Cyclopropenone Oximes: Preparation and Reaction with Isocyanates

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2,3-Diphenyl-, 2-methyl-3-phenyl-, and 2-methyl-3-(4-methylphenyl)cyclopropenone oxime hydrochlorides (**3**) were prepared in good yields from the corresponding cyclopropenones and hydroxylamine hydrochloride in methanol. The salts **3** reacted with alkyl and aryl isocyanates in the presence of triethylamine to afford 1:2 addition products 4,6-diazaspiro[2.3]hexenones in moderate yields. In contrast, acetone, acetophenone, and cyclohexanone oximes reacted with twice excess of methyl isocyanates to give linear 1:2 addition products and benzophenone oxime yielded only 1:1 addition product.

The physical and chemical properties of cyclopropenones, cyclopropenium ions, and triafulvenes have been of great interest and are currently being investigated[1] as microcyclic aromatics. In a continuation of our studies on the chemistry of cyclopropenium salts possesing heteroatom substituents[2] we have found an easy route for the preparation of cyclopropenone oximes; however, their chemical properties have not yet been well-explored.

Several studies have been repored on the reaction of diphenylcyclopropenone (**1a**) with hydroxylamine. Breslow[3] has shown that a reaction of **1a** with hydroxylamine hydrochloride **2** in aqueous ethanol yields deoxybenzoin oxime and diphenylisoxazolone. Kitahara[4] has obtained diphenylcyclopropenone oxime (**4a**) as colorless needles from **1a** and **2** in methanol, followed by treating with aqueous sodium hydrogencarbonate. On the other hand, Eicher has prepared 1-hydroxyamino-2,3-diphenylcyclopropenium tetrafluoroborate (**3a** as BF_4 salt) from 1-ethoxy-2,3-diphenylcyclopropenium salt and hydroxylamine.[5] However, only the reaction of **4a** with secondary amines has been shown.[6]

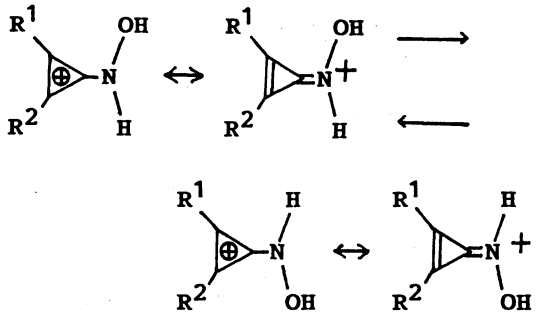
2,3-Diphenyl-, 2-methyl-3-phenyl-, and 2-methyl-3-(4-methylphenyl)cyclopropenone (**1a—c**) reacted easily with hydroxylamine hydrochloride **2** in methanol at room temperature for one day. The hydrochloride **3a** precipitated from the reaction mixture and the salts **3b, c** were obtained as a dichloromethane soluble products. The salts **3a—c** were colorless and stable at room temperature. Upon treating with aqueous sodium hydrogen carbonate or triethylamine yielded free diphenylcyclopropenone oxime **4a** as yellow needles in quantitative yield which were stable for a long-time storage at room temperature. However, the free oximes **4b, c** turned brown and decomposed at room temperature within one hour while giving a resinous mass. The structures of **3a—c** and **4a** were confirmed by IR, ^1H and ^{13}C NMR and mass spectroscopic studies. The NMR spectra ($CDCl_3$+CF_3CO_2H, 10:1) of **3b, c**, as shown in Table 1, revealed the presence of two isomers, corresponding to *E*- and *Z*-form, in nearly

Table 1. Yields and Physical Properties of Cyclopropenone Oxime Derivatives **3** and **4**

	Yield	Mp	IR(KBr)	MS	^1H NMR[a]	^{13}C NMR[a]	Found(Calcd)/%		
	%	θ_m/°C	cm^{-1}	M^+			C	H	N
3a	83	198—202	2940 2740 1920	221	7.8—8.6(m, 15H, Ph)	119.1(s), 119.2(s), 129.9(d), 130.3(d), 133.6(d), 136.2(d), 139.5(s)	69.98 (69.90)	4.53 (4.69)	5.34 (5.43)
4	98[b]	133—136[c]	3150 1880 1850	221	d)	d)	81.32 (81.43)	4.94 (5.01)	6.49 (6.63)
3b	76	137—141	2980 2720 1940	159	2.75 and 2.80(2s, 3H, Me), 7.1—8.3(m, 6H, Arom and NH)	10.1(q), 10.3(q), 118.8(s), 118.9(s), 129.8(d), 133.3(d), 134.2(d), 135.0(d), 135.3(d), 135.5(s), 136.0(d), 136.5(d), 142.4(d), 143.2(s)	61.49 (61.39)	5.01 (5.15)	6.98 (7.15)
3c	69	148—152	2980 2720 1940	173	2.50(s, 3H, Me), 2.70 and 2.75 (2s, 3H, Me), 7.8—8.6 (m, 4H, Arom)	10.0(q), 10.3(q), 20.9(q), 115.9(s), 116.0(s), 130.6(d), 132.6(s), 133.3(d), 133.4(d), 135.9(s), 137.4(s), 142.9(s), 147.2(s), 147.4(s)	62.94 (63.01)	5.88 (5.76)	6.73 (6.68)

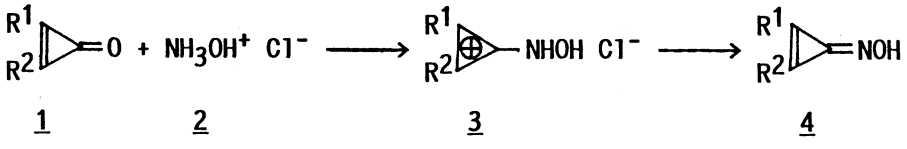
a) In a mixture of $CDCl_3$ and CF_3CO_2H (10:1). b) Yield from **3a**. c) Lit,[5] mp 116—116.5 °C. d) Insoluble in $CDCl_3$, methanol-d_4, or CD_2Cl_2.

equal amounts.



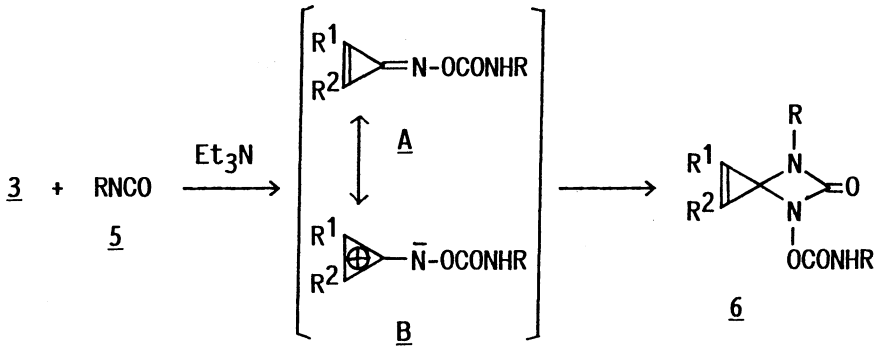
An equimolar reaction of **3a** with methyl isocyanate **5a** in the presence of triethylamine at room temperature gave 4-methyl-6-methylcarbamoyloxy-1,2-diphenyl-4,6-diazaspiro[2.3]hex-1-en-5-one (**6aa**) in a 40% yield. The use of twice excess moles of **5a** yielded **6aa** in a 75% yield. The structure of **6aa** was assigned from its ^{1}H and ^{13}CNMR, and mass spectroscopic studies and chemical transformations. Thus, upon treating with potassium methoxide in methanol **6aa** afforded 3,3-diaminocyclopropene **7** in a 61% yield. An acidic hydrolysis of **7** gave **1a**, indicating the presence of the cyclopropene ring in **6aa** and **7** (Schemes 2 and 3). A similar treatment of **3a** at room temperature or **3b** at a lower temperature with two moles of **5** yielded spiro compounds **6** in moderate yields, as listed in Table 2. No 1 : 1 addition product could be isolated by us.

It has been well-known that aldoximes and ketoximes react with isocyanates **5** to yield carbamates.[7] To check these results the reaction of ketoximes **8** and **5a** was studied in the presence of triethylamine. The reactions of acetone oxime **8a** with **5a** in 1 : 1 and 1 : 2 molar ratios afforded carbamate-type products **9a** and **10a**, respectively, in moderate yields. Similarly, acetophenone oxime **8b** and cyclohexanone oxime **8d**



1, 3, 4	R^1	R^2
a	Ph	Ph
b	Me	Ph
c	Me	4-MeC_6H_4

Scheme 1.

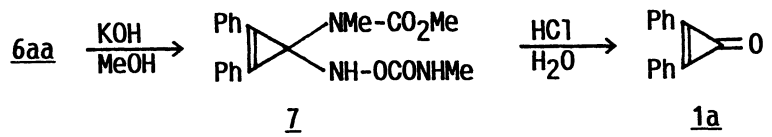


5	R
a	Me
b	n-C_3H_7
c	t-C_4H_9
d	Ph
e	3-MeC_6H_4
f	4-ClC_6H_4

6	R^1	R^2	R
aa	Ph	Ph	Me
ab	Ph	Ph	n-C_3H_7
ac	Ph	Ph	t-C_4H_9
ad	Ph	Ph	Ph
ae	Ph	Ph	3-MeC_6H_4
af	Ph	Ph	4-ClC_6H_4

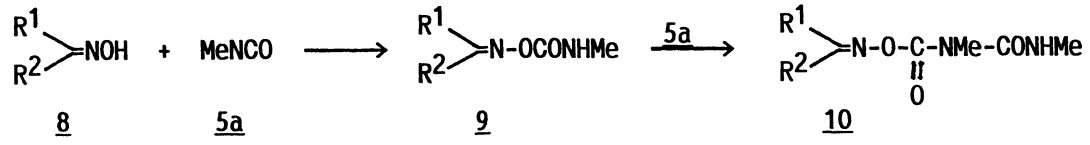
6	R^1	R^2	R
ba	Me	Ph	Me
bd	Me	Ph	Ph
be	Me	Ph	3-MeC_6H_4
bf	Me	Ph	4-ClC_6H_4

Scheme 2.



7 1a

Scheme 3.



8 5a 9 10

8, 9, 10	R^1	R^2
a	Me	Me
b	Me	Ph
c	Ph	Ph
d	$(CH_2)_5$	

Scheme 4.

Table 2. The Reaction of Oximes **3** or **8** with Isocyanates **5**

Reactants		Reaction conditions			Products	
3	**5**	Mole ratio	Temp/°C	Time/d	(Yield/%)	
3a	**5a**	1:1	20	1	**6aa**	(40)
		1:2	20	1	**6aa**	(75)
	5b	1:2	20	1	**6ab**	(63)
	5c	1:2	20	1	**6ac**	(69)
	5d	1:2	20	1	**6ad**	(71)
	5e	1:2	20	1	**6ae**	(67)
	5f	1:2	20	1	**6af**	(48)
3b	**5a**	1:2	5	1	**6ba**	(27)
	5d	1:2	5	1	**6bd**	(42)
	5e	1:2	5	1	**6de**	(38)
	5f	1:2	5	1	**6bf**	(32)
8a	**5a**	1:1	20	2	**9a**	(85)
		1:2	20	2	**10a**	(64)
8b	**5a**	1:1	20	1	**9b**	(63)
		1:2	20	2	**10b**	(28)
9b	**5a**	1:1	20	1	**10b**	(45)
8c	**5a**	1:2	20	3	**9c**	(57)
8d	**5a**	1:2	20	2	**10d**	(56)

yielded the open-chain 1:2 addition products **10b, d**. However, the bulky benzophenone oxime **8c** gave no 1:2 addition product under similar reaction conditions (Scheme 4 and Table 2). None of the cyclic product was obtained from reactions of these oxime **8** with **5a**.

Although the isolation of (carbamoyloxyimino)cyclopropene **A**, a 1:1 addition product, failed, the intermediacy of **A** was clear from the final product **6**. The reaction of the highly polarized form **B** with **5** would be faster than that of **4** with **5**. Although it has been shown that some C=N derivatives react with **5** to afford the 1:1 cycloaddition products, 1,3-diazetidines,[6-8] to our knowledge no spiro derivatives, like **6**, have been reported. The marked difference in the products between **6** from **3** and **10** from **9** can be explained in terms of the polarization of imino nitrogens of oximes **B** and **9**. The highly polarized imino nitrogen of **B** facilitate the formation of **6**, while such activation was not observed for **9**.

Experimental

General. Melting points were uncorrected. The ^{13}C NMR spectra were recorded either on a JEOL JMN FX-60 spectrometer (15.04 MHz) or JEOL JNM FX-90Q (22.49 MHz) and ^1H NMR spectra on a Hitachi R-24B (60 MHz). The IR spectra were recorded on a JASCO A-3 spectrometer.

Preparation of 1-Hydroxyamino-2,3-diphenylcyclopropenium Chloride 3a and 4a. A solution of diphenylcyclopropenone **1a** (5.26 g, 25 mmol) and hydroxylamine

hydrochloride **2** (5.30 g, 76 mmol) in 30 cm^3 of methanol was allowed to stay at room temperature for a day. The precipitated salt **3a** was collected and washed with a small amount of cold methanol and dried under reduced pressure. The salt **3a** was treated with aqueous sodium hydrogencarbonate and extracted with dichloromethane. The extract was dried over sodium carbonate, condensed in vacuo, and recrystallization from methanol yielded diphenylcyclopropenone oxime **4a**. The physical properties are shown in Table 1.

Preparations of 3b and 3c. A solution of **1b** or **1c** (10 mmol) and **2** (10.5 mmol) in methanol (6 cm^3) was reacted at room temperature for one day. The solvent was removed in vacuo and the dichloromethane soluble product was separated. Trituration of the dichloromethane soluble mass with benzene afforded pure cyclopropenone oxime hydrochloride **3b** or **3c** (Table 1).

The Reaction of 3 with Isocyanates 5. A General Procedure. A mixture of **3** (2 mmol), **5** (2 mmol), and triethylamine (4 mmol) in dichloromethane (15 cm^3) was stirred well at appropriate temperature. The resulting solution was poured into cold water and an organic layer was separated. The extract was dried over sodium carbonate, condensed in vacuo, and recrystallized from ether-petroleum ether to give the spiro derivative **6**. **6aa**: mp 135—137 °C; IR (KBr) 3430, 1780, and 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.59 (s, 3H, CNMe), 2.85 (d, J=6 Hz, 3H, NHMe), 6.13 (bs, 1H, NH), and 7.2—7.9 (m, 10H, 2Ph); ^{13}C NMR ($CDCl_3$) δ=26.5(q), 26.6(q), 65.7(s), 118.4(s), 125.9(s), 128.9(d), 129.9(d), 130.4(d), 155.4(s), and 160.0(s). Found: C, 68.23; H, 4.93; N, 12.64%; M^+, 335. Calcd for $C_{19}H_{17}N_3O_3$: C, 68.05; H, 5.11; N, 12.53%; M, 335. **6ab**: mp 118—122 °C; IR(KBr) 3370, 1770, and 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.72 (t, J=6Hz, 3H, CH_3), 0.90 (t, J=6Hz, 3H, CH_3), 1.43 (sext, J=6Hz, 4H, $2CH_2CH_3$), 2.45 (t, J=6 Hz, 2H, NCH_2), 3.24 (q, J=6 Hz, 2H, NCH_2), 6.05 (bs, 1H, NH), and 7.2—8.0 (m, 10H, 2Ph). Found: C, 70.58; H, 6.72; N, 10.89%; M^+ 391. Calcd for $C_{23}H_{25}N_3O_3$: C, 70.56; H, 6.43; N, 10.73%; M, 391. **6ac**: mp 142—143 °C; IR (KBr) 3380, 1750, and 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.29 (s, 9H, t-Bu), 1.40 (s, 9H, t-Bu), 6.0 (bs, 1H, NH), and 7.4—8.1 (m, 10H, 2Ph). Found: C, 71.43; H, 6.79; N, 10.21%; MS, 320 (M^+—t-BuNCO). Calcd for $C_{25}H_{29}N_3O_3$: C, 71.57; H, 6.96; N, 10.01%; M, 419. **6ad**: mp 142—145 °C; IR (KBr) 3330, 1770, and 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ=7.2—7.7 (m, 21H, 4Ph and NH). Found: C, 75.91; H, 4.32; N, 9.02%; M^+, 459. Calcd for $C_{29}H_{21}N_3O_3$: C, 75.80; H, 4.60; N, 9.14%; M, 459. **6ae**: mp 142—145 °C; IR (KBr) 3330, 1770, and 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.05 (s, 3H, Me), 2.30 (s, 3H, Me), and 6.8—7.6 (m, 19H, Arom+NH). Found: C, 76.15; H, 5.01; N, 8.73%; MS, 354 (M^+—4-MeC_6H_4NCO). Calcd for $C_{31}H_{25}N_3O_3$: C, 76.36; H, 5.16; N, 8.61%; M, 487. **6af**: mp 146—148 °C; IR (KBr) 3330, 1770, and 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ=7.1—8.0 (m, 19H, Arom and NH). Found: C, 67.13; H, 4.32; N, 7.82%; M^+, 556. Calcd for $C_{31}H_{23}Cl_2N_3O_3$: C, 66.91; H, 4.16; N, 7.55%; M, 556. **6ba**: mp 135—138 °C; IR (KBr) 3370, 1780, and 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.45 (s, 3H, Me), 2.55 (s, 3H, Me), 2.85 (d, J=6Hz, 3H, NHMe), 6.1 (bs. 1H, NH), and 7.2—7.8 (m, 5H, Arom). ^{13}C NMR ($CDCl_3$) δ=11.0(q), 26.4(t), 26.6(d), 66.1(s), 115.7(s), 122.7(d), 125.1(s), 128.8(d), 129.3(d), 130.1(d), 155.7(s), and 160.6(s). Found: C, 61.26; H, 5.46; N, 15.09%; M^+, 273. Calcd for $C_{14}H_{15}N_3O_3$: C, 61.55; H, 5.49; N, 15.37%; M, 273. **6bd**: mp 125—128 °C; IR (KBr) 3350, 1770, and 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.35 (s, 3H, Me) and 6.9—8.1 (m, 16H, Arom and NH). Found: C, 72.67; H, 4.55; N, 10.68%; M^+, 397. Calcd for $C_{24}H_{19}N_3O_3$: C, 72.56; H, 4.78; N, 10.57%; M, 397. **6be**: mp 98—102 °C; IR (KBr) 3050, 1780, and 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.25 (s, 3H, Me), 2.35 (s, 6H, 2Me), and 6.8—8.1 (m, 14H, Arom). Found: C, 73.25; H, 5.67; N, 9.58%; M^+, 425. Calcd for $C_{26}H_{23}N_3O_3$: C, 73.42; H, 5.40; N, 9.87%; M, 425. **6bf**: mp 141—143 °C; IR (KBr) 3350, 1770, and 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.85 (s, 3H, Me) and 6.9—8.1 (m, 14H, Arom and NH). Found: C, 61.89; H, 3.52; N, 9.31%; M^+, 474. Calcd for $C_{24}H_{17}Cl_2N_3O_3$: C, 61.83; H, 3.64; N, 9.01%; M, 474.

Methanolysis of 6aa. A solution of **6aa** (1 mmol) and KOH (3 mmol) in methanol (10 cm^3) was stirred at room temperature for 1 h. The mixture was poured into water and extracted with benzene. The benzene extract was dried over sodium carbonate, condensed in vacuo, and recrystallized from petroleum ether to yield the gem-diamine **7**: 61%; mp 122—125 °C; IR (KBr) 3340, 1820, 1770, and 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.60 (d, J=6Hz, 3H, MeNH), 2.76 (s, 3H, MeN), 3.56 (s, 3H, MeO), 5.72 (bs, 1H, NH), 7.0—8.1 (m, 10H, 2Ph), and 9.52 (bs, 1H, NHO). ^{13}C NMR ($CDCl_3$) δ=26.5(q), 33.9(q), 53.1(q), 58.9(s), 116.1(s), 126.1(s), 128.8(d), 129.7(d), 130.5(d), 159.1(s), and 159.9(s). Found: C, 65.55; H, 5.73; N, 11.23%. M^+, 367. Calcd for $C_{20}H_{21}N_3O_4$: C, 65.38; N, 5.76; N, 11.43%. M, 367. A mixture of **7** (1 mmol), concd HCl (0.3 cm^3), chloroform (3 cm^3), and water (1 cm^3) was stirred well at room temperature for 1 h. The organic extract yielded **1a** in an 89% yield.

The Reaction of Ketoximes 8 with 5a. General Procedure. A solution of **8** (1 mmol), **5a** (1.1 or 2.2 mmol), and triethylamine (1 mmol) in dichloromethane (5 cm^3) was allowed to react at room temperature until the disappearance of **8** by checking the reaction mixture with TLC. The solution was poured into water and an organic layer was separated. The extract was dried over sodium carbonate, condensed, and recrystallized from benzene or ether. The results are listed in Table 2. The physical properties are as follows. **9a**: mp 48—50 °C; IR (KBr) 3350, 1720, and 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.93 (s, 3H, Me), 1.94 (s, 3H, Me), 2.86 (d, J=6 Hz, NHMe), and 6.40 (bs, 1H, NH). MS m/z 130 (M^+). **10a**: mp 180—183 °C; IR (KBr) 3350, 1720, and 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.06 (s, 3H, Me), 2.09 (s, 3H, Me), 2.87 (d, J=6 Hz, 3H, NHMe), and 3.28 (s, 3H, CONMe). Found: C, 44.53; H, 7.21; N, 22.48%; M^+, 187. Calcd for $C_7H_{13}N_3O_3$: C, 44.91; H, 6.99; N, 22.44%; M, 187. **9b**: mp 96—98 °C; IR (KBr) 3350 and 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.38 (s, 3H, MeC=N), 2.91 (d, J=6 Hz, 3H, NHMe), 6.5 (bs, 1H, NH), and 7.2—7.8 (m, 5H, Ph). MS m/z 192 (M^+). **10b**: mp 134—136 °C; IR (KBr) 3370, 1740, and 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.42 (s, 3H, MeC=N), 2.91 (d, J=6Hz, 3H, NHMe), 3.40 (s, 3H, CONMe), and 7.3—7.9 (m, 5H, Ph). ^{13}C NMR ($CDCl_3$) δ=14.7(q), 27.2(q), 30.3(q), 126.9(d), 128.5(d), 130.7(d), 134.2(s), 154.5(s), 154.8(s), and 163.3(s). Found: C, 57.72; H, 5.87; N, 16.48%; M^+, 249. Calcd for $C_{12}H_{15}N_3O_3$: C, 57.82; H, 6.06; N, 16.85%; M, 249. **9c**: mp 162—164 °C; IR (KBr) 3370, 1740, and 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.95 (d, J=3 Hz, 3H, NHMe), 6.35 (bs, 1H, NH), and 7.2—7.6 (m, 10H, 2Ph). MS m/z 254 (M^+). **10d**: mp 134—137 °C; IR (KBr) 3350, 1720, and 1690 cm^{-1}; ^1H NMR ($CDCl_3$) 1.5—2.7 (m, 10H, $(CH_2)_5$), 2.93 (d, J=6 Hz, 3H, NHMe), and 3.28 (s, 3H, CONMeCO). Found: C, 52.63; H, 7.49; N, 18.11%. Calcd for $C_{10}H_{17}N_3O_3$: C, 52.85; H, 7.53; N, 18.48%.

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