Reduction of Allylic Nitro Compounds to Oximes with Carbon Disulfide under Solid–Liquid Phase-Transfer Catalysis Conditions

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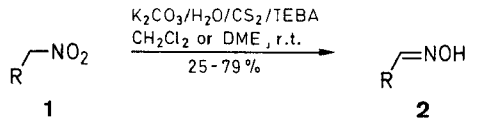
A mild procedure for the synthesis of allylic oximes **2** from the corresponding nitro derivatives **1**, using carbon disulfide as reducing agent in the presence of wet potassium carbonate and a catalytic amount of a phase-transfer agent, is described.

Barton and co-workers recently described an interesting procedure for the reduction of aliphatic nitro compounds to oximes using carbon disulfide in the presence of an excess of triethylamine under homogeneous conditions.[1] The process is particularly suitable for the reduction of allylic nitro derivatives. The choice of base was a crucial factor for a good outcome of the reaction; the use of a stronger base such as *N*-*tert*-butyl-*N'*,*N'*,*N''*,*N''*-tetramethylguanidine afforded a mixture of oxime and nitrile.

Potassium carbonate is a versatile and effective reagent for promoting base-catalyzed reactions especially under solid–liquid phase-transfer catalysis (SL-PTC) conditions.[2] Herein we report the successful reduction of allylic nitro derivatives **1** to the corresponding oximes **2** using carbon disulfide under SL-PTC conditions in the presence of wet potassium carbonate and catalytic amounts of a phase-transfer agent.

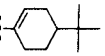


1 **2**

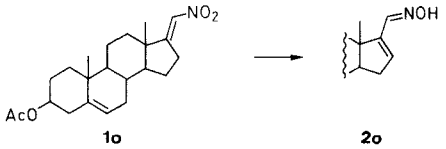
The examined substrates were 1-nitromethylcyclohexenes **1a–g**, 1-nitromethylcycloheptene (**1h**), 1-nitromethylcyclooctene (**1i**), 1-nitromethylcyclododecene (**1j**), 1-nitromethyl-3,4-dihydronaphthalene (**1k**), 4-nitromethyl-2*H*-1-benzothiopyran (**1l**), (2-nitro-1-phenylethylidene) cyclopentane (**1m**), 1-nitrooctane (**1n**) and 3-acetoxy-17-nitromethylene-5-androstene (**1o**) (Table 1). The spectroscopic data of new nitro compounds prepared and new oximes obtained are given in Tables 2 and 3.

4-Methyl-1-nitromethylcyclohexene (**1b**) was chosen as the model derivative for studying the factors affecting the reduction. Pertinent data are reported in Table 4. Entries 1–3 show that the highest yield of the oxime **2b** was obtained using 1.5 moles of carbon disulfide per mole of substrate **1b**. As expected for a reaction carried out under PTC conditions,[2,3] the reaction times decreased by increasing the amount of catalyst (entries 14, 15). In the absence of the latter the reaction was very slow and the

Table 1. Reduction of Nitro Compounds **1** to Oximes **2** with Carbon Disulfide Catalyzed by Wet Potassium Carbonate under SL-PTC Conditions[a]

	R	Reaction Time[b] (h)	Yield[c] (%)	mp (°C)	Molecular Formula[d] or Lit. mp (°C)
a		7	52	96–98	98–99[6]
b		8	60	93–94	$C_8H_{13}NO$ (139.2)
c		5	68 (72)	82–84	83–84[1]
d		14	60 (85)	131–133	132–133[1]
e		25	79	143–144	$C_{13}H_{15}NO$ (201.3)
f		25	51	135–137	$C_{13}H_{15}NO$ (201.3)
g		112[e]	25	126–129	$C_{11}H_{19}NO$ (181.3)
h		24	60	44–45	$C_8H_{13}NO$ (139.2)
i		168	60	59–60	$C_9H_{15}NO$ (153.2)
j		157	56 (83)	110–112	111–112[1]
k		8	60 (66)	75–77	75–77[1]
l		24	45	111–113	$C_{10}H_9NOS$ (191.3)
m		76[f]	50	157–158	$C_{13}H_{15}NO$ (201.3)
n	n-C_7H_{15}	120	no reaction	–	–
–[g]		200[h]	29 (59)	180–182	183–185[1]

[a] For reaction conditions, see experimental.
[b] Time for complete conversion of the substrate after the addition of CS_2 to the reaction mixture.
[c] Isolated yield.
[d] Satisfactory microanalyses obtained: C ±0.26, H ±0.24, N ±0.30.
[e] 60% Conversion of the substrate.
[f] 88% Conversion of the substrate.
[g] For the reaction.



1o **2o**

[h] 72% Conversion of the substrate.

yield of oxime was very poor (entry 20). Among the phase-transfer catalysts examined, benzyltriethylammonium chloride (TEBA) was the most efficient (entries 2, 16–19). Similar results were obtained by using dicyclohexano-18-crown-6 (DCH-18-C-6, entry 19). In the case of tetrabutylammonium bromide or hydrogen sulfate and hexadecyltributylphosphonium bromide, (entries 16–18) a complete conversion of **1b** was achieved under the same reaction time (8 h) but the yields of oxime **2b** were lower (35, 53%). The reduction was found to be very sensitive to both the nature and the amount of base employed. The best results were obtained by using 1 mole equivalent of wet potassium carbonate (entry 2). The presence of an excess of the latter gave lower yields (47%) of **2b** (entry 4). Wet potassium hydrogen carbonate (1 mole equiv.) afforded oxime **2b** with comparable yields (57%) but the reaction time was substantially longer (entry 11).

According to the results obtained in homogeneous media,[1] and also under SL-PTC conditions, the power of the base is a crucial factor for the reduction. In fact, the use of stronger bases, such as sodium hydroxide or a 1:1 mixture of sodium hydroxide and potassium carbonate, gave **2b** in 25 and 30% yields, respectively (entries 12, 13) together with comparable amounts of the corresponding nitrile. In the presence of sodium or lithium carbonate (entries 9, 10) the reaction rates were much lower, whereas the use of cesium carbonate (entry 8) gave complete conversion in 8 hours but produced **2b** in lower yields (50%).

As previously reported for reactions performed under SL-PTC conditions,[4] the presence of small amounts of water was found to be beneficial also for the reduction. The best results (entries 2, 6, 7) were obtained using 0.4–2 mole of water per mole of potassium carbonate. Under anhydrous conditions (entry 5) both reaction rates and yields were substantially lower.

The reduction carried out under liquid–liquid PTC conditions reached a 100% conversion in 1–3 hours, but

Table 2. Spectroscopic Data of New Oximes **2**

Compound	IR (Nujol) ν (cm^{-1}) OH, C=N	^{1}H-NMR ($CDCl_3$/TMS) δ, J(Hz)
2b	3210, 1640	1.00 (d, 3H, J = 6.0, CH_3), 1.60–2.60 (m, 7H_{aliph}), 5.95 (br s, 1H, CH=C), 7.70 (s, 1H, CH=N), 8.10 (br s, 1H, OH)
2e	3250, 1635	1.50–2.50 (m, 8H_{aliph}), 7.10–7.20 (m, 5H_{arom}), 7.55 (br s, 1H, CH=N), 8.30 (br s, 1H, OH)
2f	3250, 1630	1.20–2.60 (m, 6H_{aliph}), 3.80 (br s, 1H, CHC), 6.15 (br s, 1H, CH=C), 7.00–7.20 (m, 5H_{arom}), 7.50 (br s, 1H, CH=N), 8.00 (br s, 1H, OH)
2g	3260, 1640	0.90 (d, 3H, J = 5.7, CH_3), 0.95 (d, 6H, J = 6.9, CH_3CHCH_3), 1.15–2.50 (m, 7H_{aliph}), 2.90–3.20 (m, 1H, CH_3CHCH_3), 8.30 (s, 1H, CH=N), 9.20 (br s, 1H, OH)
2h	3320, 1635	1.30–2.90 (m, 10H_{aliph}), 6.10 (t, J = 6.9, 1H, CH=C), 7.45 (s, 1H, CH=N), 7.70 (s, 1H, OH)
2i	3250, 1635	1.05–2.60 (m, 12H_{aliph}), 5.90 (t, J = 9.1, 1H, CH=C), 7.05 (br s, 1H, OH), 7.61 (s, 1H, CH=N)
2l	3250, 1630	3.35 (d, 2H, J = 6.0, CH_2), 6.35 (t, 1H, J = 6.0, CH=C), 7.00–7.30 (m, 3H_{arom}), 7.50–7.70 (m, 1H_{arom}), 7.95 (s, 1H, CH=N), 8.50 (br s, 1H, OH)
2m	3250, 1635	1.30–2.70 (m, 8H_{aliph}), 7.00–7.40 (m, 5H_{arom}), 8.15 (s, 1H, CH=N), 7.80 (br s, 1H, OH)

Table 3. Physical and Spectroscopic Data of New Nitro Compounds **1** Prepared

Product[a]	Yield[b] (%)	mp (°C) or bp (°C)/Torr or n_D^{20}	^{1}H-NMR ($CDCl_3$/TMS) δ, J(Hz)	Molecular Formula[c]
1e	15	1.5521	1.00–2.30 (m, 8H_{aliph}), 4.70 (s, 2H, CH_2), 7.00–7.40 (m, 5H_{arom})	$C_{13}H_{15}NO_2$ (217.3)
1f	59	27–28	0.80–2.40 (m, 6H_{aliph}), 3.65 (s, 1H, CHPh), 4.60 (s, 2H, CH_2), 6.20 (br s, 1H, CH=C), 7.00–7.40 (m, 5H_{arom})	$C_{13}H_{15}NO_2$ (217.3)
1g	50	1.4781	0.90 (d, 3H, J = 5.7, CH_3CH), 0.95 (d, 6H, J = 6.9, CH_3CHCH_3), 1.15–2.50 (m, 7H_{aliph}), 2.80–3.10 (m, 1H, CH_3CHCH_3), 4.90 (br s, 2H, CH_2)	$C_{11}H_{19}NO_2$ (197.3)
1i	63	72/0.6	1.30–2.60 (m, 12H_{aliph}), 4.90 (s, 2H, CH_2), 5.90 (t, 1H, J = 7.5, CH)	$C_9H_{15}NO_2$ (169.3)
1l	70	1.5227	3.40 (d, 2H, J = 5.5, CH_2S), 5.25 (s, 2H, CH_2N), 6.25 (t, 1H, J = 6.0, CH), 7.00–7.20 (m, 4H_{arom})	$C_{10}H_9NO_2S$ (207.3)
1m	76	1.5579	1.50–2.00 (m, 4H_{aliph}), 2.20–2.70 (m, 4H_{aliph}), 5.25 (s, 2H, CH_2), 7.10–7.50 (m, 5H_{arom})	$C_{13}H_{15}NO_2$ (217.3)
1o	60	200–203	0.90–2.40 (m, 20H_{aliph}), 0.95 (s, 3H, 19-CH_3), 1.05 (s, 3H, 18-CH_3), 2.00 (s, 3H, CH_3CO), 5.30–5.40 (m, 1H, CH=C), 6.85 (t, 1H, J = 2.5, $CHNO_2$)	$C_{22}H_{31}NO_4$ (373.5)

[a] All compounds exhibit characteristic absorptions in their IR spectra at ν = 1360–1380 and 1530–1550 cm^{-1}.

[b] Isolated yields.

[c] Satisfactory microanalyses obtained: C ±0.30, H ±0.15, N ±0.28.

Table 4. Factors Affecting the Reduction of 4-Methyl-1-nitromethylcyclohexene (**1b**) (1 mole equiv.) with Carbon Disulfide under SL-PTC Conditions at Room Temperature[a]

Entry	CS_2 (mole equiv.)	Base[b] (mole equiv.)	Water (mol equiv.)	Catalyst (mole equiv.)	Time (h)	Conversion[c] (%)	Yield[d] (%)
1	1.0	K_2CO_3 (1.0)	0.2	TEBA (0.1)	8	100	46
2	1.5	K_2CO_3 (1.0)	0.2	TEBA (0.1)	8	100	60
3	3.0	K_2CO_3 (1.0)	0.2	TEBA (0.1)	8	100	32
4	1.5	K_2CO_3 (2.0)	0.1	TEBA (0.1)	8	100	47
5	1.5	K_2CO_3 (1.0)	0.0	TEBA (0.1)	8	50	20
6	1.5	K_2CO_3 (1.0)	0.5	TEBA (0.1)	8	100	61
7	1.5	K_2CO_3 (1.0)	1.0	TEBA (0.1)	8	100	62
8	1.5	Cs_2CO_3 (1.0)	0.2	TEBA (0.1)	3	100	50
9	1.5	Na_2CO_3 (1.0)	0.2	TEBA (0.1)	8	43	38
10	1.5	Li_2CO_3 (1.0)	0.2	TEBA (0.1)	8	15	8
11	1.5	$KHCO_3$ (1.0)	0.4[e]	TEBA (0.1)	12	100	57
12	1.5	NaOH (1.0)	0.4	TEBA (0.1)	8	100	30
13	1.5	NaOH (1.0) K_2CO_3 (1.0)	0.6	TEBA (0.1)	8	100	30
14	1.5	K_2CO_3 (1.0)	0.2	TEBA (0.2)	3	100	61
15	1.5	K_2CO_3 (1.0)	0.2	TEBA (0.05)	8	80	50
16	1.5	K_2CO_3 (1.0)	0.2	Bu_4NBr (0.1)	8	100	53
17	1.5	K_2CO_3 (1.0)	0.2	Bu_4NHSO_4 (0.1)	8	100	35
18	1.5	K_2CO_3 (1.0)	0.2	$C_{16}H_{33}PBu_3Br$ (0.1)	8	100	35
19	1.5	K_2CO_3 (1.0)	0.2	DCH-18-C-6 (0.1)	8	100	56
20	1.5	K_2CO_3 (1.0)	0.2	–	8	30	11

[a] In CH_2Cl_2 (1 mL/1 mmol of substrate).
[b] Anhydrous bases were used.
[c] By TLC and/or NMR analyses.
[d] Yield of pure isolated Compounds.
[e] When reaction was performed in the 5% aq $KHCO_3/CH_2Cl_2$ two-phase system a 100% conversion was reached in 8 h and **2b** was isolated in 57% yield.

Table 5. Solvent Effect on the Reduction of 4-Methyl-1-nitromethylcyclohexene (**1b**) (1 mol) with Carbon Disulfide (1.5 mol) under SL-PTC Conditions at Room Temperature[a]

Entry	Solvent[b]	Time (h)	Conversion[c] (%)	Yield[d] (%)
1	CH_2Cl_2	8	100	60
2	DME[e]	6	100	58
3	dioxane	8	100	42
4	CH_3CN	8	100	52
5	benzene	8	12	3
6	toluene	8	15	4
7	DMF	3	100	10

[a] Potassium carbonate (0.5 mol) and water (0.2 mol).
[b] 1 mL/1 mmol of substrate.
[c] By NMR analyses.
[d] Yield of isolated pure products.
[e] 1,2-Dimethoxyethane.

reaction products were mainly tars with minor amounts of oxime **2b** (5–10%). Among the bases examined, only potassium hydrogen carbonate could be used under these conditions, complete conversion being reached in 8 hours and oxime **2b** isolated in 57% yield (Table 4, footnote e).

As shown in Table 5, dichloromethane was found to be the solvent of choice for the process (entry 1). Comparable results were obtained using 1,2-dimethoxyethane (entry 2). Longer reaction times were required and very poor yields of oxime **2b** were obtained when the reduction was performed in benzene or toluene (entries 5, 6). The use of solvents such as dioxane, acetonitrile or dimethylformamide afforded complete conversions of substrate in 3–8 h but the yields of **2b** were poor, especially in dimethylformamide. As shown in Table 1, the SL-PTC procedure afforded oximes in respectable to good yields (45–79%) in the case of allylic nitro compounds **1a–m**. Steric requirements probably account for the poor yields (25%) realized in the reduction of the (**1g**). Poor yields were also obtained in the case of the vinylic nitroderivative **1o**, while the 1-nitrooctane (**1n**) did not react at all.

The nitro derivatives **1a–m,o** were prepared by condensation of the corresponding ketones with CH_3NO_2 in the presence of a catalytic amount of ethylendiamine, according to a previously reported procedure:[1] **1a**,[7] **1b**,[8] **1h**,[9] **1e,d,j,k,n**[1] are known compounds. Physical and spectroscopic data of the unknown substrates **1e–g,l,m,o** are reported in Table 3. 1-Nitrooctane (**1n**) was synthesized from 1-bromooctane by treatment with $AgNO_2$ in anhydrous Et_2O.[5] Commercial $KHCO_3$, Cs_2CO_3, Li_2CO_3 and K_2CO_3 were carefully dried by heating at 140°C under vacuum (0.07 mbar) for 6 h and stored in a dessicator. Analar grade organic solvents were dried over molecular sieves and used without further purification. CS_2 was used as purchased. ^{1}H-NMR spectra were recorded on a Varian EM-390 90 MHz or a Bruker WP 80 SY spectrometers. IR spectra were obtained with a Perkin-Elmer 377 spectrophotometer. Melting points were determined using a Büchi melting point apparatus and are uncorrected.

Oximes 2; General Procedure:

A mixture of nitro compound **1** (0.1 mol), CH_2Cl_2 (100 mL) benzyltriethylammonium chloride (2.28 g, 0.01 mol), solid anhydrous K_2CO_3(6.90 g, 0.05 mol) and H_2O (0.36 mL, 0.02 mol) is placed in a round-bottomed flask equipped with a reflux condenser, drying tube, and magnetic stirrer. The heterogeneous mixture is stirred for 15 min at r.t. and then CS_2 (9.02 mL, 0.15 mol) is added all at once. Stirring is continued until maximum conversion of **1** is reached (see Table 1). The progress of the reaction is monitored by TLC (eluent:

Et_2O/petroleum ether) and/or ^1H-NMR spectra. At the end of the reaction, the mixture is filtered on Celite and the solvent evaporated under reduced pressure to give the crude oxime **2**, which is purified by column chromatography on silica gel (230–400 mesh) using Et_2O/petroleum ether (bp 40–60°C, 1:9) as eluent.

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