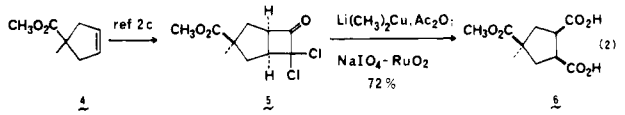

4 5 6

Experimental Section

Solvents were generally distilled prior to use. Tetrahydrofuran and ether were distilled from sodium hydride–lithium aluminum hydride. Phosphorus oxychloride was distilled from potassium carbonate. Reaction mixtures were generally stirred under a nitrogen or argon atmosphere. Thin-layer chromatography was performed on Merck $60F_{254}$ (0.25 mm) sheets, which were visualized with molybdophosphoric acid in ethanol. Merck 70–230-mesh silica gel 60 and Florisil (60–100 mesh) were employed for column chromatography. A Perkin-Elmer Model 397 spectrophotometer was used to record the IR spectra. A Bruker WP 80 SY spectrometer was employed for the ^1H NMR spectra (Me_4Si as the internal reference). Mass spectra were obtained on a VG Micromass 70 70F instrument. Melting points were obtained with a Büchi-Tottoli apparatus and are not corrected. Microanalyses were performed by the Central Service of the CNRS.

Dichlorocyclobutanones. The cycloadducts **2a–g** and **5** were obtained from the commercially available olefins **1a–c** and **1e–g** and the known olefins **1d**[9] and **4**,[2c] by using the procedure of Krepski and Hassner.[3b] The cycloadducts **2a**,[2a] **2b**,[10] **2d**,[11] **2e**,[3c] **2f**,[3b,c] **2g**,[3b,c] and **5**[2c] have been reported previously.

***trans*-2,2-Dichloro-3,4-dimethylcyclobutanone (2c)**: bp 30 °C (0.5 torr); ^1H NMR (CCl_4) δ 1.30 (d, J = 7.1 Hz, 3 H), 1.44 (d, J = 6.3 Hz, 3 H), 2.30–2.70 (m, 1 H), 2.95–3.25 (m, 1 H); IR (film) 1802 cm^{-1}; mass spectrum, m/e 168 (M^+ + 1), 167 (M^+), 166, 140, 139, 138, 109 (100%).

Succinic Acids. General Procedure. To a stirred solution of 4 mmol of the α,α-dichlorocyclobutanone in 16 mL of dry tetrahydrofuran at −78 °C was added over 1 min 2.84 mL (4.4 mmol) of 1.55 M n-butyllithium[12] in hexane. After 15 min, 2.8 mL (29.7 mmol) of acetic anhydride were added and the solution was allowed to come to room temperature. After being stirred for 1.5 h, the reaction mixture was concentrated under reduced pressure[13] and the resulting solid residue was dissolved in 28 mL of acetonitrile–carbon tetrachloride–water (8:8:12) and treated with 4.8 g (22.4 mmol) of sodium metaperiodate and 100 mg (0.75 mmol) of ruthenium dioxide.[7] After being efficiently stirred for 14 h, the mixture was treated with 24 mL of 10% aqueous sodium hydroxide and stirring was continued for an additional 6 h in order to hydrolyze any anhydride present.[14] The mixture was extracted with ether and the aqueous phase was acidified to pH 2–3 with 10% aqueous hydrochloric acid and then thoroughly extracted with ether or ethyl acetate. After being washed with 2% aqueous sodium thiosulfate, the organic phase was dried over sodium sulfate and concentrated under reduced pressure to yield the diacid, which generally crystallized spontaneously. Diacids **3a**,[1d,15] **3b**,[16] **3c**,[16] **3e**,[17] **3f**,[18] and **3g**[19] have been described previously.

5α-Cholestane-2α,3α-dicarboxylic acid (3d): mp 207–208 °C (dichloromethane–pentane); ^1H NMR ($CDCl_3$) δ 0.65 (s), 0.82 (s), 0.90 (s), 2.50–2.85 (m), 3.20–3.40 (m), 8.60 (br, s); IR (Nujol) 3080, 2660, 1710 cm^{-1}. Anal. Calcd for $C_{29}H_{48}O_4 \cdot {}^1/_2H_2O$: C, 74.16; H, 10.52. Found: C, 74.18; H, 10.44.

(1*R*,2*S*,4*r*)-4-(Methoxycarbonyl)-4-methylcyclopentane-1,2-dicarboxylic acid (6): mp 132 °C (dichloromethane–hexane); ^1H NMR ($CDCl_3$) δ 1.31 (s, 3 H), 1.78–2.13 (m, 2 H), 2.54–2.87 (m, 2 H), 3.05–3.45 (m, 2 H), 3.68 (s, 3 H), 10.70 (br s, 2 H); IR (Nujol) 3030, 2700, 1730, 1700 cm^{-1}. Anal. Calcd for $C_{10}H_{14}O_6$: C, 52.17; H, 6.13. Found: C, 52.03; H, 6.02.

Acknowledgment. We thank Professor A. Rassat, Dr. J. L. Luche, and Dr. C. Morat for their interest in this work, the CNRS (LA 332) for financial support, and the C.N.Pq. for a fellowship award to F.C.

Registry No. **1a**, 872-05-9; **1b**, 590-18-1; **1c**, 624-64-6; **1d**, 570-73-0; **1e**, 513-35-9; **1f**, 591-49-1; **1g**, 563-79-1; **2a**, 71221-64-2; **2b**, 64512-26-1; **2c**, 95864-67-8; **2d**, 28415-02-3; **2e**, 68212-49-7; **2f**, 32166-29-3; **2g**, 66239-90-5; **3a**, 2530-32-7; **3b**, 608-40-2; **3c**, 57694-62-9; **3d**, 95864-68-9; **3e**, 2103-16-4; **3f**, 76704-91-1; **3g**, 630-51-3; **4**, 95864-69-0; **5**, 95864-70-3; **6**, 95864-71-4; $Cl_2C{=}C{=}O$, 4591-28-0; n-BuLi, 109-72-8; Ac_2O, 108-24-7; RuO_2, 12036-10-1; $NaIO_4$, 7790-28-5.

(9) Douglas, G. H.; Ellington, P. S.; Meakins, G. D.; Swindells, R. *J. Chem. Soc.* **1959**, 1720–1723.
(10) Huber, M. K.; Martin, R.; Rey, M.; Dreiding, A. S. *Helv. Chim. Acta* **1977**, *60*, 1781–1800.
(11) Fletcher, V. R.; Hassner, A. *Tetrahedron Lett.* **1970**, 1071–1074. Cragg, G. M. L. *J. Chem. Soc. C* **1970**, 1829–1832.
(12) Treatment of **2a** and **5** with lithium dimethylcopper[2b,c] in lieu of n-butyllithium led to considerably higher yields of the diacids **3a** and **6**, respectively. (In these cases, the enol acetates were isolated by extraction prior to oxidative cleavage.) Generally, however, the greater simplicity of the n-butyllithium procedure more than compensates for any lower yield.
(13) With volatile substrates, the reaction mixture was instead treated with aqueous sodium bicarbonate and the crude enol acetate was then isolated with 1:1 ether–hexane [IR (film) 1770, 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ ~2.15 (s, 3 H)].
(14) This step was omitted in the conversion of **5** to **6**.
(15) Barry, V. C.; Twomey, D. *Proc. R. Ir. Acad., Sect. B* **1947**, *51*, 137–144; *Chem. Abstr.* **1947**, *41*, 4453e.
(16) Pollock, J. R. A., Stevens, R., Eds. "Dictionary of Organic Compounds", 4th ed.; Eyre and Spottiswoode Ltd.: London, 1965; Vol. II, p 1225.
(17) Reference 16, Vol. V, p 3189.
(18) Johnson, W. S.; Allen, D. S., Jr.; Hindersinn, R. R.; Sausen, G. N.; Pappo, R. *J Am. Chem. Soc.* **1962**, *84*, 2181–2196.
(19) Reference 16, Vol. V, pp 3028–3029.

A Synthesis of β-Methylene-γ-butyrolactones

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In contrast to the many procedures that exist for obtaining α-methylene-γ-butyrolactones,[1] there are relatively few methods available for the synthesis of β-methylene-γ-butyrolactones.[2] Not unexpectedly, a direct approach to α,α-disubstituted lactones of this type by successive alkylation of 3-methylbut-2-enolide fails due to preferential proton abstraction at C-4.[3] While in principle this problem could be overcome through the use of β-methylene-γ-butyrolactone, in practice the instability to conjugation of this molecule[2a,4] (and its α-monoalkyl derivatives[4a]) renders its use in synthesis impractical at best.

It seemed quite likely that a suitably protected γ-hydroxy dimethylacrylate derivative would, in contrast, undergo selective deprotonation at the methyl position[5] and

(1) See: Grieco, P. A. *Synthesis* **1975**, 67–82. Newaz, S. S. *Aldrichimica Acta* **1977**, *10*, 64–71, and references cited therein.
(2) (a) Haslouin, J.; Rouessac, F. *Tetrahedron Lett.* **1976**, 4651–4654. (b) Wenkert, E.; Alonso, M. E.; Buckwalter, B. L.; Chou, K. J. *J. Am. Chem. Soc.* **1977**, *99*, 4778–4782. (c) Evans, D. A.; Sims, C. L.; Andrews, G. C. *Ibid.* **1977**, *99*, 5453–5461. (d) Brocksom, T. J.; Constantino, M. G.; Ferraz, H. M. C. *Synth. Commun.* **1977**, *7*, 483–493. (e) Petragnani, N.; Brocksom, T. J.; Ferraz, H. M. C.; Constantino, M. G. *Synthesis* **1977**, 112–113. (f) Inoue, Y.; Hibi, T.; Satake, M.; Hashimoto, H. *J. Chem. Soc., Chem. Commun.* **1979**, 982. (g) Okabe, M.; Tada, M. *J. Org. Chem.* **1982**, *47*, 5382–5384. (h) Kano, K.; Hayashi, K.; Mitsuhashi, H. *Chem. Pharm. Bull.* **1982**, *30*, 1198–1203. For natural products with this function, see ref 2c.
(3) Gedge, D. R.; Pattenden, G. *Tetrahedron Lett.* **1977**, 4443–4446. See also: Donaubauer, J. R.; Greaves, A. M.; McMorris, T. C. *J. Org. Chem.* **1984**, *49*, 2833–2834.
(4) (a) F. Coelho, unpublished observations. (b) McMurry, J. E.; Donovan, S. F. *Tetrahedron Lett.* **1977**, 2869–2872.
(5) Harris, F. L.; Weiler, L. *Tetrahedron Lett.* **1984**, *25*, 1333–1336.

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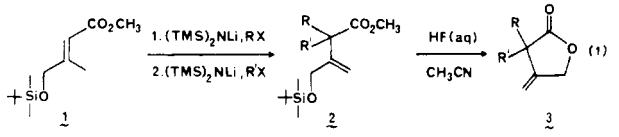
Table I. Synthesis of β-Methylene-γ-butyrolactones 3

lactone	RX, R′X	yield, % 2	3	overall
3a	CH_3I, CH_3I	82, 92	92	69
3b	$(CH_3)_2CHI$	86	94	81
3c	CH_2=$CHCH_2Br$, CH_3OCH_2Cl	84, 95	61	49
3d	$Br(CH_2)_3Br$	81, 66	92	49
3e	$Br(CH_2)_4Br$	88, 86	95	72
3f	$Br(CH_2)_5Br$	77, 62	93	44

that the resultant dienolate would suffer alkylation at the α-site to give a methylene derivative significantly less prone than its cyclic counterpart to undergo isomerization.[6] A second alkylation followed by deprotection would then yield the α,α-dialkyl-β-methylene-γ-butyrolactone. In practice this approach has led to an effective synthesis of these lactones.

The easily prepared dimethylacrylic acid derivative 1 is selectively deprotonated with lithium bis(trimethylsilyl)amide in tetrahydrofuran to give an ester dienolate, which on alkylation affords exclusively the quite stable deconjugated ester 2 (R′ = H, eq 1). This intermediate



can be lactonized under mild conditions to give relatively unstable[7] α-alkyl-β-methylene-γ-butyrolactone 3 (R′ = H) or alkylated anew and then subjected to lactonization to produce 3 (R = R′ = alkyl). Examples of this sequence are given in Table I.

The overall yields (nonoptimized) range from 44% to 81% and average 61%. Secondary alkyl groups can be efficiently introduced (e.g., **3b**) as well as certain functional groups (e.g., **3c**). For effecting the lactonization of **2**, 40% aqueous hydrofluoric acid in acetonitrile[8] is by far the most efficacious of the numerous methods examined.

In that there are few effective procedures currently available for the synthesis of β-methylene-γ-butyrolactones, this simple method should prove useful.

Experimental Section

Solvents were generally distilled prior to use. Tetrahydrofuran and ether were distilled from sodium hydride–lithium aluminum hydride, and *N*,*N*-dimethylformamide was distilled from calcium hydride under reduced pressure. Reaction mixtures were generally stirred under a nitrogen or argon atmosphere. Thin-layer chromatography was performed on Merck $60F_{254}$ (0.25 mm) sheets, which were visualized with molybdophosphoric acid in ethanol. Merck 70–230-mesh silica gel 60 was employed for column chromatography. A Perkin-Elmer Model 397 spectrophotometer was used to record the IR spectra. A JEOL PMX 60 or a Bruker WP 80 SY spectrometer was employed for the ^1H NMR spectra (Me_4Si as the internal reference). Mass spectra were obtained on a VG Micromass 70 70F or a MS-30 AEI instrument. Melting points were obtained with a Büchi-Tottoli apparatus and not corrected. Microanalyses were performed by the Central Service of the CNRS.

Methyl (*E*)-4-[(*tert*-Butyldimethylsilyl)oxy]-3-methyl-2-butenoate (1). A 3.48-g (30.0 mmol) sample of (*E*)-4-hydroxy-3-methyl-2-butenoic acid, prepared from dimethylacrylic acid as previously described,[9] was esterified with ethereal diazomethane. The resultant crude methyl ester[10] was dissolved in 7 mL of *N*,*N*-dimethylformamide and treated with 5.10 g (75.0 mmol) of imidazole and 5.43 g (36.0 mmol) of *tert*-butyldimethylsilyl chloride.[11] After being stirred under argon for 10 h, the reaction mixture was processed with ether in the usual manner and the crude product was purified by dry silica gel chromatography with 5% ether in pentane to yield 6.50 g (89%) of **1**: ^1H NMR ($CDCl_3$) δ 0.10 (s, 6 H), 0.79 (s, 9 H), 1.96 (s, 3 H), 3.61 (s, 3 H), 4.02 (s, 2 H), 5.93 (m, 1 H); IR (film) 1720, 1660, 840 cm^{-1}. Anal. Calcd for $C_{12}H_{24}O_3Si$: C, 58.97; H, 9.90; M_r 244.1494. Found: C, 58.84; H, 9.96; M_r (mass spectrum) 244.1497.

Synthesis of β-Methylene-γ-butyrolactones 3. General Procedure. A stirred solution of 100 mg (0.41 mmol) of ester **1** in 0.5 mL of dry tetrahydrofuran at −78 °C under argon was treated with 450 μL (0.45 mmol) of a 1.0 M solution of lithium bis(trimethylsilyl)amide in tetrahydrofuran.[12] Following the addition, the reaction mixture was allowed to warm to 0 °C over 1 h, after which it was recooled to −78 °C and treated with 2 mmol[13] of the alkyl halide and 200 μL of hexamethylphosphoric triamide. After being warmed to room temperature over 2 h, the reaction mixture was processed with ether in the usual fashion to give the crude ester **2** (R′ = H), which was purified by dry silica gel chromatography with 5% ether in pentane. Spectroscopic values typically include the following: ^1H NMR (CCl_4) δ 0.1 (s, 6 H), 0.9 (s, 9 H), ~2.9 (m, 1 H), 3.6 (s, 3 H), 4.1 (s, 2 H), 5.0 (s, 1 H), 5.2 (s, 1 H); IR (film) 3075, 1735, 1640, 840, 780 cm^{-1}. A stirred solution of the monoalkylated ester in tetrahydrofuran (1.4 mL/mmol) at −78 °C under argon was treated with 1.1 equiv of 1.0 M lithium bis(trimethylsilyl)amide in tetrahydrofuran. For cyclizations, hexamethylphosphoric triamide (0.5 mL/mmol) was added and the reaction mixture was allowed to warm to room temperature over 2 h and then processed with ether. For the introduction of second alkyl groups, the reaction mixture was allowed to warm to 0 °C over 1 h, recooled to −78 °C, and treated with 5 equiv of the alkyl halide and hexamethylphosphoric triamide (0.5 mL/mmol) and then allowed to warm to room temperature over 2 h and worked up as usual. The ester **2** was purified by dry silica gel chromatography with 5% ether in pentane and then lactonized by stirring with aqueous hydrofluoric acid in acetonitrile[8] (3.5 mL of a 5% solution of 40% aqueous HF/mmol of **2**) at room temperature for 4 h. The crude product was isolated with ether and then purified by dry silica chromatography with 10% ether in pentane to give **3**.

α,α-Dimethyl-β-methylene-γ-butyrolactone (3a):[2f] ^1H NMR ($CHCl_3$) δ 1.33 (s, 6 H), 4.83 (t, *J* = 2 Hz, 2 H), 5.08 (t, *J* = 2 Hz, 2 H); IR (film) 3075, 1775, 1670, 1020, 900 cm^{-1}; mass spectrum, *m*/*e* 126 (M^+).

α-Isopropyl-β-methylene-γ-butyrolactone (3b): ^1H NMR (CCl_4) δ 1.00 (d, *J* = 2 Hz, 3 H), 1.10 (d, *J* = 2 Hz, 3 H), 2.2 (m, 1 H), 2.95 (m, 1 H), 4.67 (m, 2 H), 5.15 (m, 2 H); IR (film) 3075, 1770, 1665, 1025, 900 cm^{-1}; mass spectrum, *m*/*e* 140 (M^+). Anal. Calcd for $C_8H_{12}O_2$: M_r 140.0837. Found: M_r (mass spectrum) 140.0832.

2-Isopropyl-3-methylbut-2-enolide:[7] ^1H NMR (CCl_4) δ 1.18 (d, *J* = 7 Hz, 6 H), 2.03 (s, 3 H), 2.72 (hpt, *J* = 7 Hz, 1 H), 4.5 (s, 2 H); IR (film) 1740, 1665, 1025, 780 cm^{-1}; mass spectrum, *m*/*e* 140 (M^+). Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.15; H, 8.66.

α-Allyl-α-(methoxymethyl)-β-methylene-γ-butyrolactone (3c): ^1H NMR ($CDCl_3$) δ 2.38 (pseudo t, *J* = 6 Hz, 2 H), 3.32 (s, 3 H), 3.55 (AB q, *J* = 9 Hz, $\delta_a - \delta_b$ = 14.4 Hz, 2 H), 4.75 (m, 2 H), 4.9–5.9 (m, 5 H); IR (film) 3075, 1770, 1670, 1640, 1025, 915 cm^{-1}; mass spectrum, *m*/*e* 182 (M^+). Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found: C, 65.77; H, 8.00.

β-Methylene-α,α-trimethylene-γ-butyrolactone (3d): ^1H NMR (CCl_4) δ 1.9–2.9 (m, 6 H), 4.70 (t, *J* = 2 Hz, 2 H), 5.13 (t, *J* = 2 Hz, 1 H), 5.33 (t, *J* = 2 Hz, 1 H); IR (film) 3070, 1765, 1675, 1020, 900 cm^{-1}; mass spectrum, *m*/*e* 138 (M^+). Anal. Calcd for

(6) Petragnani, N.; Yonashiro, M. *Synthesis* **1982**, 521–578, and references cited therein.

(7) Lactone **3b** is completely isomerized to 2-isopropyl-3-methylbut-2-enolide under conditions (toluene, neutral Al_2O_3, 20 °C, 1 h)[4b] that leave ester **2b** >90% unchanged.

(8) Newton, R. F.; Reynolds, D. P.; Finch, M. A. W.; Kelly, D. R.; Roberts, S. M. *Tetrahedron Lett.* **1979**, 3981–3982.

(9) Colonge, J.; Reymermier, M. *Bull. Soc. Chim. Fr.* **1956**, 195–198.

(10) Epstein, W. W.; Sonntag, A. C. *J. Org. Chem.* **1967**, *32*, 3390–3394.

(11) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190–6191.

(12) Aldrich Chemical Co.

(13) The use of just 0.53 mmol (1.3 equiv) of monohalide for the alkylation resulted in only a very slightly reduced yield [e.g., allyl bromide 81% (vs. 84%), isopropyl iodide 82% (vs. 86%)].

$C_8H_{10}O_2$: M_r 138.0681. Found: M_r (mass spectrum) 138.0684.

β-Methylene-α,α-tetramethylene-γ-butyrolactone (3e):[2d,e] ^1H NMR ($CDCl_3$) δ 1.6–2.4 (m, 8 H), 4.80 (t, J = 2 Hz, 2 H), 5.06 (m, 2 H); IR (film) 3075, 1770, 1670, 1020, 900 cm^{-1}; mass spectrum, m/e 152 (M^+).

β-Methylene-α,α-pentamethylene-γ-butyrolactone (3f):[2b,f,g] mp 41–42 °C (lit. mp 46 °C,[2b] 42–43 °C[2g]); ^1H NMR ($CDCl_3$) δ 1.3–2.2 (m, 10 H), 4.78 (t, J = 2 Hz, 2 H), 5.09 (t, J = 2 Hz, 1 H), 5.18 (t, J = 2 Hz, 1 H); IR (film) 3070, 1770, 1665, 1020, 900 cm^{-1}; mass spectrum, m/e 166 (M^+).

Acknowledgment. We thank Professor A. Rassat and Dr. J. L. Luche for their interest in this work, the CNRS (LA 332) for financial support, and the C.N.Pq. for a fellowship award to F.C.

Registry No. 1, 95864-49-6; 2 (R = CH_3, R′ = H), 95864-50-9; 2 (R = $(CH_3)_2CH$, R′ = H), 95864-51-0; 2 (R = CH_2=$CHCH_2$), 95864-52-1; **2a**, 95892-00-5; **2c**, 95864-56-5; **2d**, 95864-53-2; **2e**, 95864-54-3; **2f**, 95864-55-4; **3a**, 73461-19-5; **3b**, 95864-57-6; **3c**, 95864-58-7; **3d**, 95864-59-8; **3e**, 57429-72-8; **3f**, 63965-86-6; CH_3I, 74-88-4; $(CH_3)_2CHI$, 75-30-9; CH_2=$CHCH_2Br$, 106-95-6; $Br(CH_2)_3Br$, 109-64-8; $Br(CH_2)_4Br$, 110-52-1; $Br(CH_2)_5Br$, 111-24-0; CH_3OCH_2Cl, 107-30-2; diazomethane, 334-88-3; *tert*-butyldimethylsilyl chloride, 18162-48-6; (*E*)-4-hydroxy-3-methyl-2-butenoic acid, 44647-19-0; methyl (*E*)-4-hydroxy-3-methyl-2-butenoate, 13866-57-4; 2-isopropyl-3-methylbut-2-enolide, 95864-60-1; 2 (R = $Br(CH_2)_3$, R′ = H), 96020-93-8; 2 (R = $Br(CH_2)_4$, R′ = H), 96020-94-9; 2 (R = $Br(CH_2)_5$, R^1 = H), 96020-95-0.

A Direct Synthesis of [(*tert*-Butoxycarbonyl)methylidene]azacycloalkanes from *N*-Alkyl Lactams

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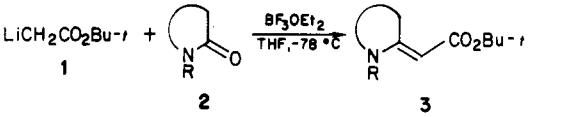
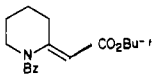
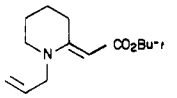
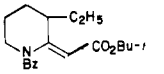
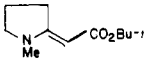
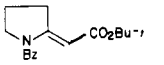
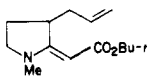
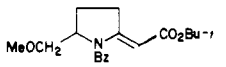
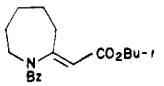
[(Alkoxycarbonyl)methylidene]azacycloalkanes **3** are useful compounds for the synthesis of various nitrogen-containing natural products. These compounds have been prepared by Knoevenagel reactions on lactam-derived acetals,[1] imino ethers,[2] iminium chlorides,[3] or (alkylthio)alkylidenium salts[4] followed by decarboxylation. Other routes include Eschenmoser's sulfide-contraction procedure via thiolactams[5] and a novel Wittig reaction of *N*-sulfonyl lactams.[6] These procedures, however, require the conversion of lactams to activated derivatives, and overall yields are often low.[7]

During our studies on new synthetic methods utilizing the combination of organolithium compounds and BF_3·OEt_2,[8] we found that lithium *tert*-butyl accetates **1** readily reacts with *N*-alkyl lactams **2** in the presence of this Lewis acid to give the enamino esters **3** (Table I). The details of this investigation are described herein.

Table I.
2-[(*tert*-Butoxycarbonyl)methylidene]azacycloalkanes 3



3		yield,[a] %
3a		54 (quant)[b]
3b		42
3c		30
3d		48, 47[c]
3e		45 (87)[b]
3f		21
3g		28
3h		41[d]

[a] Isolated yields are given. [b] Conversion based on starting material consumed. [c] The reaction was carried out with 2.5 mmol of **2d** and 5 mmol of *tert*-butyl acetate. [d] The reaction was quenched with piperidine and the product was isolated by chromatography on alumina.

The lithium salt **1** was derived from *tert*-butyl acetate and lithium diisopropylamide (LDA) in THF at −78 °C. Treatment of **1** with 1-benzyl-2-piperidone (**2a**) followed by BF_3·OEt_2 for 30 min at −78 °C, gave 1-benzyl-2-[(*tert*-butoxycarbonyl)methylidene]piperidine (**3a**) in 54% yield. Unchanged starting material could be recovered, and the conversion to **3a** based on consumed **2a** was high. The reaction of **1** with BF_3·OEt_2 seems to be competitive as the addition of BF_3·OEt_2 prior to **2a** did not give **3a** at all. Stereochemical assignments are based on ^1H NMR shift reagent studies, using tris(dipivalomethanato)europium(III) ($Eu(DPM)_3$). With $Eu(DPM)_3$ large deshielding effects were observed for C-3 hydrogens of **3a**, indicating it to be the *E* isomer.[2c,9]

Various reaction conditions were investigated in the synthesis of 1-allyl-2-[(*tert*-butoxycarbonyl)-methylidene]piperidine (**3b**). The use of THF as the solvent is essential; other solvents such as ether, toluene, or hexane gave no detectable amount of **3b**. The use of $TiCl_4$ instead of BF_3·OEt_2 as the Lewis acid gave, as well as enamine **3b** (33%), 1-allyl-2,2-bis[(*tert*-butoxycarbonyl)methyl]piperidine (**4b**) in 35% yield. The dialkylated piperidine **4b** is considered to be formed by attack of **1** on the iminium intermediate. However, we

(1) (a) Meerwein, H.; Florian, W.; Schön, N.; Stopp, G. *Justus Liebigs Ann. Chem.* **1961**, *641*, 1. (b) Shov, Y.; Shanan-Atidi, H. *J. Am. Chem. Soc.* **1969**, *91*, 6683, 6689.

(2) (a) Horii, Z.; Morikawa, K.; Ninomiya, I. *Chem. Pharm. Bull.* **1969**, *17*, 2230. (b) Oishi, T.; Nagai, M.; Onuma, T.; Moriyama, H.; Tsutae, K.; Ochiaia, M.; Ban, Y. *Ibid.* **1969**, 17. 2306. (c) Célérier, J.-P.; Deloisy, E.; Lhommet, G.; Maitte, P. *J. Org. Chem.* **1979**, *44*, 3089.

(3) Bredereck, H.; Bredereck, K. *Chem. Ber.* **1961**, *94*, 2278.

(4) (a) Restle, S.; Wermuth, C. G. *Tetrahedron Lett.* **1979**, 4837. (b) Gugelchuk, M. M.; Hart, D. J.; Tsai, Y.-M. *J. Org. Chem.* **1981**, *46*, 3671.

(5) Roth, M.; Dubs, P.; Götschi, E.; Eschenmoser, A. *Helv. Chim. Acta.* **1971**, *54*. 710.

(6) Natsume, M.; Takahashi, M.; Kiuchi, K.; Sugaya, H. *Chem. Pharm. Bull.* **1971**, *19*, 2648.

(7) A reaction of lithio-*N*,*N*-dimethyl(trimethylsily)acetamide with a lactam is known: Woodbury, R. P.; Rathke, M. W. *Tetrahedron Lett.* **1978**, 709.

(8) (a) Yamaguchi, M.; Hirao, I. *Tetrahedron Lett.* **1983**, *24*, 391, 1719. (b) Yamaguchi, M.; Waseda, T.; Hirao, I. *Chem. Lett.* **1983**, 35. (c) Yamaguchi, M.; Nobayashi, Y.; Hirao, I. *Tetrahedron Lett.* **1983**, *24*, 5121. (d) Yamaguchi, M.; Shibato, K.; Hirao, I. *Ibid.* **1984**, *24*, 1159. (e) Yamaguchi, M.; Hirao, I. *J. Chem. Soc., Chem. Commun.* **1984**, 202.

(9) Krueger, S. A.; Bryson, T. A. *J. Org. Chem.* **1974**, 39, 3167.

0022-3263/85/1950-1975$01.50/0