STANNOUS CHLORIDE REDUCTION OF α,β-UNSATURATED NITROALKENES: A DIRECT SYNTHESIS OF 2-ARYL-2H-1-BENZOPYRAN-3(4H)-ONE OXIMES

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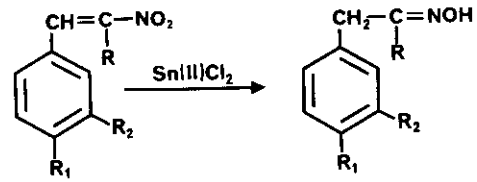
Abstract - Stannous chloride, in acetone, readily reduced the α,β-unsaturated nitroalkenes to the corresponding oximes at room temperature. A series of 2-aryl-3-chromanone oximes were obtained via the reduction of 3-nitrochromenes.

Nitro-2H-1-benzopyrans have attracted attention in recent years because of their potential as precursors to a variety of medicinally important 2H-1-benzopyran derivatives[1] such as flavonols,[2] amines[3] etc. Our continued interest in the chemistry of benzopyran derivatives[4-12] led us to investigate the preparation of 3-chromanone oximes from Δ^3-nitrochromenes. In a preliminary communication we reported [13] that oximes are accessible via the reduction of α,β-unsaturated nitroalkenes with stannous chloride in acetone. The details of this reaction are presented in Table I. Indeed, in a separate study, we discovered that α-substituted oximes[15] and their corresponding ketone[16] derivatives are obtained when stannous chloride is used to reduce conjugated nitroalkenes in non-aqueous and non-acidic media. We wish to report that stannous chloride reduction of 3-nitrochromenes, in acetone, provides stable 2-aryl-2H-1-benzopyran-3(4H)-one oximes in a single step. This methodology affords essentially pure products in good yields and provides an easy entry into a number of previously unknown 3-chromanone oximes. Our results are summarized in Tables II and III.

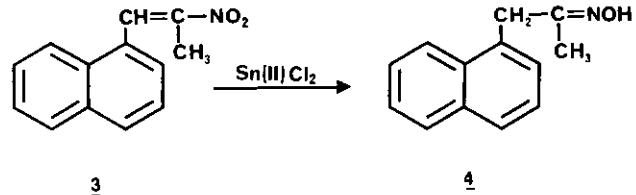
It should be pointed out that although 4-chromanones and flavanones have been studied extensively, relatively little has been reported on the 3-chromanones,[17] apparently due to their inherent reactivity. Unlike the ketone precursors, 3-chromanones, the oximes are very stable. This new approach may provide a simple route to a variety of 3-chromanones via hydrolysis[18] or to 3-chromanamines via the reduction[19] of the corresponding oximes. We anticipate that this work will stimulate interest in the chemistry of 3-chromanone system.

TABLE I

Reduction of α,β-Unsaturated Nitroalkenes to Oximes 2a-d and 4[a]



1 2



3 4

Compound No.	R_1	R_2	R	yield[c] [%]	Time (Min.)	^{1}H-NMR δ (ppm)[b] CH_2 (Z)	CH_2 (E)	CH_3/H (Z)	CH_3/H (E)	^{13}C-NMR δ (ppm)[b] C=NOH (Z)	C=NOH (E)	CH_2 (Z)	CH_2 (E)	CH_3 (Z)	CH_3 (E)	Lit. Ref.
2a	H	H	H	46	50	-	-	3.52	3.74	150.8	150.8	31.7	36.0	-	-	20
2b	H	H	CH_3	74	45	3.76	3.51	1.82	1.83	157.0	157.7	34.9	42.2	19.8	13.3	21
2c	Br	H	CH_3	69	60	3.68	3.44	1.80	1.80	156.3	157.2	34.3	41.6	19.7	13.4	22
2d	OC_2H_5	OC_2H_5	CH_3	70[d]	70	3.66	3.41	1.80	1.80	157.3	157.9	34.3	41.7	19.7	14.9	22
4	-	-	-	71	60	4.20	3.98	1.67	1.82	157.1	157.7	32.5	39.6	19.4	13.3	23

[a] Products are mixtures of E- and Z-isomers (E:Z ≈ 3:1).

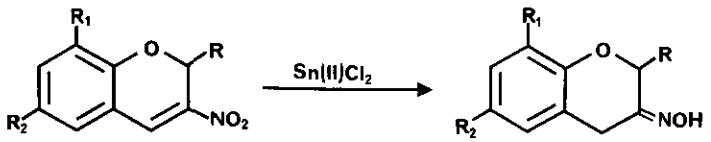
[b] NMR spectra were recorded in deuteriochloroform.

[c] Isolated and unoptimized yields; all products are thick oils except 2b (colorless needles, mp 90-91°C).

[d] Six molar equivalents of stannous chloride was used.

Table II

Physical and Analytical Data for Compounds 6a-f[a]



5 6

Compound No	R_1	R_2	R	yield[b] [%]	mp[°C][c]	Molecular Formula	Analyses (%) Calcd/Found C	H	N
6a	H	H	Phenyl	77	205-206	$C_{15}H_{13}NO_2$	75.31 75.12	5.44 5.50	5.86 5.72
6b	OCH_3	H	Phenyl	73	211-212	$C_{16}H_{15}NO_3$	71.36 71.25	5.61 5.60	5.20 5.25
6c	H	H	p-Isopropylphenyl	82	169-170	$C_{18}H_{19}NO_2$	76.83 76.70	6.81 6.56	4.98 5.21
6d	H	NO_2	Phenyl	68	214-215	$C_{15}H_{12}N_2O_4$	63.34 63.45	4.26 4.40	9.85 9.85
6e	H	H	1-Naphthyl	63	217-218	$C_{19}H_{15}NO_2$	78.86 78.88	5.23 5.16	4.84 4.84
6f	OCH_3	H	1-Naphthyl	63	211-212	$C_{20}H_{17}NO_3$	75.22 75.25	5.37 5.35	4.39 4.53

[a]Single isomer formed in each reaction (presumably the E-isomer based on examination of molecular models).

[b]Isolated and unoptimized yields.

[c]Recrystallization solvent:ethyl acetate.

Table III

Spectral Data of 2-Aryl-2H-1-benzopyran-3(4H)-one Oximes (6a-f)

Compound No	I.R. ν_{max} cm^{-1}	^{1}H-NMR δ(ppm)[a] Chroman ring protons					^{13}C-NMR δ(ppm)[a] Chroman ring carbons		
		2-H	4-H	Other signals			2-C	3-C	4-C
6a	3260,1587,1485,1455 1240,1110,1040,960	5.75 (s,1H)	3.50,3.92 (AB,J=22.42)	7.4-6.9 (m,9H,Ar-H)			76.87	152.31	23.95
6b	3270,1585,1487,1267 1240,1210,1092,960	5.74 (s,1H)	3.47,3.88 (AB,J=22.82)	7.4-6.7 (m,8H,Ar-H)	3.79 (s,3H,OCH_3)		76.79	152.39	23.99
6c	3270,1585,1485,1460, 1235,1110,1030,960	5.70 (s,1H)	3.56,3.91 (AB,J=21.76)	7.3-6.8 (m,8H,Ar-H)	2.84 (Septet,1H,CH)	1.15 (d,6H,CH_3)	76.85	152.37	24.00
6d	3260,1580,1510,1338 1242,1205,1089,955	5.96 (s,1H)	3.78,4.04 (AB,J=21.76)	8.2-7.1 (m,8H,Ar-H)			77.74	150.47	23.97
6e	3270,1580,1482,1235 1190,1110,1057,960	6.32 (2,1H)	3.94 (s,2H)	8.3-6.7 (m,11H,Ar-H)			76.47	152.21	25.33
6f	3220,1580,1478,1256 1234,1215,1082,950	6.21 (s,1H)	3.91 (s,2H)	8.2-6.7 (m,10H,Ar-H)	3.67 (s,3H,OCH_3)		76.98	153.21	25.46

[a]NMR spectra were recorded in hexadeuteriodimethylsulfoxide.

EXPERIMENTAL

Melting points were determined in capillary tubes on a Mel-Temp melting point apparatus and are uncorrected. Infrared spectra (potassium bromide) were recorded using a Perkin-Elmer 1330 spectrophotometer. The ^{1}H and ^{13}C nmr spectra were obtained on a JEOL-FX90Q spectrometer using deuteriochloroform and hexadeuteriodimethylsulfoxide as the solvent and are referenced to TMS as the internal standard. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN.

General Procedure for the Synthesis of Oximes 2a-d and 4

A mixture of β-nitrostyrene (4 mmol) and stannous chloride (10 mmol) was stirred together in an Erlenmeyer flask at room temperature in acetone. After stirring for appropriate time, the reaction mixture was poured onto ice-water, pH adjusted to ~8 with 10% aqueous sodium bicarbonate, stirred for 15 min and saturated with sodium chloride. The product was extracted into ether (6x30 ml), dried over anhydrous magnesium sulfate and the solvent removed under reduced pressure. The crude product on column chromatography (silica gel; ether: petroleum, 1:9) gave pure product as a thick oil.

General Procedure for the Synthesis of 2-Aryl-3-Chromanone Oximes 6a-f.

2-Aryl-3-nitrochromene (2.5 mmol) was placed in an Erlenmeyer flask containing a magnetic stirring bar and ~20 ml of acetone at room temperature. Stannous chloride (7.5 mmol) was then added in one portion to the well stirred solution. The mixture was stirred for 3 h at room temperature while a yellow suspension of product forms (progress of the reaction was monitored by TLC analysis). The reaction mixture was then poured onto ice-water, pH adjusted to ~8 with 10% aqueous sodium bicarbonate and the suspension stirred for 15 min. The pale yellow suspension was then filtered using a buchner funnel and the precipitate washed with water. To obtain the product, the precipitate was macerated repeatedly with ethyl acetate (5x25 ml), the combined organic layers dried with magnesium sulfate, and the solvent removed under reduced pressure. The crude product was purified by recrystallization from ethyl acetate.

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