Peroxide-Initiated Cyclizations of Olefinic N-Chloro Amides. Electronic Configuration of Amido Radicals

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It is shown that intramolecular additions of N-methylcarboxamido radicals are conveniently achieved in high yields by benzoyl peroxide initiation, whereas the analogous acetamido radicals either do not cyclize or cyclize less efficiently under the same conditions. In a few cases, a comparison is made with photochemically initiated cyclizations. Some mechanistic and stereoelectronic aspects are discussed, leading to the conclusion that a Σ_N electronic configuration of the carboxamido radicals could be involved.

Introduction

Extensive experimental studies on amido radicals have shown that these species do react similarly to aminium radicals in nonactivated hydrogen abstraction processes.[2-6] Concerning the reactivity toward double bonds, aminium radicals are known to add efficiently to olefins,[7,8] but the reactivity of amido radicals was shown to depend markedly on the presence or absence of an N-alkyl substituent. Thus, the intermolecular radical additions of primary N-halo amides (additions of unsubstituted amido radicals) to olefins, either photochemically induced[9] or initiated by chromous chloride,[10] proceed in good to excellent yields, whereas N-alkyl-N-halo amides (N-alkylamido radicals) do not usually add under the same conditions.[6,9-11] However, intramolecular additions of a few N-alkylamido radicals have recently been reported; these amido radicals were photochemically generated from olefinic N-chloro amides[12,13] or N-nitroso amides.[12,14,15]

The purpose of the present work was to make a comparative study of the radical cyclization of olefinic N-chloro carboxamides A and of the corresponding N-chloro acetamides B

A B

using various methods of initiation. Cyclizations initiated by chromous chloride reduction are described and discussed in the accompanying paper.[16] In this paper, we wish to report that, as in the case of olefinic N-chloramines,[17] cyclization of olefinic N-chloro carboxamides A can efficiently be achieved by using benzoyl peroxide as initiator. However, cyclization of the corresponding olefinic N-chloro acetamides B was far from being as efficient. Our results give interesting information on the electronic structure of N-alkylamido radicals and their relative reactivity toward double bonds and/or allylic hydrogens.

Results

We have studied the cyclization of N-chloro carboxamides **1b, 4b,** and **7b,** and of the corresponding N-chloro acetamides **9b, 11b,** and **12b** (Table I). These N-chloro compounds have been easily prepared by treatment of the corresponding amides with commercial bleach and the crude products were used without further purification. Full details about the preparation, yields, and purity of the N-chloro derivatives are given in the accompanying paper.[16]

Benzoyl peroxide initiated reactions were performed by heating (80 °C) a dioxane solution of the N-chloro amide under a nitrogen atmosphere. Addition of bases (e.g., calcium carbonate) and water in the reaction medium, which was shown to increase markedly the yield of transannular cyclization reactions of N-chloro lactams,[18] was unnecessary. In order to allow comparison of the yields and of the structures of the products, we also performed the photolysis of N-chloro carboxamides **1b, 4b,** and **7b.** The results are recorded in Table I together with literature data on the photolysis of N-chloro amides **1b** and **9b.**

Model compound **1b** was chosen in order to compare our results with those already described in the literature.[12,13] Photolysis of N-chloro carboxamide **1b** in methylene chloride solution led to a 97% cyclization yield. An identical yield (95%) was obtained by the dioxane–benzoyl peroxide method. Two isomers, **2** and **3,** were obtained along with traces of parent amide **1a.**

Model compound **4b** was studied because, in this system, intramolecular allylic hydrogen abstraction by the amido radical could "a priori" compete more effectively with the intramolecular addition to the double bond than in the N-chloro carboxamide **1b** (see discussion below). Cyclization of this compound by irradiation led to a 55% yield of isomers **5** and **6,** whereas the peroxide initiated reaction afforded 79% of these bicyclic amides. The material balance (cyclization products plus parent amide) was much higher in the peroxide-initiated cyclization. No attempt was made to isolate the other products from the photolysis.

Similarly, cyclization of N-chloro carboxamide **7b** led, under photolysis, to a 70% yield of tricyclic chloride **8,** whereas benzoyl peroxide initiated cyclization gave a much higher yield (92%) of the same product[19] and again a much better material balance. The benzoyl peroxide initiated cyclization of the corresponding N-chloro acetamide **12b** was much less efficient, however, leading to the formation of only 50% of tricyclic chloride **13.** The exclusive formation of the exo isomers **8** and **13** can be assigned to steric factors[20] as well as to the probable pyramidal structure of the intermediate adduct radical.[21] The same stereoselectivity was observed for the cyclization of the corresponding N-chloramine.[17]

Surprisingly, the parent amides **9a** and **11a** were the sole products isolated from the treatment of N-chloro acetamides **9b** and **11b** with benzoyl peroxide. Cyclization of **9b** has been achieved by photolysis[13] and more efficiently using chromous chloride.[16]

Discussion

The possible reactions of the olefinic amido radicals are depicted in Scheme I with the amido radical I derived from

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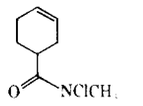
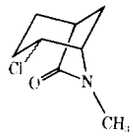
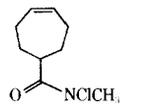
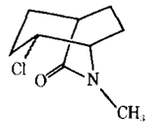
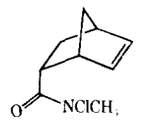
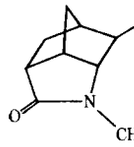
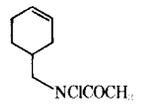
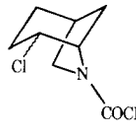
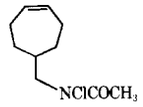
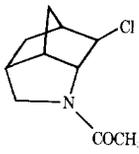
Table I. Radical Cyclization of Olefinic *N*-Chloro Amides

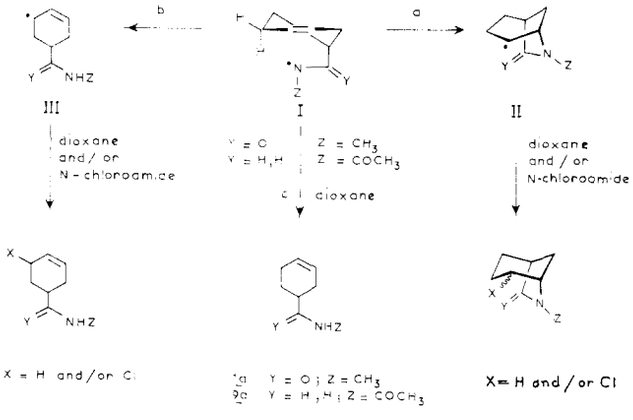
N-chloro amide	no.	cyclization products	no.	% yield[a] of cyclization products Bz_2O_2	% yield[a] of cyclization products $h\nu$	% yield[a] of cyclization products lit. ($h\nu$)[b]	% parent amide no.	% parent amide Bz_2O_2	% parent amide $h\nu$
	**1b**		**2** (exo) **3** (endo)	51 44	42 55	47,[c] 39[d] 44,[c] 30[d]	**1a**	3	tr
	**4b**		**5** (exo) **6** (endo)	57 22	35 20		**4a**	18	12
	**7b**		**8**	92	70		**7a**	5	<5
	**9b**		**10**	0		55[d,c]	**9a**	90	
	**11b**			0			**11a**	90	
	**12b**		**13**	50			**12a**	20	

[a] Yields based on the *N*-chloro amide and determined by VPC. [b] Photolyses carried out in benzene. [c] Reference 12. [d] Reference 13; yields of isolated products after distillation. [e] Probably a mixture of endo and exo isomers.

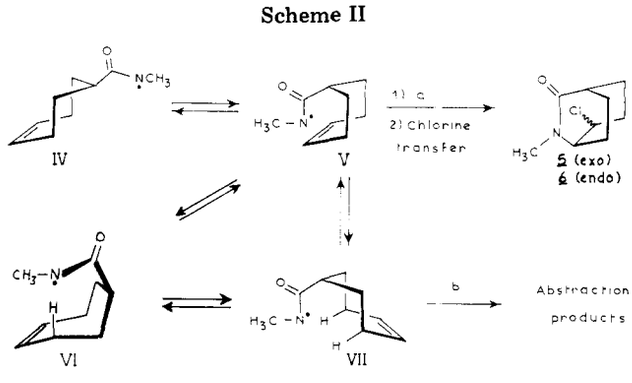
N-chloro carboxamide **1b**: intramolecular addition to the double bond (path a); intramolecular allylic hydrogen abstraction through the normally highly favored six-membered ring transition state[22,24] (path b); and hydrogen abstraction from the solvent to yield the parent amide (path c). The carbon-centered radicals II and III resulting from paths a and b, respectively, could abstract hydrogen from the solvent and/or react with another *N*-chloro amide molecule by chlorine-atom transfer.

Interestingly, the *N*-methylamido radicals I (Y = O, Z = CH_3; Scheme I) and IV (Scheme II) derived from *N*-chloro carboxamides **1b** and **4b**, respectively, follow almost exclusively path a, a result which is in marked contrast with the assumed preference for allylic hydrogen abstraction in intermolecular reactions of *N*-alkylamido radicals with olefins.[6,25] This high preference for path a is particularly noteworthy in the case of **4b**, since this process would be expected to be less favorable than in the case of **1b** and **7b** because of the formation of a six-membered ring (**5** and **6**, Scheme II), usually less favored than the formation of a five-membered ring in intramolecular radical additions to double bonds;[27] furthermore, the cycloheptene ring has to adopt a boat-like conformation[28] (V, Scheme II). On the other hand the intramolecular allylic hydrogen abstraction process involves the normally prefered 1,5-transfer[22,24] with either a twist-boat form (VI) or a chair-like conformation (VII) of the seven-membered ring (Scheme II).

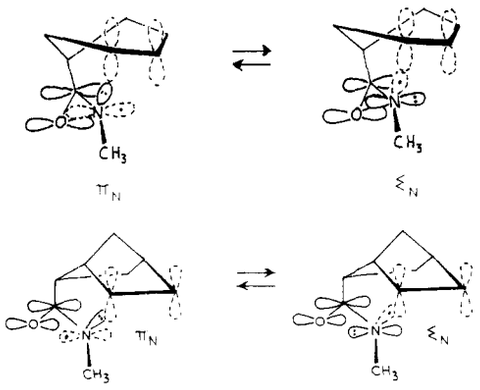
Scheme I



Scheme II



Scheme III



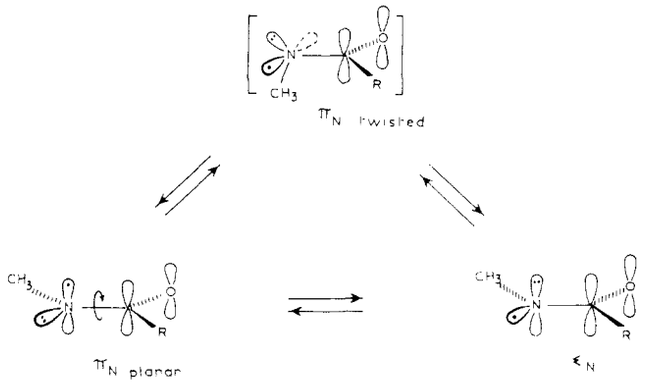
The contrasting behavior of the *N*-alkenylacetamido radicals derived from *N*-chloro acetamides **9b** and **11b** is also very interesting; they do not follow path a. The sole products isolated in high yields were the parent amides **9a** and **11a.** These amides could have arisen directly via path c and/or via path b. Their formation presumably occurs via path c for the following reasons. First of all, since the carbon-centered radicals II (Scheme I) obtained via path a did react exclusively by chlorine-atom transfer, there is no reason to believe that the more stable allylic radicals III formed via path b would prefer to abstract hydrogen from dioxane. Secondly, it will be shown, by chromous chloride reduction of **11b** carried out in a fully deuterated medium, that such an allylic radical is not formed.[16]

The less efficient cyclization of *N*-chloro acetamide **12b,** as compared to *N*-chloro carboxamide **7b,** and the failure to cyclize *N*-chloro acetamides **9b** and **11b,** suggest that an *N*-alkylamido radical would be less reactive toward a double bond on the *N*-alkyl chain than toward a double bond on the acyl chain.[16]

Our results show that benzoyl peroxide cyclization of the olefinic *N*-chloro carboxamides leads to better yields than photochemical cyclization. This can be easily understood as chlorine atoms are formed in the initiation step of the photochemical process. These are known to be quite reactive hydrogen abstractors[29] and may perform competing reactions of the type proposed by Goldfinger et al.[30] They are also known to add efficiently to olefins.[31] On the other hand no such chlorine atoms are formed during the peroxide initiation process.

One of the main points of interest concerns the electronic structure of the amido radical. ESR evidence and calculations suggest that the ground-state electronic configuration of amido radicals is of the Π_N type.[32] This has recently been used by Chow et al.[4] to satisfactorily explain, on the basis of stereoelectronic arguments, the behavior of *N*-halo carboxamides in intramolecular hydrogen abstraction processes. Examination of Dreiding models of the *N*-methylcarboxamido radicals derived from *N*-chloro carboxamides **1b** and **7b** show that, for a Π_N configuration, the Π orbital of the carbon–carbon double bond and the orbital containing the unpaired electron would be about orthogonal (Scheme III); in contrast, for a Σ_N configuration, there is maximum overlap[33,34] (Scheme III). In the case of the *N*-methylcarboxamido radical derived from **4b,** the overlap appears to be better for the Σ_N configuration. As for the acetamido radicals derived from **9b, 11b,** and **12b,** a good overlap is possible with both the Π_N and Σ_N configurations (there seems to be more nonbonded interactions with the Π_N configuration, however). Hence the failure to cyclize **9b** and **11b** and the less efficient cyclization of **12b** (as compared to **7b**) do not seem to be related to the electronic structure of the amido radicals; it is most probably due to steric effects.[16]

Scheme IV



If we assume that, in the cyclization of the amido radicals derived from **1b, 4b,** and **7b,** the Σ_N configuration is the reacting species and the Π_N planar configuration is nevertheless more stable,[4,32] the former could be in equilibrium with the latter through the Π_N twisted configuration[32b] (Scheme IV). The activation energy for the rotation around the C–N bond should be quite low because, according to ESR experiments,[32a] there is no extensive delocalization of the unpaired electron onto the carbonyl group. The Π_N planar and Σ_N configurations could also be directly interconverted by electronic reorganization (Scheme IV) as recently suggested by Goosen et al.[35] to explain their results on the intramolecular reactions of *N*-methylcarboxamido radicals with aromatic rings. Finally, the amido radical could react in a Π_N twisted configuration without rehybridization to a Σ_N configuration.[4] Interestingly, ab initio calculations predict the most stable configuration of the formamido radical as being the 50° Π_N twisted configuration.[32b]

Experimental Section

Infrared spectral data were obtained from a Perkin-Elmer 257 spectrophotometer. Routine ^{1}H NMR spectra were recorded on a Varian A60 or on a Varian XL100 WG spectrophotometer, and 250 MHz ^{1}H NMR spectra were obtained from a Cameca spectrophotometer. Mass spectra were taken on a Hitachi RMU-6E or on a AEI-MS9 spectrometer. All melting points and boiling points are uncorrected. VPC analyses and separations were performed on the following columns: OS-138 (15% on AW–DMCS Chromosorb W); OV-17 (3% on AW–DMCS Chromosorb W).

Preparation of Olefinic Amides. *N*-Methyl-3-cyclohexenecarboxamide (1a) and *N*-[(3-Cyclohexen-1-yl)methyl]acetamide (9a). Amide **1a** was prepared from 3-cyclohexenecarboxylic acid: 78% yield; mp 88–89 °C (lit.[13] mp 89–90 °C). Amide **9a** was prepared from 3-cyclohexenecarbonitrile: 63% yield; bp 109–114 °C (0.15 mm) [lit.[13] bp 88–95 °C (0.07 mm)].

***N*-Methyl-4-cycloheptenecarboxamide (4a).** A solution of 1.94 g (0.014 mol) of 4-cycloheptenecarboxylic acid[36] in 10 mL of dry benzene was cooled at 0 °C and 2.3 g (0.018 mol) of freshly distilled oxalyl chloride was added slowly with stirring. The mixture was stirred overnight at room temperature. The benzene and the excess oxalyl chloride were then stripped off. The crude acid chloride was distilled to give 1.87 g (85%) of colorless liquid: bp 80 °C (10 mm). A solution of 1.87 g (0.012 mol) of distilled acid chloride in 5 mL of dry benzene was added dropwise to 10 mL of dry benzene saturated at 0 °C with methylamine. The solution was stirred for 1 h, water was added, and the organic layer was dried over magnesium sulfate. The solvent was evaporated and the crude residue was crystallized from hexane to give 1.65 g (92%) of *N*-methyl-4-cycloheptenecarboxamide (**4a**): mp 125–127 °C; IR ($CHCl_3$) 3460, 3300, 1660 and 1520 cm^{-1}; NMR ($CDCl_3$) δ 1.4–2.5 (m, 9 H), 2.8 (d, 3 H), 5.8 (m, 2 H), and 6.5 (br, 1 H).

***N*-Methyl-5-bicyclo[2.2.1]hept-2-enecarboxamide (7a).** This amide has been prepared following standard procedures: 57 g (0.4 mol) of *endo*-5-carbomethoxybicyclo[2.2.1]hept-2-ene[37] was treated with an excess of saturated solution of methylamine in methanol at room temperature during 5 days. The solvent was stripped off to leave 44 g (78%) of a white solid which was recrystallized from a methylene chloride–pentane mixture: mp 104 °C; IR (CCl_4) 3450, 3300, 1645, and 1530 cm^{-1}; NMR δ 1.2–2.2 (m, 5 H), 2.75 (d, 3 H), 3.0 (m, 2 H), 6.1 (ddd, 2 H), and 6.5 (br, 1 H).

***N*-[(4-Cyclohepten-1-yl)methyl]acetamide (11a).** 4-Cycloheptenecarboxamide was prepared by bubbling ammonia into a solution of 5 g (0.031 mol) of the acid chloride in dry tetrahydrofuran. The solvent was stripped off and the residue was recrystallized in hexane to give 3.77 g (86%) of the amide: mp 176 °C; IR ($CHCl_3$) 3560, 3440, and 1690 cm^{-1}; NMR (Me_2SO-d_6) δ 1.2–2.55 (m, 9 H), 5.75 (m, 2 H), 6.6 (br, 1 H), and 7.15 (br, 1 H). This amide (7.36 g, 0.053 mol) was placed in a Soxhlet apparatus and reduced by means of lithium aluminium hydride in boiling tetrahydrofuran during 50 h. After normal workup and distillation under vacuum [bp 37 °C (4 mm)] one gets 5.13 g (78%) of (4-cyclohepten-1-yl)methylamine: IR (CCl_4) 3420, 3050, and 710 cm^{-1}; NMR ($CDCl_3$) δ 0.9–2.3 (m, 7 H), 1.22 (s, 2 H), 2.57 (d, 2 H), and 5.5 (m, 2 H). Treatment of 4.9 g (0.039 mol) of the primary amide by 4 g of acetic anhydride dissolved in dry benzene afforded, after workup and recrystallization from cyclohexane, 6.3 g (96%) of the pure acetamide **11a**: mp 52 °C; IR ($CHCl_3$) 3460, 1670, and 1520 cm^{-1}; NMR ($CDCl_3$) δ 1.0–2.2 (m, 9 H), 2.0 (s, 3 H), 3.12 (t, 2 H), and 5.8 (m, 3 H).

***N*-[(2-Bicyclo[2.2.1]hepten-5-yl)methyl]acetamide (12a).** 5-Bicyclo[2.2.1]hept-2-enecarboxamide was obtained by a Diels–Alder reaction between cyclopentadiene and acrylamide.[38] Reduction of this primary amide following the above described procedure (using a Soxhlet apparatus) gave the primary amine in 40% yield. Acetylation by means of acetic anhydride afforded the acetamide **12a**, which was distilled under vacuum: bp 125–126 °C (0.3 mm); IR ($CHCl_3$) 3450, 3330, 1660, and 1520 cm^{-1}; NMR ($CDCl_3$) δ 0.55 (ddd, 1H), 1.15–3.1 (m, 8 H), 1.98 (s, 3 H), and 6.05 (ddd + br, 3 H).

Preparation of Olefinic *N*-Chloro Amides. The various *N*-chloro amides have been obtained by treating the olefinic amides, dissolved in methylene chloride, with an excess of commercial bleach. Full details about the preparation, the yields, and the purity of the *N*-chloro compounds are given in the accompanying paper.[16]

Typical Procedure for the Photolysis of Olefinic *N*-Chloro Amides. Cyclization of *N*-Chloro-*N*-methyl-4-cycloheptenecarboxamide (4b). In a 50-mL Vycor irradiation cell, 1 g (0.0053 mol) of **4b** was dissolved in 20 mL of methylene chloride (freshly distilled over phosphorus pentoxide). Oxygen-free dry nitrogen was bubbled through the solution for 10 min and the solution was then irradiated in a Rayonet reactor (2500-Å lamps). Irradiation was carried out at room temperature during 1 h (until a negative starch–iodide paper test). The solution was concentrated and transfered in a 10-mL volumetric flask. The yields were determined by VPC (OS-138) using authentic samples as standards: 35% of exo isomer **5**, 20% of endo isomer **6**, and 12% of parent amide **1a**. Minor products have not been identified. The authentic samples were obtained by preparative VPC on a 5-mL aliquot.

The less polar isomer was identified as *exo*-4-chloro-6-methyl-6-azabicyclo[3.2.2]nonan-7-one (**5**). It was recrystallized from hexane: mp 67–68 °C; IR (CCl_4) 1670 cm^{-1}; NMR ($CDCl_3$) δ 1.7–2.9 (m, 9 H), 3.05 (s, 3 H), 3.65 (m, 1 H), and 4.0 (m, 1 H).

Anal. Calcd for $C_9H_{14}ClNO$: C, 57.60; H, 7.52; N, 7.46. Found: C, 57.53; H, 7.33; N, 7.46.

The more polar isomer was *endo*-4-chloro-6-methyl-6-azabicyclo[3.2.2]nonan-7-one (**6**): IR (CCl_4) 1670 cm^{-1}; NMR ($CDCl_3$) δ 1.5–2.6 (m, 8 H), 2.8 (m, 1 H), 3.18 (s, 3 H), 3.85 (m, 1 H), and 4.25 (m, 1 H).

Anal. Calcd for $C_9H_{14}ClNO$: C, 57.60; H, 7.52; N, 7.46. Found: C, 56.74; H, 7.40; N, 7.04.

The mass spectra of the two isomers were identical: *m/e* (rel intensity) 187 (M^+, 27), 151 (100), 109 (40), 95 (37), 57 (41); for these and all the other cyclization products, P/(P + 1) = 2.8–3.

The olefinic *N*-chloro amides **1b** and **7b** were irradiated respectively for 1.5 and 2 h under the same conditions. Yields were determined by VPC analyses (see Table I) and authentic samples were obtained either by preparative VPC or by preparative TLC.

Cyclization of *N*-Chloro-*N*-methyl-3-cyclohexenecarboxamide (1b). The bicyclic exo isomer **2** was recrystallized from hexane, mp 37–40 °C. The endo isomer **3** was obtained as an oil. IR and ^1H NMR spectra were consistent with those reported.[12,13]

Cyclization of *N*-Chloro-*N*-methyl-5-bicyclo[2.2.1]hept-2-enecarboxamide (7b). The tricyclic exo isomer **8** has been recrystallized from hexane to give pure *exo*-9-chloro-3-methyl-3-azatricyclo[4.2.1.$0^{1,5}$]nonan-2-one (**8**): mp 57–59 °C; IR (CCl_4) 1710 and 1400 cm^{-1}; NMR ($CDCl_3$) δ 1.5–1.63 (2 m, 2 H), 1.84–2.65 (m, 5 H), 2.85 (s, 3 H), 3.04 (m, 1 H), 3.58 (m, 1 H), and 3.64 (m, 1 H); mass spectrum *m/e* (rel intensity) 185 (M^+, 36), 150 (17), 122 (31), 110 (100), 43 (31).

Anal. Calcd for $C_9H_{12}ClNO$: C, 58.23; H, 6.52; Cl, 19.1. Found: C, 58.27; H, 6.36; Cl, 18.97.

Typical Procedure for Benzoyl Peroxide Initiated Reactions of Olefinic *N*-Chloro Amides. Cyclization of *N*-Chloro-*N*-methyl-5-bicyclo[2.2.1]hept-2-enecarboxamide (7b). In 10 mL of peroxide-free dioxane (distilled over sodium and passed through alumina) containing a catalytic amount (10 mg) of benzoyl peroxide was dissolved 927 mg (0.004 mol) of **7b**. Dry nitrogen was bubbled through the solution for 5 min. The solution was then stirred at 80 °C under nitrogen. The reaction took 29 h as checked by an iodometric test. The solvent was stripped off and the crude product dissolved in a 10-mL volumetric flask. VPC analyses were carried out as in the photochemical reaction and gave 92% of the tricyclic exo isomer **8** and <5% of the starting amide. The same procedure was used with the olefinic *N*-chloro amides **1b, 4b, 9b, 11b,** and **12b;** the reactions took respectively 4.5, 21, 22, 48, and 48 h. No cyclizations have occurred for the *N*-chloro compounds **9b** and **11b** and the parent amides were recovered in a 90% yield.

Cyclization of *N*-Chloro-*N*-[(2-bicyclo[2.2.1]hepten-5-yl)-methyl]acetamide (12b). Cyclization of the olefinic *N*-chloro amide **12b** afforded only the tricyclic exo isomer **13** in a 50% yield plus 20% of the starting amide **12a**. Recrystallization from cyclohexane gave the pure *exo*-9-chloro-3-acetyl-3-azatricyclo[4.2.1.$0^{1,5}$]nonane (**13**): mp 87–88 °C; IR ($CHCl_3$) 1630 cm^{-1}; NMR ($CDCl_3$, 250 MHz) δ 1.0 (d, 1 H), 1.6 (d, 1 H), 1.9–2.9 (m, 5 H), 2.05 and 2.2 (2 s, 3 H). 3.35 (q, 1 H), 3.4 (s, 1 H), 3.6 (s, 1 H), 4.2 (d, 1 H); mass spectrum *m/e* (rel intensity) 201 (43), 199 (M^+, 93), 159 (45), 157 (100), 110 (47), 80 (98), 43 (53).

Anal. Calcd for $C_{10}H_{14}ClNO$: C, 60.15; H, 7.07; Cl, 17.75. Found: C, 60.22; H, 6.93; Cl, 17.78.

Registry No.—**1a,** 54385-24-9; **1b,** 36393-98-3; **2,** 36294-04-4; **3,** 36394-03-3; **4a,** 53102-89-9; **4b,** 66769-77-5; **5,** 66769-88-8; **6,** 66791-98-8; **7a,** 13295-40-4; **7b,** 66769-79-5; **8,** 66769-89-9; **9a,** 54385-23-8; **9b,** 54385-09-0; *endo*-**10,** 66769-87-7; *exo*-**10,** 66769-86-6; **11a,** 66769-67-3; **11b,** 66769-78-6; **12a,** 66769-68-4; **12b,** 66769-80-0; **13,** 66769-90-2; 3-cyclohexenecarboxylic acid, 4771-80-6; 3-cyclohexenecarbonitrile, 100-45-8; 4-cycloheptenecarboxylic acid 1614-73-9; oxalyl chloride, 79-37-8; 4-cycloheptenecarbonyl chloride 3454-74-8; *endo*-5-carbomethoxybicyclo[2.2.1]hept-2-ene, 2903-75-5; 4-cycloheptenecarboxamide, 1626-63-7; (4-cyclohepten-1-yl)methylamine, 38288-79-8; 5-bicyclo[2.2.1]hept-2-enecarboxamide, 51757-85-8.

References and Notes

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Chromous Chloride Promoted Cyclization of Olefinic *N*-Chloro Amides. Synthesis of Nitrogen Heterocycles[1]

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The chromous chloride promoted cyclization of a variety of olefinic *N*-chloro-*N*-methyl carboxamides was compared to the cyclization of the analogous *N*-chloro-*N*-alkenylacetamides. In all cases but one, the yields were higher with the former than with the latter. The high yield of cyclization (95%) of *N*-chloro-*N*-methylcycloheptenecarboxamide (**13b**) is noteworthy since a six-membered ring is formed and contrasts with the failure of the analogous *N*-chloro-*N*-cycloheptenylacetamide (**16b**) to cyclize. A number of nitrogen heterocycles were synthesized in good to excellent yields, including the azahomoadamantanone derivative **28** and the azaadamantane derivatives **30** and **31**. An attempt to prepare an azatwistanone derivative from *N*-chloro carboxamide **26b** failed. Comparison with photochemical and peroxide cyclizations of a few *N*-chloro amides showed that better yields were usually obtained with the chromous chloride method. The reaction mechanism is discussed from the following points of view: comparison of reactivity of the *N*-chloro carboxamides and *N*-chloro acetamides; comparison of the relative reactivity of amido radicals (complexed or not) in intramolecular addition to double bonds and intramolecular allylic hydrogen abstraction; stereochemistry; nature of the transfer step of the radical chain reaction.

Introduction

The chromous chloride promoted intermolecular addition of *N*-halo amides (ZCONHX) to a variety of olefins has been shown to proceed in good to excellent yields,[2] whereas *N*-alkyl-*N*-halo amides (ZCONRX) failed to add under the same conditions.[2a] This failure could be due to the fact that chromium(II) reduction of an *N*-alkylamido radical would be faster than its addition to the olefin as already suggested.[2b] However, intramolecular addition of *N*-alkylamido radicals would be expected to compete favorably with their chromium(II) reduction (an intermolecular process). Indeed, as we will see, the chromous chloride promoted cyclization of olefinic *N*-chloro amides does occur in good to excellent yields.

In the preceding paper,[3] we have compared the intramolecular behavior of *N*-chloro amides toward double bonds under photochemically and peroxide-initiated decomposition. Due to the special design of the models used, it was possible to gain information on the electronic structure of *N*-alkylamido radicals. Because of the possible complexation of these radicals with chromium ions,[2b] their electronic structure will not be considered in this paper.

In the present paper, we are going to (i) evaluate the scope and limitations of the chromous chloride method for the synthesis of nitrogen heterocycles, comparing the cyclization of olefinic *N*-chloro carboxamides A and *N*-chloro acetamides B; (ii) see whether the cyclization would occur when a six-membered transition state is involved; (iii) examine the competition between intramolecular abstraction of allylic hydrogens by the amido radical, and its intramolecular addition to double bonds; and (iv) study the stereochemistry of the cyclization reaction.

A B

As will be seen, most of the questions raised could be answered in a satisfactory manner and an efficient process for the synthesis of functionalized nitrogen heterocycles was devised. This method constitutes a useful complement to the synthesis of azabicyclic and polycyclic molecules efficiently

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