Intramolecular [3 + 2] Annulation of Olefin-Tethered Cyclopropylamines

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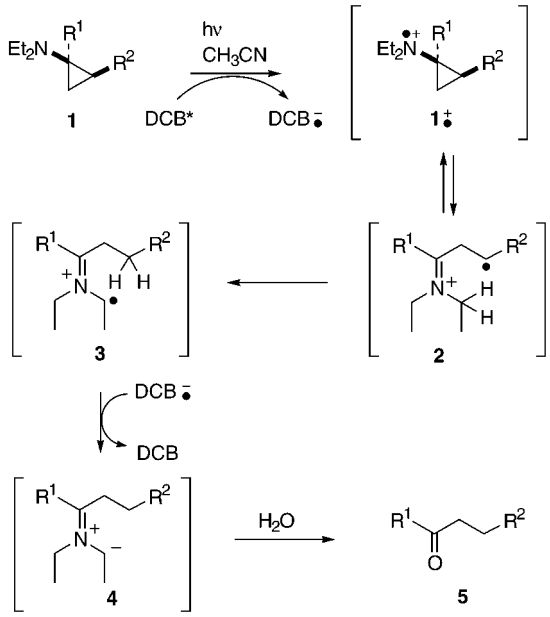
Starting from readily available olefin-tethered tertiary aminocyclopropanes, we have developed a convenient [3 + 2] annulation reaction by means of one-electron oxidation which can be induced photochemically or chemically, followed by two sequential 5-exo radical cyclizations. The rate constants for the competing 1,5-hydrogen transfer in the β-immonium carbon radical intermediate have been estimated to fall between 1000 (6-exo) and 100 (7-exo and/or 8-endo) s^{-1} at room temperature.

Tertiary aminocyclopropanes **1** can be prepared in good yields by the Simmons−Smith cyclopropanation of enamines or, more conveniently, by Ti(II)-mediated coupling of terminal olefins and *N*,*N*-dialkylcarboxamides.[1−5] They resist ring cleavage by acids, bases, or electrophiles.[6] We recently developed a convenient method for facile ring opening of these cyclopropylamines by photosensitized oxidation (Scheme 1).[7] The cyclopropylamine cation radicals **1**$^{\bullet+}$ undergo facile ring opening, followed by 1,5-hydrogen shift(s) of the resulting β-immonium carbon radicals **2**, to afford the ring-opened ketones **5** upon hydrolysis. Analogous ring opening of the cyclopropylamine radical cations has been implicated as the mode of inactivation by cyclopropylamines of cytochrome P-450 and monoamine oxidase.[8] In light of the synthetic potential and biological significance of cyclopropylamine cation radicals, we decided to assess the relative rates of 1,5-hydrogen transfer (i.e., **2a** → **3a**) of the β-immonium carbon radical intermediate by employing competitive 5-, 6-, and 7-exo cyclization (e.g., **2a** → **6**) to the tethered olefin (eq 1).[9,10] Herein we report a new, intramolecular

Scheme 1



[3 + 2] annulation of olefin-tethered cyclopropylamines by photosensitized and chemical oxidation.[11−13]

(1) Chaplinski, V.; de Meijere, A. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 413.

(2) Lee, J.; Cha, J. K. *J. Org. Chem.* **1997**, *62*, 1584.

(3) This new synthetic method for electron-donor substituted cyclopropanes, in turn, evolved from the original Kulinkovich procedure: (a) Kulinkovich, O. G.; Sviridov, S. V.; Vasilevskii, D. A.; Prityts kaya, T. S. *Zh. Org. Khim.* **1989**, *25*, 2244. (b) Kulinkovich, O. G.; Sviridov, S. V.; Vasilevskii, D. A.; Savchenko, A. I.; Prityts kaya, T. S. *Zh. Org. Khim.* **1991**, *27*, 294. (c) Kulinkovich, O. G.; Sorokin, V. L.; Kel'in, A. V. *Zh. Org. Khim.* **1993**, *29*, 66.

(4) (a) Lee, J.; Kang, C. H.; Kim, H.; Cha, J. K. *J. Am. Chem. Soc.* **1996**, *118*, 291. (b) Lee, J.; Kim, H.; Cha, J. K. *J. Am. Chem. Soc.* **1996**, *118*, 4198. (c) Lee, J.; Kim, Y. G.; Bae, J.; Cha, J. K. *J. Org. Chem.* **1996**, *61*, 4878. (d) Cho, S. Y.; Lee, J.; Lammi, R. K.; Cha, J. K. *J. Org. Chem.* **1997**, *62*, 8235. See also: (e) Lee, J.; Kim, H.; Cha, J. K. *J. Am. Chem. Soc.* **1995**, *117*, 9919. (f) Lee, J.; Cha, J. K. *Tetrahedron Lett.* **1996**, *37*, 3663. (g) U, J. S.; Lee, J.; Cha, J. K. *Tetrahedron Lett.* **1997**, *38*, 5233. (h) Lee, J.; Ha, J. D.; Cha, J. K. *J. Am. Chem. Soc.* **1997**, *119*, 8127.

(5) See also: (a) Corey, E. J.; Rao, S. A.; Noe, M. C. *J. Am. Chem. Soc.* **1994**, *116*, 9345. (b) Kasatkin, A.; Sato, F. *Tetrahedron Lett.* **1995**, *36*, 6079. (c) Kasatkin, A.; Kobayashi, K.; Okamoto, S.; Sato, F. *Tetrahedron Lett.* **1996**, *37*, 1849 and references therein.

(6) Kuehne, M. E.; King, J. C. *J. Org. Chem.* **1973**, *38*, 304.

(7) Lee, J.; U, J. S.; Blackstock, S. C.; Cha, J. K. *J. Am. Chem. Soc.* **1997**, *119*, 10241.

(8) See, inter alia: (a) Guengerich, F. P.; Macdonald, T. L. *Adv. Electron Transfer Chem.* **1993**, *3*, 191. (b) Hanzlik, R. P.; Tullman, R. H. *J. Am. Chem. Soc.* **1982**, *104*, 2048. (c) Silverman, R. B. *J. Biol. Chem.* **1983**, *258*, 14766. See also: (d) Pirrung, M. C. *J. Am. Chem. Soc.* **1983**, *105*, 7207.

(9) For recent investigations on kinetics of other aminium radical reactions, see: (a) Goez, M.; Satorius, I. *J. Am. Chem. Soc.* **1993**, *115*, 11123. (b) Horner, J. H.; Martinez, F. N.; Musa, O. M.; Newcomb, M.; Shahin, H. E. *J. Am. Chem. Soc.* **1995**, *117*, 11124. (c) Musa, O. M.; Horner, J. H.; Shahin, H.; Newcomb, M. *J. Am. Chem. Soc.* **1996**, *118*, 3862. Cf.: (d) Maeda, Y.; Ingold, K. U. *J. Am. Chem. Soc.* **1980**, *102*, 328.

(10) For recent examples of intramolecular hydrogen atom transfer, see inter alia: (a) Beckwith, A. L. J.; Ingold, K. U. In *Rearrangements in the Ground and Excited States*; de Mayo, P., Ed.; Academic: New York, 1980; Vol. 1, p 161. (b) Baldwin, J. E.; Adlington, R. M.; Robertson, J. *Tetrahedron* **1989**, *45*, 909. (c) Snieckus, V.; Cuevas, J.-C.; Sloan, C. P.; Liu, H.; Curran, D. P. *J. Am. Chem. Soc.* **1990**, *112*, 896. (d) White, J. D.; Jeffrey, S. C. *Synlett* **1995**, 831.

(11) In a previous communication (footnote 17 of ref 7), we had disclosed that the ring-opened, β-immonium carbon radical can be trapped effectively by a tethered olefin by means of 5-exo cyclization, affording efficient bicyclic annulation.

(12) A recent report on the related CAN-mediated cyclization prompted us to report our own results: Takemoto, Y.; Yamagata, S.; Furuse, S.-i.; Hayase, H.; Echigo, T.; Iwata, C. *J. Chem. Soc., Chem. Commun.* **1998**, 651.

(13) Cyclopropyl sulfides bearing a benzylidene moiety were shown to undergo similiar cyclization: Takemoto, Y.; Furuse, S.-i.; Koike, H.; Ohra, T.; Iwata, C.; Ohishi, H. *Tetrahedron Lett.* **1995**, *36*, 4085.

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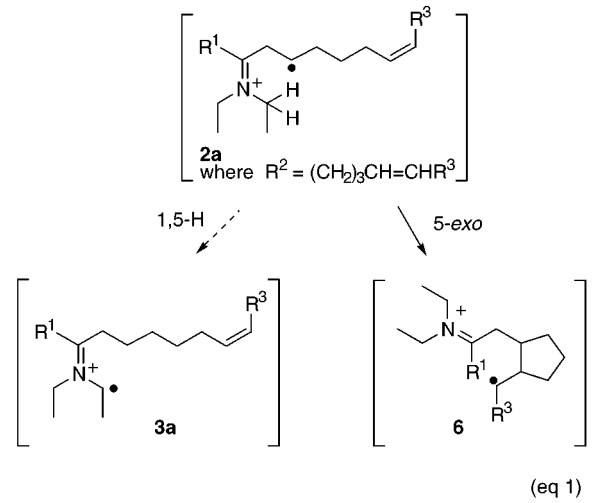
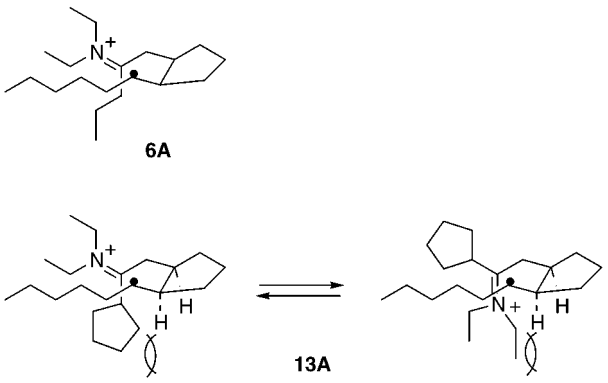


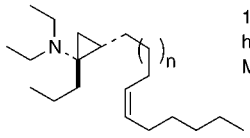
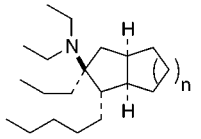
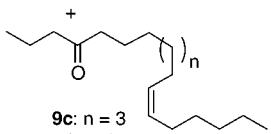
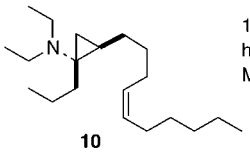
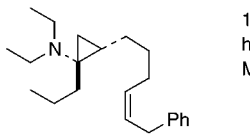
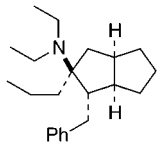
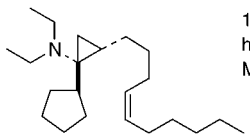
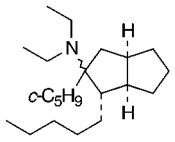
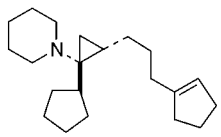
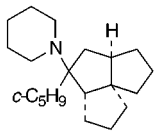
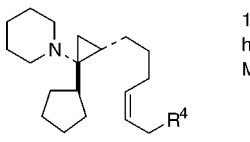
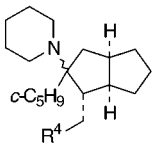
(eq 1)

The starting materials **1** were readily prepared in a single step by Ti(II)-mediated coupling of the corresponding dienes.[2] The *trans*-1,2-dialkyl (major) isomers were used for photooxidation experiments (Table 1). In a typical experiment, a deaerated solution of cyclopropylamine **7a** in 10:1 MeCN−H_2O containing 1.5 equiv of 1,4-dicyanobenzene (DCB) was irradiated for 1 h; the bicyclic amine **8a** was isolated as a single diastereomer in 91% yield (based on 66% conversion) (entry 1, Table 1). The expected β-immonium carbon radical **2a** preferentially undergoes 5-exo cyclization over the competing 1,5-hydrogen transfer to afford a new radical **6**. A second intramolecular cyclization, followed by reduction with $DCB^{\bullet-}$, then affords the annulation product. On the basis of steric considerations (see **6A**), its stereochemistry is tentatively assigned as **8a**. The observation that replacement of the propyl group by the bulkier cyclopentyl unit (see **13A**) resulted in the stereorandom (1:1) production of two diastereomers **14** (entry 6) supports this stereochemical assignment (compare also entry 5 vs entries 8 and 9). Both *trans*- and *cis*-1,2-dialkyl diastereomers, **7a** and **10**, gave the identical photooxidation product **8a** (entry 4). Photooxidation of the homologue **7b** also furnished the amino-substituted bicyclo[4.3.0]nonane **8b** in 47% (unoptimized) yield (based on 75% conversion). On the other hand, no cyclization product **8c**, but only the ketone **9c**, was obtained (60% yield) from the homologue **7c**. The rate constants for 1,5-hydrogen transfer in these systems are estimated to fall between 1000 (6-exo) and 100 (7-exo and/or 8-endo) s^{-1} at room temperature.



The fused tricyclic product **16** was obtained as a single isomer in 50% yield (based on 60% conversion).[14] Although the yield remains to be optimized, it is noteworthy that the two-step sequence involving cyclopropanation of

Table 1.

entry	cyclopropylamines	product(s)
1	 **7a**: n = 1	1.5 equiv DCB, hν, MeCN-H_2O, 1 h →  **8a**: n = 1 (60%) + **7a**: n = 1 (34% recovered)
2	**7b**: n = 2	**8b**: n = 2 (35%) + **7b**: n = 2 (25% recovered)
3	**7c**: n = 3	**8c**: n = 3 (0%) +  **9c**: n = 3 (60%)
4	 **10**	1.5 equiv DCB, hν, MeCN-H_2O, 0.8 h → **8a** (48%) + **7a** (41% recovered)
5	 **11**	1.5 equiv DCB, hν, MeCN-H_2O, 1.3 h →  **12** (60%) + **11** (30% recovered)
6	 **13**	1.5 equiv DCB, hν, MeCN-H_2O, 1.3 h →  **14** ~1 : 1 (60%) + **13** (17% recovered)
7	 **15**	1.5 equiv DCB, hν, MeCN-H_2O or MeCN-MeOH, 1 h →  **16** (30%) + **15** (40% recovered)
8	 **17**: $R^4 = (CH_2)_3CH_3$	1.5 equiv DCB, hν, MeCN-MeOH, 10 h →  **18** ~ 1.4 : 1 (36%) + **17** (52% recovered)
9	**19**: R^4 = *i*Pr	**20** ~ 1.2 : 1 (48%) + **19** (42% recovered)

(14) Whereas the stereochemistry has not been assigned yet, it is likely that **16** has the piperidine ring in the β configuration (with the α configuration of the cyclopentyl group).

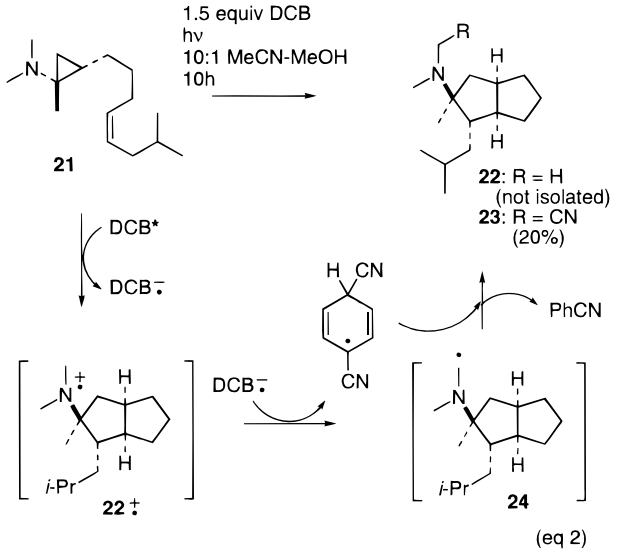
Table 2. Photosensitized Oxidation of Cyclopropylamines 7a and 13 in Several Solvent Systems

starting materials	*reaction conditions*	*products*			*recovered starting material(s)*
7a	1.5 equiv DCB, hν	**8a**	+ **7a**	+ **10**	
	10:1 MeCN-H_2O, 1h	60%	28%		6%
	10:1 MeCN-H_2O, 2h	56%	10%		4%
	10:1 MeCN-NH_4Cl, 1h	45%	trace		trace
	10:1 MeCN-pH 9, 1.6h	34%	trace		trace
13	1.5 equiv DCB, hν	**14**	+ **13**	+ **13-*C***	
	10:1 MeCN-H_2O, 1.3h	60%	14%		3%
	10:1 MeCN-NH_4Cl, 2h	50%	0%		0%
	10:1 MeCN-pH 7, 2h	42%	12%		trace
	10:1 MeCN-MeOH, 1h	26%	43%		3%

a readily available diene and subsequent photooxidation provides convenient, easy access to the structurally complex triquinane ring system.

As can be seen from the examples in Table 1, a shortcoming of this novel [3 + 2] annulation reaction centers around low conversion. The crux of the problem is posed by the fact that the tertiary amine functionality of the annulation products is also susceptible to photooxidation; in fact, the amine products are anticipated to possess lower ionization and oxidation potentials than the starting materials because of the greater s character of the cyclopropyl group (compared to an sp^3 alkyl).[15] Indeed, prolonged irradiation resulted in poor yields due to further oxidative degradation of the desired product. In attempts to protect the tertiary amine products from such degradation by means of selective protonation, use of a (pH 7 or 9 phosphate) buffer and aqueous NH_4Cl solution, in addition to 10:1 $CH_3CN-MeOH$,[16a] was investigated (Table 2). Unfortunately, none of the variations afforded the desired selective shield to the products; the best results were obtained by use of 10:1 CH_3CN-H_2O.[16b] Only when sterically demanding groups are present at and near the amine (i.e., entries 7−9 vs entries 1−6, Table 1) could 10:1 $CH_3CN-MeOH$ be utilized as the solvent to achieve comparable yields. It is interesting to note that the annulation reaction proceeds faster in 10:1 CH_3CN-H_2O than in $CH_3CN-MeOH$.

The undesired oxidative decomposition likely involves α-CH deprotonation, a well-documented reaction, of the aminium radicals[17] and appears to be more pronounced for small alkyl substituents (such as methyl) at the amine group. For example, the nitrile **23** was obtained as the only isolable product (as a single diastereomer) in 20% yield from photooxidation of cyclopropylamine **21** (eq 2).



(eq 2)

Next, α-CH deprotonation of the aminium radicals was explored concurrently with the oxidation of the resulting neutral α-amino radicals of type **27** (or **24**) to generate immonium ions **28**, which should be inert to further oxidation (eq 3). Treatment of **7a** with ceric ammonium nitrate (CAN) (5 equiv of CAN, 5 equiv of $NaHCO_3$, in 5:1 $MeOH-CH_2Cl_2$) afforded the secondary amine **25** in 61% yield, along with amide **26** (15%), ketone **9a** (5%), and unreacted **7a** (10%).[18] The results of the use of other solvents are tabulated in Table 3. Mechanistically, the CAN-mediated [3 + 2] annulation reaction parallels the photooxidative process, but the main difference emerges only after the formation of the initial annulation products. Under CAN oxidation, the original annulation products undergo further oxidation to result in dealkylation, whereas such a pathway is precluded in the photosensitized oxidation by the presence of $DCB^{\bullet-}$. The [3 + 2] annulation reaction is anticipated to be general and tolerant of a wide range of substitution patterns: it is by no means limited to *N*-benzylamino cyclopropanes.[19]

(15) For example, cyclopropyl(dimethyl)amine was found to be less basic (pK_{BH^+} = 7.7) than cyclohexyl(dimethyl)amine (pK_{BH^+} = 9.2): Roberts, J. D.; Chambers, V. C. *J. Am. Chem. Soc.* **1951**, *73*, 5030.

(16) (a) This solvent system was originally and successfully employed for the generation of the ring-opened ketones by photosensitized oxidation of tertiary aminocyclopropanes (ref 7). (b) While the reason for the beneficial effect of water is presently unclear, it is tempting to speculate that it might be in part due to H-bonding between water and the tertiary amine.

(17) Cf.: (a) Nelsen, S. F. In *Free Radicals*; Kochi, J. K., Ed.; Wiley: New York, 1973; Vol. 2, Chapter 21. (b) Chow, Y. L.; Danen, W. C.; Nelsen, S. F.; Rosenblatt, D. H. *Chem. Rev.* **1978**, *78*, 243. (c) Stella, L. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 337. (d) Newcomb, M.; Deeb, T. M. *J. Am. Chem. Soc.* **1987**, *109*, 3163. (e) Zhang, X.; Yeh, S.-R.; Hong, S.; Freccero, M.; Albini, A.; Falvey, D. E.; Mariano, P. S. *J. Am. Chem. Soc.* **1994**, *116*, 4211 and references therein.

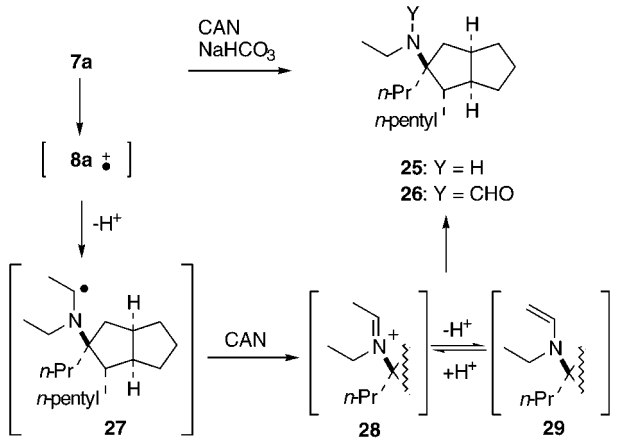
(18) The formamide formation is presumed to arise from oxidation of the enamine intermediate **29**. The detailed mechanism must await further study. Cf.: (a) Jerussi, R. A. *J. Org. Chem.* **1969**, *34*, 3648. (b) Blau, K.; Voerckel, V. *J. Prakt. Chem.* **1989**, *331*, 285.

(19) Iwata and co-workers have recently reported facile debenzylation in similar CAN-mediated annulation reactions of *N*-benzyl cyclopropylamines.[12] On the basis of our present findings, we believe their proposed timing of debenzylation is incorrect; the correct debenzylation mechanism involves the identical sequence as described for **8a** → **27** → **28** → **25**.

Table 3. CAN Oxidation of Cyclopropylamine 7a Under Several Conditions

starting materials	*reaction conditions*	*products*				*recovered starting material(s)*
7a	5 equiv CAN 5 equiv $NaHCO_3$	**25**	+ **26**	+ **9a*** (n = 1)	+	**7a**
	DMF (24m*M*) 2h	22%	25%	49%		
	DMF (6m*M*) 2h	22%	40%	25%		
	10:1 DMF-H_2O 24h	trace				82%
	5:1 MeOH-CH_2Cl_2 24h	61%	15%	5%		10%
	5:1 MeOH-THF 25h	61%	5%	5%		20%
	10 equiv CAN 10 equiv $NaHCO_3$ 5:1 MeOH-CH_2Cl_2 25h	55%	20%	18%		0%

*The ketone **9a** was admixed with inseparable, unidentified byproducts.



(eq 3)

In summary, starting from readily available olefin-tethered cyclopropylamines, we have developed a convenient [3 + 2] annulation reaction by means of one-electron oxidation which can be induced photochemically or chemically, followed by two sequential 5-exo radical cyclizations. The rate constants for the competing 1,5-hydrogen transfer in the β-immonium carbon radical intermediate have been estimated to fall between 1000 (6-exo) and 100 (7-exo and/or 8-endo) s^{-1} at room temperature. Further optimization and comparison studies of the photochemical and chemical [3 + 2] annulation methods, along with synthetic applications, will be reported in due course.

Experimental Section

A Representative Procedure for Photosensitized Oxidation of Olefin-Tethered *N,N*-Dialkylcyclopropylamines. A mixture of the tertiary aminocyclopropane **7a** (29 mg, 0.1 mmol) and 1,4-dicyanobenzene (19 mg, 0.15 mmol) in 10:1 CH_3CN-H_2O (33 mL) was placed in a Hanovia 450-W immersion photochemical reactor (equipped with a medium-pressure mercury lamp) and deaerated with nitrogen. The reaction mixture was irradiated at room temperature for 1 h under a nitrogen atmosphere. After the lamp was turned off, the resulting mixture was extracted with EtOAc (2 × 20 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (5:1 hexane−EtOAc) to afford the bicyclic annulation product **8a** (17 mg, 60%), along with 10 mg (34%) of the recovered cyclopropylamine (as a ~4:1 mixture of *cis*- and *trans*-1,2-dialkyl isomers, **7a** and **10**).

8a: ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.88 (t, J = 7.2 Hz, 3 H), 0.89 (t, J = 6.9 Hz, 3 H), 0.96 (t, J = 7.0 Hz, 6 H), 1.15−1.65 (m, 20 H), 1.74 (dd, J = 8.0, 12.4 Hz, 1 H), 1.94 (m, 1 H), 2.25 (m, 1 H), 2.59 (q, J = 7.0 Hz, 4 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 14.1, 15.2, 17.0, 17.5, 22.7, 25.7, 28.9, 32.1, 32.7, 33.2, 34.9, 35.0, 39.4, 41.3, 43.3, 49.1, 52.6, 71.2; MS *m*/*z* 293 (M^+, 2), 222 (49), 191 (58), 149 (100), 121 (76); HRMS (M^+) 293.3082 calcd for $C_{20}H_{39}N$, found 293.3078.

8b: ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.89 (t, J = 7.2 Hz, 6 H), 1.01 (t, J = 7.1 Hz, 6 H), 1.10−1.57 (m, 19 H), 1.58 (m, 1 H), 1.64−1.81 (m, 4 H), 2.02 (m, 1 H), 2.44 (dq, J = 14.0, 7.1 Hz, 2 H), 2.51 (dq, J = 14.0, 7.1 Hz, 2 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 14.1, 15.1, 17.1, 17.9, 22.6, 26.3, 26.6, 29.7, 29.9, 31.4, 31.7, 32.3, 32.9, 38.7, 43.9, 44.0, 44.5, 50.8, 53.1, 69.6; MS *m*/*z* 307 (M^+, 1), 216 (53), 187 (78), 163 (76), 121 (100); HRMS (M^+) 307.3239 calcd for $C_{21}H_{41}N$, found 307.3232.

9c: IR (CH_2Cl_2) 1709 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.88 (t, J = 7.1 Hz, 3 H), 0.91 (t, J = 7.5 Hz, 3 H), 1.28 (m, 14 H), 1.58 (m, 4 H), 2.00 (m, 4 H), 2.36 (t, J = 7.3 Hz, 2 H), 2.37 (t, J = 7.4 Hz, 2 H), 5.35 (m, 2 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 13.8, 14.1, 17.3, 22.6, 23.8, 27.2, 29.1, 29.2, 29.3, 29.4, 29.7, 31.5, 32.5, 42.8, 44.7, 129.8, 129.9, 211.5; MS *m*/*z* 266 (M^+, 22), 223 (79), 178 (49), 153 (86), 125 (100); HRMS (M^+) 266.2609 calcd for $C_{18}H_{34}O$, found 266.2599.

12: ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.94 (t, J = 7.2 Hz, 3 H), 1.04 (t, J = 7.1 Hz, 6 H), 1.14−1.45 (m, 12 H), 1.65 (m, 1 H), 1.79 (m, 2 H), 2.05 (m, 1 H), 2.25 (m, 1 H), 2.72 (q, J = 7.1 Hz, 4 H), 7.21 (m, 5 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 15.2, 17.1, 17.5, 25.4, 33.2, 33.8, 34.8, 38.1, 39.0, 40.9, 43.2, 48.2, 54.7, 71.3, 125.4, 128.1, 129.0, 142.6.

14 (one diastereomer): ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.89 (t, J = 6.7 Hz, 3 H), 1.01 (t, J = 7.0 Hz, 6 H), 1.15−1.69 (m, 24 H), 1.94 (dd, J = 8.4, 14.1 Hz, 1 H), 2.22 (m, 1 H), 2.34 (m, 1 H), 2.47 (m, 1 H), 2.68 (dq, J = 14.0, 7.0 Hz, 2 H), 2.77 (dq, J = 14.0, 7.0 Hz, 2 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 14.2, 17.1, 22.7, 25.3, 25.7, 26.4, 29.2, 29.3, 30.0, 31.9, 33.0, 34.1, 34.3, 39.0, 41.3, 44.3, 45.1, 50.8, 55.9, 75.7; MS *m*/*z* 319 (M^+, 1), 246 (17), 222 (20), 175 (100), 133 (37); HRMS (M^+) 319.3239 calcd for $C_{22}H_{41}N$, found 319.3220.

14 (the other diastereomer): ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.89 (t, J = 6.7 Hz, 3 H), 0.96 (t, J = 7.0 Hz, 6 H), 1.15−1.70 (m, 24 H), 1.91 (dd, J = 8.8, 13.3 Hz, 1 H), 1.99 (m, 1 H), 2.11 (m, 1 H), 2.30 (m, 1 H), 2.55 (ddq, J = 13.5, 13.5, 7.0 Hz, 4 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 14.2, 17.4, 22.8, 24.9, 25.8, 26.1, 27.5, 29.1, 30.4, 32.8, 33.2, 34.5, 35.7, 39.4, 41.1, 43.7, 44.7, 50.4, 54.4, 74.2.

16: ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.25−1.83 (m, 27 H), 1.91−2.02 (m, 2 H), 2.09 (m, 1 H), 2.30 (m, 1 H), 2.68 (m, 4 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 25.2, 25.6, 26.0, 26.7, 27.9, 28.4, 29.4, 29.8, 32.3, 40.2, 42.0, 42.3, 46.1, 48.7, 50.0, 60.4, 73.3; MS *m*/*z* 301 (M^+, 2), 232 (100), 216 (58), 187 (67), 173 (64), 147 (42), 119 (46); HRMS (M^+) 301.2769 calcd for $C_{21}H_{35}N$, found 301.2762.

18 (one diastereomer): ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.89 (t, J = 6.5 Hz, 3 H), 1.06 (dd, J = 10.2, 13.7 Hz, 1 H), 1.11−1.63 (m, 30 H), 1.86 (dd, J = 7.7, 13.7 Hz, 1 H), 2.20 (m, 1 H), 2.35 (m, 1 H), 2.63 (br s, 4 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 14.2, 22.7, 25.2, 25.7, 26.0, 28.0, 28.9, 29.1, 29.7, 29.8, 32.0, 32.9, 33.6, 33.8, 36.9, 40.4, 43.1, 50.0, 50.4, 55.8, 73.8; MS *m*/*z* 331 (M^+, 3), 262 (59), 217 (18), 175 (100), 133 (30); HRMS (M^+) 331.3239 calcd for $C_{23}H_{41}N$, found 331.3231.

20 (one diastereomer): ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.83 (d, J = 6.4 Hz, 3 H), 0.91 (d, J = 6.4 Hz, 3 H), 1.08 (dd, J = 10.3, 13.7 Hz, 1 H), 1.16−1.62 (m, 23 H), 1.64 (m, 1 H), 1.86

(dd, J = 7.8, 13.7 Hz, 1 H), 2.18 (m, 1 H), 2.25 (m, 2 H), 2.63 (br s, 4 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 22.2, 24.7, 25.3, 25.7, 25.9, 26.0, 26.2, 28.0, 28.7, 29.8, 33.4, 33.7, 37.0, 40.6, 41.7, 43.0, 50.0, 50.7, 52.6, 74.0; MS m/z 317 (M^+, 4), 274 (30), 248 (87), 176 (100), 133 (50); HRMS (M^+) 317.3082 calcd for $C_{22}H_{39}N$, found 317.3099.

23: ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.89 (d, J = 6.4 Hz, 3 H), 0.92 (d, J = 6.4 Hz, 3 H), 1.01 (s, 3 H), 1.17 (m, 2 H), 1.37 (m, 1 H), 1.44 (m, 2 H), 1.50−1.77 (m, 6 H), 1.72 (dd, J = 10.3, 13.7 Hz, 1 H), 1.97 (m, 1 H), 2.36 (m, 1 H), 2.41 (s, 3 H), 3.50 (d, A of ABq, J = 17.5 Hz, 1 H), 3.66 (d, B of ABq, J = 17.5 Hz, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 19.5, 21.6, 24.7, 25.6, 25.7, 33.1, 33.9, 35.8, 38.8, 39.9, 40.2, 40.5, 47.9, 48.0, 68.0, 118.3.

A Representative Procedure for CAN Oxidation of Olefin-Tethered *N,N*-Dialkylcyclopropylamines. To a solution of cyclopropylamine **7a** (29 mg, 0.1 mmol) in 5:1 MeOH−CH_2Cl_2 (6 mL) were added CAN (0.27 g, 0.5 mmol) and $NaHCO_3$ (42 mg, 0.5 mmol). The resulting mixture was stirred at room temperature for 24 h and concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (10 mL) and 1 N NaOH (2 mL). After the organic solution layer was separated, the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography (hexane; 10:1 hexane−EtOAc; 30:1 CH_2Cl_2−EtOH) to afford the bicyclic products **25** and **26**, in addition to the ring-opened ketone **9a** and the unreacted starting material **7a**.

25: ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.88 (t, J = 6.7 Hz, 3 H), 0.94 (t, J = 6.6 Hz, 3 H), 1.19−1.70 (m, 19 H), 1.35 (t, J = 7.2 Hz, 3 H), 1.88 (m, 1 H), 2.06 (m, 1 H), 2.17 (dd, J = 7.9, 12.6 Hz, 1 H), 2.39 (m, 1 H), 2.93 (m, 1 H), 3.04 (m, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 12.2, 14.0, 14.7, 16.7, 22.7, 25.1, 28.2, 30.8, 32.4, 32.7, 32.9, 34.5, 38.5, 39.8, 40.3, 49.0, 52.9, 70.6.

26: IR (CH_2Cl_2) 2934, 1659 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.89 (t, J = 6.7 Hz, 3 H), 0.92 (t, J = 7.3 Hz, 3 H), 1.11 (t, J = 7.0 Hz, 3 H), 1.15−1.72 (m, 20 H), 2.03 (m, 1 H), 2.08 (dd, J = 7.7, 12.3 Hz, 1 H), 2.41 (m, 1 H), 3.12 (dq, J = 14.0, 7.0 Hz, 1 H), 3.52 (dq, J = 14.0, 7.0 Hz, 1 H), 8.21 (s, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 14.0, 14.4, 14.6, 16.3, 22.6, 25.3, 28.4, 30.3, 32.3, 32.4, 32.6, 34.4, 35.6, 39.3, 41.1, 47.7, 54.2, 70.4, 162.5.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra (24 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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