in any suitable solvent (15 mL or requisite amount) and hydrazinium monoformate (20 mmole) was stirred under nitrogen atmosphere at room temperature. After the completion of the reaction (monitored by TLC or by colour disappearance of starting material), the reaction mixture was filtered through celite pad and washed with solvent. The combined filtrate and washings were evaporated under vacuum. The residue was taken into 15 mL chloroform or ether, washed twice with 15 mL saturated brine solution and finally with water. The organic layer was dried over anhydrous magnesium sulfate and the solvent was removed using rotary evaporator. Further, the products were purified either by preparative TLC or column chromatography. After the purification, the products were characterized by IR spectra and the melting points were compared with authentic samples.

(c) Procedure for the reduction of azo compounds to Amines: A suspension of an appropriate azo compound (10 mmole), Raney nickel (30 mmole) in methanol or in any suitable solvent (15 mL) and hydrazinium monoformate (30 mmole) was stirred under nitrogen atmosphere at reflux temperature. After the completion of the reaction (monitored by TLC), the reaction mixture was filtered through celite pad and washed with solvent. The combined filtrate and washings were evaporated under vacuum. The residue was taken into 15 mL chloroform or ether, washed twice with 15 mL saturated brine solution and finally with water. The organic layer was dried over anhydrous magnesium sulfate and the solvent was removed using rotary evaporator. Further, the products were separated and purified either by preparative TLC or column chromatography. After the purification, the products were characterized by IR spectra and the melting points were compared with authentic samples.

ACKNOWLEDGMENT

The authors wish to thank the University Grants Commission, New Delhi, India, for financial assistance.

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Received in the USA July 24, 2003