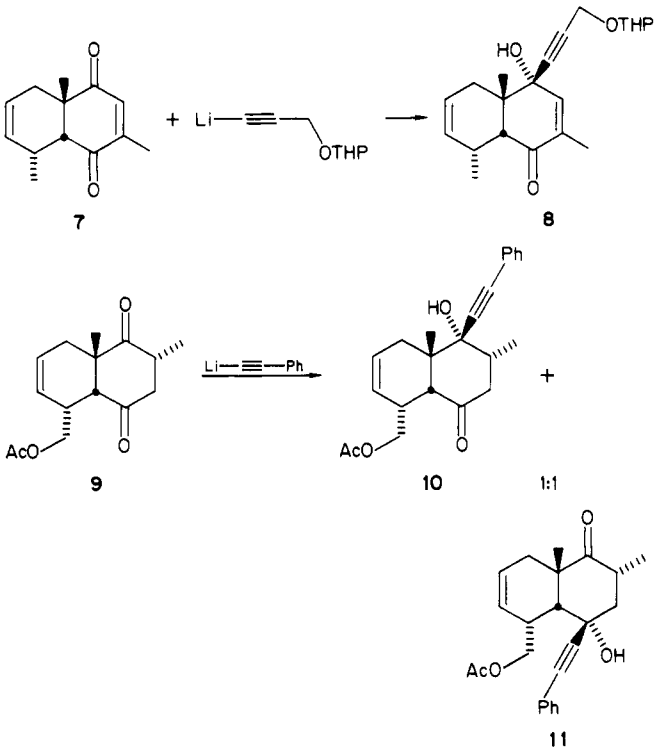

Acknowledgment. This work was supported by the National Institutes of Health and, in part, by Schering-Plough Corporation. We also thank the National Science Foundation for providing funds for the purchase of a Nicolet 360-MHz NMR spectrometer.

(9) A typical experimental procedure follows. To a solution of 1.17 g (8.35 mmol, 2 equiv of propargyl alcohol and tetrahydropyranyl ether in 20 mL of dry THF at ~78 °C under argon was added 7.11 mL (7.52 mmol, 1.8 equiv) of a 1.06 M solution of *n*-BuLi. The mixture was allowed to stir at ~78 °C for $^1/_2$ h and at 0 °C for an additional $^1/_2$ h. At this point it was cooled to ~78 °C again and added via syringe to a solution of 1.25 g (4.18 mmol, 1 equiv) of 1 (X = H, Y = SPh) in 20 mL of THF at ~78 °C under argon. The mixture was allowed to stir at ~78 °C for 2 h and at 0 °C for $^1/_2$ h. The reaction mixture was then quenched with a saturated NH_4Cl solution and the solvent was removed under vacuum. The residue was diluted with water and extracted with ether (3 × 50 mL). The combined extracts were washed successively with 5% HCl solution, saturated brine, and water. The ether was removed under reduced pressure and the residue was purified by MPLC (silica gel) to give 2 (X = H, Y = SPh, R = C≡CCH_2OTHP) (1.73 g, 97% yield): 90-MHz ^1H NMR ($CDCl_3$) 7.15-7.61 (m, 5 H), 5.88-6.12 (m, 1 H), 5.84 (brs, 1 H), 5.48-5.72 (m, 1 H), 4.78-4.93 (m, 1 H), 4.32 (s, 2 H), 3.58-4.05 (m, 2 H), 3.25 (d, J = 3 Hz, 1 H), 2.25-2.61 (m, 1 H), 2.03 (d, J = 1 Hz, 3 H), 1.39-1.98 (m, 8 H), 1.35 (s, 3 H); mass spectrum, m/e, 438.

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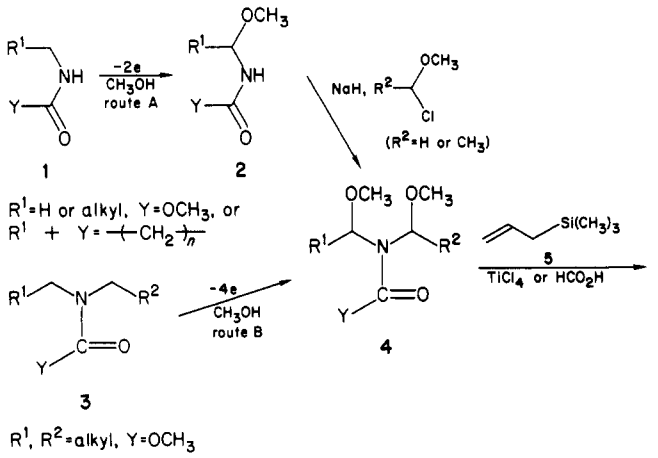
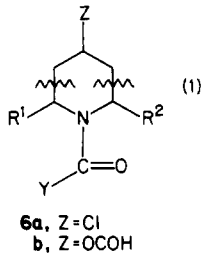
A New [3+3]-Type Annelation Useful for the Formation of Piperidine Skeletons[1]

Summary: A [3 + 3]-type annelation between α,α'-dimethoxylated amides **4** and allyltrimethylsilane (**5**) gave piperidine derivatives **6**. It was applied to the synthesis of piperidine, indolizidine, quinolizidine, 1-azabicyclo[5.4.0]undecane, 1-aza-8-oxabicyclo[4.3.0]nonane, 8-azabicyclo[3.2.1]octane, and 9-azabicyclo[3.3.1]nonane derivatives.

Sir: Ring formation through [m + n]-type annelation[2] is highly useful to the synthesis of new cyclic compounds. We wish to report a convenient method for the formation of piperidine skeletons by utilizing a new [3 + 3]-type annelation between allyltrimethylsilane (**5**) and α,α'-dimethoxylated amides **4** easily prepared either by anodic α-monomethoxylation[3] of *N*-monoalkylamides **1** followed by methoxyalkylation of the α-methoxylated products **2** (route A) or by anodic α,α'-dimethoxylation[4] of *N,N*-dialkylamides **3** (route B) (eq 1).





(1)

6a, Z=Cl
b, Z=OCOH

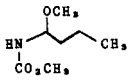
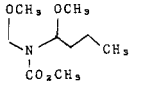
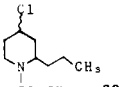
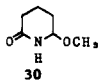
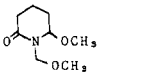
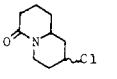
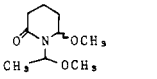
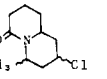
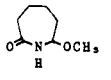
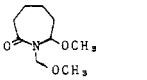
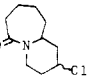
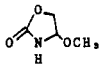
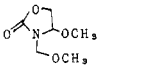
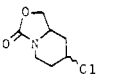
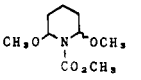
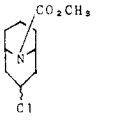
A typical procedure is exemplified by the synthesis of a piperidine derivative **10** from α,α'-dimethoxylated carbamate **9**. Thus, the anodic oxidation[3] of **7** followed by methoxymethylation of the product **8** gave **9** (route A).[5] A solution of **9** (2 mmol) in CH_2Cl_2 (3 mL) was added dropwise to a solution of $TiCl_4$ (4 mmol) in CH_2Cl_2 (5 mL) at room temperature, and then a solution of **5** (3.3 mmol) in CH_2Cl_2 (2 mL) was added to the mixture. After the solution was stirred overnight it was treated with water, and the isolation by column chromatography gave **10** in 65% yield (eq 2). $SnCl_4$ gave a similar result (yield 60%) to $TiCl_4$, and using (2-bromoallyl)trimethylsilane (**11**) instead of **5** yielded **12** (eq 2). The annelation between **9** and **5** also took place in formic acid to give **6b** ($R^1 = R^2 = H$; $Y = OCH_3$) in 73% yield.[6]

One of the advantages of our method consists in the wide applicability as exemplified by the facile synthesis of bi-

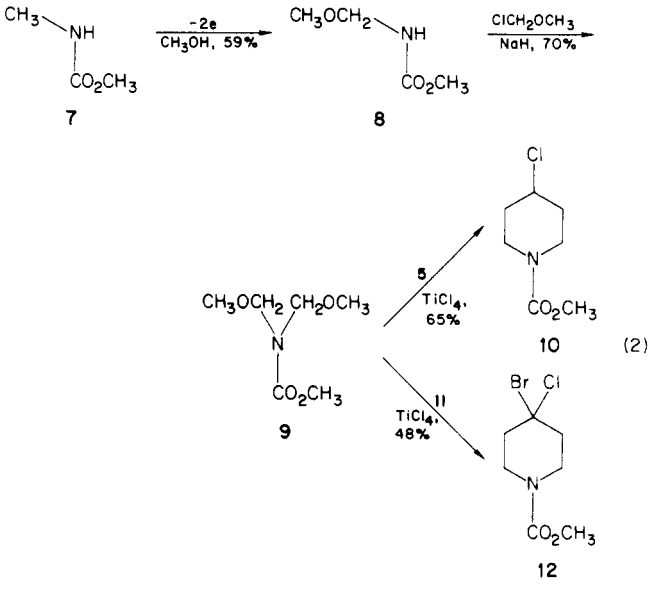
(1) Electroorganic Chemistry. 89.
(2) (a) Pine, S. H.; Hendrickson, J. B.; Cram, D. J.; Hammond, G. S. "Organic Chemistry"; 4th ed.; McGraw-Hill: New York, 1981; p 710. (b) For examples of the recent studies on the synthesis of nitrogen heterocycles, see the following. [3 + 2] annelation: Vedejs, E.; West, F. G. *J. Org. Chem.* **1983**, *48*, 4773. Livinghouse, T.; Smith, R. *J. Chem. Soc., Chem. Commun.* **1983**, 210. [4 + 2] annelation: Bailey, T. R.; Garigipati, R. S.; Morton, J. A.; Weinreb, S. M. *J. Am. Chem. Soc.* **1984**, *106*, 3240 and references cited therein.
(3) Shono, T.; Hamaguchi, H.; Matsumura, Y. *J. Am. Chem. Soc.* **1975**, *97*, 4264.
(4) Shono, T.; Matsumura, Y.; Tsubata, K.; Sugihara, Y.; Yamane, S.; Aoki, T. *J. Am. Chem. Soc.* **1982**, *104*, 6697.
(5) Synthesis of **9** was also achievable by the anodic α,α'-dimethoxylation of *N*-carbomethoxydimethylamine in methanol (route B).
(6) The annelation of **15** or **20** with **5** in formic acid resulted in low yields.

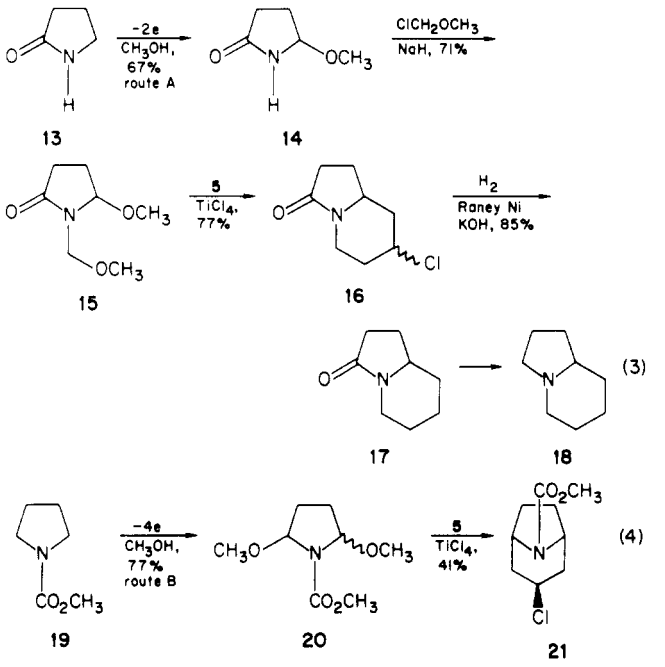
0022-3263/85/1950-3243$01.50/0

Table I. [3 + 3]-Type Annelation between 4 and 5

run	anodic methoxylation of 1			methoxymethylation of 2		6a	
		yield of 2, %[a]	passed electricity, F/mol		yield of 4, %[a]		yield of 6a, %[d]
1		88	10.2	 28	70	 29	75[e,f]
2	 30	93	3.6		68		83
3		30			42[c]		50
4		94	10.0		44		62
5		89	3.0		86		77
6		71[b]	10			 31	85[f]

[a] Route A, see text. Isolated yield. [b] Route B, see text. [c] Methoxyethylation. [d] A mixture of stereoisomers. Isolated yield. The ratios were unknown unless otherwise noted. [e] Stereoisomers were separable by column chromatography (85:15). [f] See ref 17.





cyclic nitrogen heterocycles such as indolizidine **16**[7] and 8-azabicyclo[3.2.1]octane **21**[8] derivatives from lactam **13** (route A) and pyrrolidine **19** (route B), respectively (eq 3 and 4). Since the chloro substituent of **16** was easily removed by hydrogenation, (±)-δ-coniceine (**18**)[10] could be synthesized from **16** (eq 3). Similarly, (±)-coniine[12] was prepared from the annelated product **29** (Table I) by hydrogenation followed by alkaline hydrolysis (overall yield 43% from **28**).

Furthermore, this [3 + 3]-type annelation makes the preparation of methyl-substituted indolizidine derivative **25** possible by using methoxyethylation instead of methoxymethylation through route A (eq 6). Other examples are summarized in Table I.

These annelations may proceed through the intermolecular allylation at the α-position of **4** followed by the intramolecular addition of the cation developed at the α′-position to the allylic double bond.[13] In fact, the treatment of **23** with Lewis acid gave **21** (eq 5).

(7) NMR spectrum (400 MHz) of **16** showed that **16** was a mixture of stereoisomers, the ratio of which was 40 to 60.

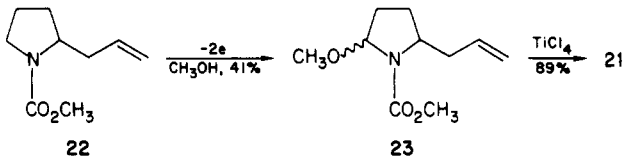
(8) The stereochemistry of **21** was confirmed by comparing the melting point[9] of the picrate of 3β-chlorotropane with that of the product obtained by the reduction of **21** with LAH.

(9) Archer, S.; Lewis, T. R.; Zenitz, B. *J. Am. Chem. Soc.* **1958**, *80*, 958.

(10) The spectra of **17** were identical with those of reported data.[11] The conversion of **17** to **18** has already been reported.[11]

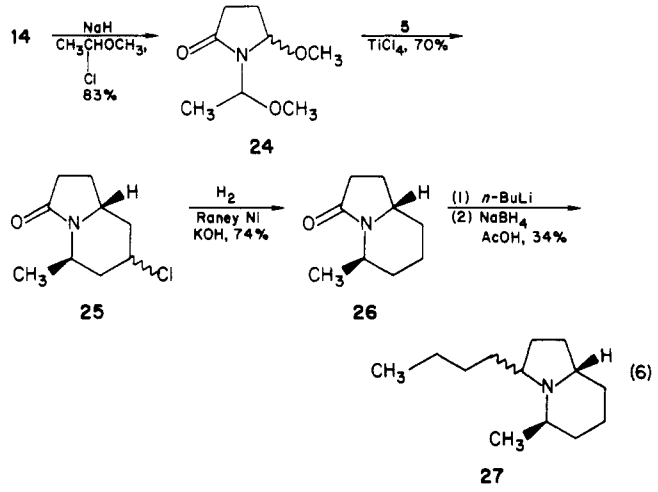
(11) Khatri, N. A.; Schmitthenner, H. F.; Shringarpure, J.; Weinreb, S. M. *J. Am. Chem. Soc.* **1981**, *103*, 6387.

(12) Glasby, J. S. "Encyclopedia of the Alkaloids"; Plenum Press: New York, 1975; Vol 1, p 321.



22 23 (5)

The stereochemistry of this [3 + 3]-type annelation was investigated in the preparation of **25**. Although **25** can have four stereoisomers, the product actually obtained showed the stereostructure depicted in eq 6,[14] though the stereochemistry of the chloro substituent was not clear.[15]



24 25 26 27 (6)

The pharaoh ant trail pheromone stereoisomers **27**[16] could be prepared from **25**. Thus, the hydrogenation of **25** under basic conditions followed by butylation of the dechlorinated product **26** with *n*-BuLi and reduction with $NaBH_4$ gave a mixture of stereoisomers **27** in the ratio of about 2:1 (eq 6).

Nucleophilic olefinic reagents other than **5** can lead to other new [3 + *n*]-type annelations, which will be reported elsewhere.

Acknowledgment. One of the authors (T.S.) wishes to thank the Asahi Glass Foundation for Industrial Technology for supporting this work.

Registry No. **5**, 762-72-1; **6b**, 97316-65-9; **7**, 6642-30-4; **8**, 28482-71-5; **9**, 6781-03-9; **10**, 97316-66-0; **11**, 81790-10-5; **12**, 97316-67-1; **13**, 616-45-5; **14**, 63853-74-7; **15**, 97316-68-2; **16**, 97316-69-3; **17**, 71779-55-0; **18**, 62279-67-8; **19**, 56475-80-0; **20**, 66893-74-1; **21**, 97316-70-6; **22**, 97316-71-7; **23**, 97316-72-8; **24**, 97316-73-9; **25** (isomer I), 97316-74-0; **25** (isomer II), 97371-87-4; **26**, 97316-75-1; **26** (butylated, isomer I), 97316-77-3; **26** (butylated, isomer II), 97371-90-9; **27** (isomer I), 97371-88-5; **27** (isomer II), 97371-89-6; **28**, 97316-56-8; *cis*-**29**, 97316-60-4; *trans*-**29**, 97316-76-2; **30**, 63853-82-7; **31**, 97316-64-8; methyl butylcarbamate, 2594-21-0; 2-piperidinone, 675-20-7; hexahydro-2-azepinone, 105-60-2; 2-oxazolidinone, 497-25-6; methyl 1-piperidinecarboxylate, 1796-27-6; methyl (1-methoxybutyl)carbamate, 76469-96-0; hexahydro-7-methoxy-2-azepinone, 63853-81-6; 4-methoxy-2-oxazolidinone, 14441-94-2; methyl 2,6-dimethoxy-1-piperidinecarboxylate, 66893-72-9; 1-(methoxymethyl)-6-methoxy-2-piperidinone, 97316-57-9; 1-(1-methoxyethyl)-6-methoxy-2-piperidinone, 97316-58-0; 1-(methoxymethyl)-7-methoxy-2-oxohexamethyleneimine, 80953-74-8; 3-(methoxymethyl)-4-methoxy-2-oxazolidinone, 97316-59-1; 8-chlorooctahydro-2*H*-quinolizin-4-one, 97316-61-5; 6-methyl-8-chlorooctahydro-2*H*-quinolizin-4-one, 97316-62-6; 2-oxo-9-chloro-1-azabicyclo[5.4.0]undecane, 97316-63-7; 4-chloro-9-oxo-1-aza-8-oxabicyclo[4.3.0]nonane, 97336-12-4; 1-chloroethyl methyl ether, 1538-87-0; (±)-δ-coniine, 3238-60-6; 1-(methoxycarbonyl)-2-propylpiperidine, 92599-71-8.

Supplementary Material Available: Experimental details and spectral and physical data for new compounds (11 pages). Ordering information is given on any current masthead page.

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(13) For a review of *N*-acyliminium ions cyclization, see: Speckamp, W. N. *Recl. Trav. Chim. Pays-Bas* **1981**, *100*, 345.
(14) The high stereoselectivity of the intramolecular cyclization of *N*-acyliminium ion with a C–C double bond has been reasonably explained in terms of $A^{(1,3)}$ strain: Hart, D. J. *J. Am. Chem. Soc.* **1980**, *102*, 397. The high stereoselectivity observed in the formation of **25** may be elucidated by the same factor.
(15) The stereochemistry between 8a-H and 5-CH_3 in **25** was determined at the step of **26**. The ratio of stereoisomers of **25** was 26 to 74, which was determined by GLC.
(16) Macdonald, T. L. *J. Org. Chem.* **1980**, *45*, 193 and references cited therein.
(17) The yields of **29** and **31** were improved by modification of the typical procedures. Thus, a solution of **4** and **5** in CH_2Cl_2 was added dropwise into a solution of $TiCl_4$ in CH_2Cl_2 at room temperature.

Additions and Corrections

Vol. 49, 1984

L. F. R. Cafferata,* G. N. Eyler, and M. V. Mirífico. Kinetics and Mechanism of Acetone Cyclic Diperoxide (3,3,6,6-Tetramethyl-1,2,4,5-tetraoxane) Thermal Decomposition in Benzene Solution.

Page 2107. At 165.0 °C, the ACDP thermolysis in benzene solution (0.05 mol kg^{-1}) yields the following gaseous products (ρ, mol of products per mol ACDP decomposed): O_2, 0.6 ± 0.1; CO_2, 0.6 ± 0.1; MeH, 0.21 ± 0.02; EtH, 0.005 ± 0.001. Considering the CO_2 and $MeCO_2Me$ yields, the ACDP decomposed through the intermediate biradical C–C bond rupture step (32%) is practically coincident with the value obtained from the acetone (35%) and oxygen (40%) yields. Then, the rate constant ratio (k_{C-O}/k_{C-C}) = $\rho_{MeCOMe}/(\rho_{MeCO_2Me} + \rho_{CO_2})$ is 2, which is a temperature-independent value.

Andrew A. Chiu, R. Russel Gorby, John E. H. Hancock,* and Eric J. Hustedt. Malonic Ester Derivatives. 2.

Page 4314, column 1, line 1–14. Prof. T. J. Curphey (Department of Pathology, Dartmouth Medical School, Hanover, NH 03756) has supplied a further mechanism which can explain the published results: Michael addition of dimethyl malonate anion to **3**, furnishing **4**, the anion of an unstable heptaester, which then undergoes retrograde Michael reaction forming **1a** and the anion of the triester **5**; this latter exchanges a proton with **1a** (the tetramethyl 1,1,3,3-propenetetracarboxylic ester), forming **2b** and **5**. There appear to be analogies, e.g.: Ingold, C. K.; Perren, E. A. *J. Chem. Soc.* **1921**, *119*, 1582; **1922**, *121*, 1414. We had considered this mechanism but thought it unlikely because of the severe steric hindrance in the initial approach. The two mechanisms lend themselves to distinction via use of an isotopic label, and such aspects will be examined.