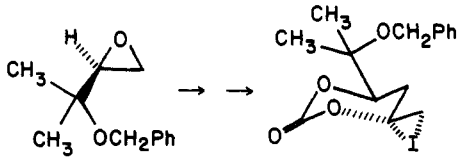
ducibly determined to be between 10–14.5:1, based on VPC analyses of the derived acetonides. Chromatographic separation, however, was best carried out at the diol olefin stage to afford pure **5** ($[\alpha]^{22}_D = -1.2°$ (*c* 10, $CHCl_3$)).

In the next iodocyclization, diol **5** required 2 equiv of base (MeLi) to form the bis alkoxide, only the homoallylic oxyanion of which reacted productively with CO_2[18] and thence I_2 at −78 °C to give a new mixture of epoxy diols (**6** + isomers) in ca. 75% yield.[19] Ketalization (dimethoxypropane, CH_2Cl_2, PPTS; 98%) led to a single new spot by TLC, the capillary VPC trace, however, indicating an 18–20:1 ratio of syn:anti products **7**.[20] Separation was best effected on homoallylic alcohol **8**, arrived at via subsequent cuprate-induced opening of **7**, thereby culminating in a stereochemically homogeneous, derivatized polyol [**7** → **8**,[21] 90%, $[\alpha]^{22}_D = +16.7°$ (*c* 3.6, $CHCl_3$)].

Interestingly, improved stereoselectivity is obtained from the second epoxidation sequence. This raises the attractive possibility that additional steric bulk on the side chain, in this case relative to that of the benzyloxymethyl moiety in the cyclization of **2**, as in the dimethyl analogue **9**, should better encourage its equatorial-like positioning in a cyclic transition state, thereby further improving the syn:anti ratio.



9

Finally, there are two other aspects of this work that are worthy of note. Upon completion of the polyol portion of interest using this route, each 1,3-diol unit is already in protected (potentially differentiated) form, most likely an essential feature for eventual macrocyclization. Moreover, each terminus exists as a latent aldehyde, which may be individually unleashed under unique chemical circumstances (i.e., ozonolysis or, e.g., $Pb(OAc)_4$).

In summary, epoxide **1** has been parlayed into a chiral, *syn*-1,3-polyol by means of a cuprate-mediated cleavage, re-epoxidation. This series can be repeated until the fragment corresponding to that of a target molecule has been attained. In each step the efficiency is high, as is the stereoselectivity, which thus far varies from 10–20:1. Improvements in this ratio may be forthcoming with refinements in the substitution pattern of the initial educt. The specific applications of these concepts to polyene macrolide synthesis will be reported in due course.

Acknowledgment. Financial support from the National Science Foundation (CHE 83-02421) and the donors of the Petroleum Research Fund, administered by the American Chemical Society, is gratefully acknowledged. We thank Dr. H. Webb for obtaining mass spectral data and Ms. Holly Pederson for technical assistance.

Registry No. **1**, 14618-80-5; **2**, 88981-35-5; **3**, 88981-36-6; **4**, 88981-37-7; **5**, 88981-38-8; **6**, 88981-39-9; **7**, 88981-40-2; **8**, 88981-41-3; $(vinyl)_2Cu(CN)Li_2$, 87136-18-3.

Supplementary Material Available: Full experimental and spectral details for compounds **2** and **4**–**8** (5 pages). Ordering information is given on any current masthead page.

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Received October 12, 1983

(18) Treatment of the bis alkoxide with dry CO_2 leads to a fairly viscous mixture at −78 °C. The addition of 10% HMPA to a THF solution of **5** prior to its conversion to **6** solubilized a good deal of the dianion; however, the product to starting material ratio did not improve.

(19) Presumably due to occlusion at −78 °C,[18] ca. 10% starting material was also usually isolated (thus, the yield based on recovered educt was ca. 86%).

(20) Not surprisingly, if the reaction mixture is warmed to 0 °C in an attempt to further solubilize the dioxyanion, the ratio of syn:anti products drops to ca. 11:1.

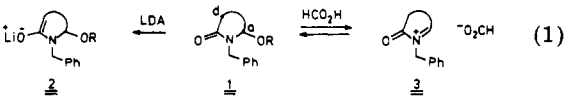
(21) All compounds derived from epoxide **1** gave satisfactory IR, NMR, and mass spectral data, as well as acceptable combustion or high-resolution MS analyses.

(22) A. P. Sloan Foundation Fellow, 1984–1986.

ω-Alkoxy Lactams as Dipolar Synthons. Silicon-Assisted Synthesis of Azabicycles and a γ-Amino Acid

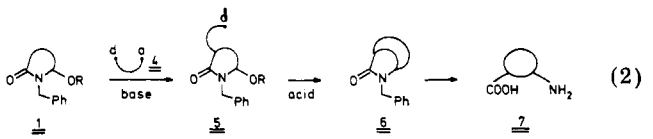
Summary: Alkylation of the lithium enolates derived from ω-alkoxy lactams **1a–c** with unsaturated iodides **4** affords **5** in high yields (Table I). Those alkylation products **5**, which contain an allyl- or propargylsilane moiety, undergo cyclization on acid treatment to furnish a variety of bicyclic nitrogen compounds, one of which has been further transformed into a γ-amino acid.

Sir: Simple and stable reagents possessing a nucleophilic (donor, d) and an electrophilic (acceptor, a) site,[1] which can be deployed selectively and sequentially, are of great potential use in synthesis.[2] It occurred to us that ω-alkoxy lactams (**1**, eq 1) might show such dipolar behavior. De-



(1)

protonation using LDA was expected to afford the nucleophilic amide enolate anion **2**[3] whereas acid treatment should result in formation of the electrophilic *N*-acyliminium ion **3**.[4] We were particularly interested in performing the second of the two C–C bond-forming reactions in an intramolecular fashion by using another dipolar reagent of type **4** in order to arrive at bicyclic systems **6** via alkylation products **5** (eq 2). Both the azabicycles **6**



(2)

and the amino acids **7**, which result from hydrolysis of the amide bond in **6**, are interesting molecules for which a general synthetic approach did not yet exist. We now disclose our results, which provide a facile entry to these molecules.

(1) Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 239.

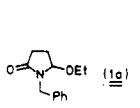
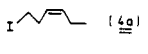
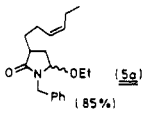
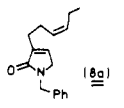
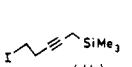
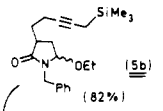
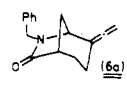
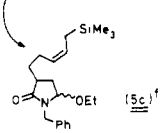
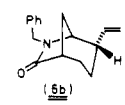
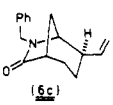
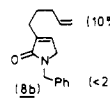
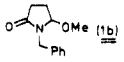
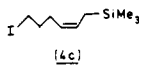
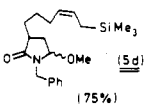
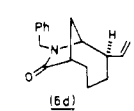
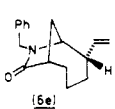
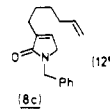
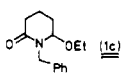
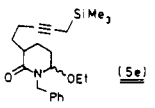
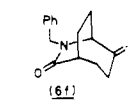
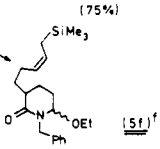
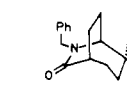
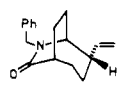
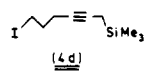
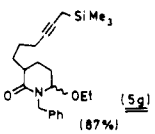
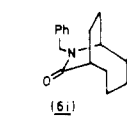
(2) For recent reports on dipolar conjunctive reagents, see: Piers, E.; Karunaratne, V. *J. Chem. Soc., Chem. Commun.* **1983**, 935. Piers, E.; Karunaratne, V. *J. Org. Chem.* **1983**, *48*, 1774. Trost, B. M.; Cossy, J.; Burks, J. *J. Am. Chem. Soc.* **1983**, *105*, 1052.

(3) Seebach, D.; Leitz, H. F. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 501. Durst, T.; LeBelle, M. J. *Can. J. Chem.* **1972**, *50*, 3196. Trost, B. M.; Kunz, R. A. *J. Org. Chem.* **1974**, *39*, 2475. Hullot, P.; Cuvigny, T.; Larchevêque, M.; Normant, H. *Can. J. Chem.* **1976**, *54*, 1098.

(4) For a review, see: Speckamp, W. N. *Recl. Trav. Chim. Pays-Bas* **1981**, *100*, 345.

0022-3263/84/1949-1149$01.50/0

Table I

entry	ω-alkoxy lactam 1	reagent 4[a]	alkylation product 5[b] (yield)[c]	acid for cyclization[d]	product of (attempted) cyclization[e] (yield)[c]
1a	 (1a)	 (4a)	 (5a) (85%)	CF_3CO_2H	 (8a) (90%)
1b				HCO_2H	(50%) + mixture of unknown compounds
2	1a	 (4b)	 (5b) (82%)	CF_3CO_2H	 (6a) (88%)
3a	—	—	 (5c)[f]	CF_3CO_2H	 (6b) (73%)  (6c) (4%)  (8b) (10%)
3b				HCO_2H	(82%) (5%) (<2%)
4	 (1b)	 (4c)	 (5d) (75%)	CF_3CO_2H	 (6d) (67%)  (6e) (6%)  (8c) (12%)
5	 (1c)	4b	 (5e) (75%)	HCO_2H	 (6f) (93%)
6	—	—	 (5f)[f]	HCO_2H	 (6g) (49%)  (6h) (36%)
7a	(1c)	 (4d)	 (5g) (87%)	HCO_2H	 (6i) (<10%)
7b				$SnCl_4$	(81%)

[a] For their preparation see ref 9. [b] About 60:40 mixtures of stereoisomers. [c] Isolated yields. [d] Reactions were carried out at room temperature; reaction time (0.5–1 h) except for entries 1a (21 h) and 1b (105 h); HCO_2H was used neat (10 mL per mmol of 5); CF_3CO_2H (10 equiv) and $SnCl_4$ (1.5 equiv) were used in CH_2Cl_2 (25 mL per mmol of 5). [e] For spectral data see ref 17. [f] Obtained from **5b** or **5e** in 97% yield according to ref 12.

The alkoxy lactams **1a–c**[5](see Table I) were prepared from the corresponding *N*-benzylimides in a one-pot reaction via the known acid-catalyzed $NaBH_4$ reduction in methanol or ethanol, followed by strong acid induced substitution of the hydroxyl function with an alkoxy group.[6] Yields of *ethoxy* lactams ranged from 80% to 90%, whereas *methoxy* lactams were obtained in yields of only 50–60%, due to an unfavorable hydroxy lactam–methoxy lactam equilibrium. Since ethoxy and methoxy lactams show the same reactivity in subsequent reactions, the former are the preferred substrates.

Deprotonation of **1b** using 1.2 equiv of LDA in THF at −78 °C was virtually complete within 30 min to yield a light yellow solution of lithium enolate **2**,[7] as shown by deuteration. The enolate was perfectly stable at −78 °C but slowly decomposed at temperatures above −25 °C. In this context, it is worth mentioning that attempts to prepare the monolithium enolate of *N*-benzylsuccinimide itself by using 1.2 equiv of LDA in THF at −78 °C were unsuccessful. Quenching with aqueous acetic acid gave no starting material back.[8]

Alkylation of the lithium enolates derived from **1a–c** (prepared at −78 °C with 1.2 equiv of LDA in THF) occurred in good yields upon addition of 1.3 equiv of iodide **4**[9] at −78 °C, stirring for 30 min at this temperature and allowing the reaction mixture to warm up to 0 °C over 2 h. The products **5**[5] were mixtures of stereoisomers (about 60:40), but this was of no concern, since the asymmetry

(5) These structures were established with the aid of IR and ^1H NMR spectroscopy and exact mass determination.[17]

(6) Hubert, J. C.; Wijnberg, J. B. P. A.; Speckamp, W. N. *Tetrahedron* **1975**, *31*, 1437.

(7) For a similar lithiation, see: Nagasaka, T.; Esumi, S.; Ozawa, N.; Kosugi, Y.; Hamaguchi, F. *Heterocycles* **1981**, *16*, 1987.

(8) Preparation of the lithium enolate of a 3,4-disubstituted *N*-protected succinimide has been published to be more successful: Schlecker, R.; Seebach, D. *Helv. Chim. Acta* **1977**, *60*, 1459.

(9) Iodides **4a–d** were derived from the corresponding alcohols through their mesylates. *cis*-3-Hexen-1-ol was commercially available. 1-(Trimethylsilyl)-2-pentyn-5-ol was prepared via reaction of the diethyl alane[10] of propargylsilane[11] with oxirane. 1-(Trimethylsilyl)-2-hexyn-6-ol was obtained via alkylation of the lithium acetylide derived from the THP ether of 4-pentyn-1-ol with (iodomethyl)trimethylsilane.[11] Hydrogenation[12] led to the corresponding cis olefin. These syntheses will be detailed in a forthcoming publication.

(10) Danishefsky, S.; Kitahara, T.; Tsai, M.; Dynak, J. *J. Org. Chem.* **1976**, *41*, 1669.

(11) Pornet, J.; Kolani, N. B.; Mesnard, D.; Miginiac, L.; Jaworski, K. *J. Organomet. Chem.* **1982**, *236*, 177.

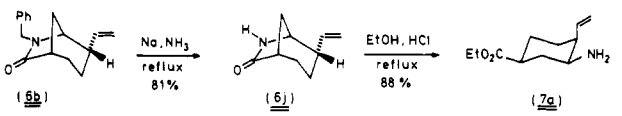
(12) Brown, C. A.; Ahuja, V. K. *J. Chem. Soc., Chem. Commun.* **1973**, 553. Brown, C. A., Ahuja, V. K. *J. Org. Chem.* **1973**, *38*, 2226.

of the carbon adjacent to nitrogen is lost on forming the planar *N*-acyliminium ion. The allylsilanes **5c** and **5f** were prepared from the corresponding propargylsilanes in excellent yields by using the partial hydrogenation procedure of Brown.[12]

The products[5] of the cyclization experiments are shown in the last column of Table I. Comparison of entries 1 and 3 reveals the favorable effect of silicon in the *N*-acyliminium ion cyclization reaction.[13] Whereas **5a** yielded only the product of ethanol elimination **8a** on treatment with CF_3CO_2H in CH_2Cl_2, **5c** afforded a good yield of cyclization products **6bc**, along with a slight amount of **8b**, resulting from protodesilylation and ethanol elimination. In general, formic acid appeared to be a better medium for cyclization, since the amount of elimination was reduced (entries 1 and 3). In the cyclization of **5a** with formic acid there was obtained, in addition to 50% of **8a**, a complex mixture of three rather unstable products (possibly resulting from ring closure) which was not further investigated. Cyclization of the other allylsilanes (entries 4 and 6) induced by Brønsted acid proceeded in good to excellent yields, leading to bicyclic amides with a vinyl substituent. The stereochemistry of the vinyl isomers (**6bc**, **6de**, **6gh**) was determined by using difference NOE in ^1H NMR spectroscopy. Cyclization of propargylsilanes (entries 2, 5, and 7) effected by Brønsted acid led to 1,1-disubstituted allenes in excellent yields except in the case of **5g**, where protodesilylation was probably faster than closure of the eight-membered ring. However, 1.5 equiv of $SnCl_4$ in CH_2Cl_2[13d] did cause the desired ring closure to yield **6i**. In future experiments we will further explore this Lewis acid mediated procedure.

Our results indicate that **1a–c** are well suited as dipolar synthons for a general approach to various bicyclic nitrogen compounds.[14] The vinyl and vinylidene substituents lend themselves for further manipulations. Starting materials **1** and **4** containing more functionality are easily available, which then may lead to more heavily substituted azabicycles. The presence of silicon appears to be crucial to the method in terms of yield and regiocontrol.

The cyclization products can readily be converted into amino acid derivatives as is shown in eq 3. Removal of



(3)

the *N*-benzyl group from **6b** with sodium in refluxing ammonia[15] afforded a lactam **6j**, which underwent ring opening to the carbocyclic amino acid ester **7a** in refluxing acidic ethanol. γ-Amino acids are interesting compounds for neurochemical research, as they are analogues of the inhibitory neurotransmitter GABA.[16]

Acknowledgment. We thank Mr. C. Kruk for providing the 250-MHz ^1H NMR spectra, in particular the NOE difference spectra.

(13) For reactions of *N*-acyliminium ions with allyl- and propargylsilanes, see: (a) Hiemstra H.; Speckamp, W. N. *Tetrahedron Lett.* **1983**, *24*, 1407. (b) Hart, D. J.; Tsai, Y.-N. *Ibid.* **1981**, *22*, 1567. (c) Aratani, M.; Sawada, K.; Hashimoto, M. *Ibid.* **1982**, *23*, 3921. (d) Kraus, G. A.; Neuenschwander, K. *J. Chem. Soc., Chem. Commun.* **1982**, 134.

(14) Many methods are known for the synthesis of the 6-azabicyclo-[3.2.1]octane skeleton **6a–c**; see, e.g.: Bonjoch, J.; Mestre, E.; Cortes, R.; Granados, R.; Bosch, J. *Tetrahedron* **1983**, *39*, 1723. Krow, G. R.; Shaw, D. A.; Jovais, C. S. *Synth. Commun.* **1983**, *13*, 575. The other bicyclic systems have incidentally been prepared by specialized methods. For 7-azabicyclo[4.2.1]nonanes **6d,e**, see, e.g.: Kawashima, K.; Agata, I. *Yakugaku Zasshi* **1969**, *89*, 1426; *Chem. Abstr.* **1970**, *72*, 21571*p*. Moriconi, E. J.; Hummel, C. F. *J. Org. Chem.* **1976**, *41*, 3583. For 6-azabicyclo-[3.2.2]nonanes **6f–h**, see, e.g.: Mackiewicz, P.; Furstoss, R.; Waegell, B.; Cote, R.; Lessard, J. *Ibid.* **1978**, *43*, 3746, 3750. For 7-azabicyclo[4.2.2]-decanes **6i**, see, e.g.: Wegener, P. *Tetrahedron Lett.* **1967**, 4985. Paquette, L. A.; Barton, T. J. *J. Am. Chem. Soc.* **1967**, *89*, 5480.

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(17) Some spectral data are as follows. **6a**: IR ($CHCl_3$) 1965, 1680 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.33 (m, Ph), 4.94 (d, *J* = 15 Hz, C*H*Ph), 4.70 (m, C=CH_2), 3.92 (d, *J* = 6 Hz, NCH), 3.88 (d, *J* = 15 Hz, C*H*Ph), 2.62 (m, COCH), 1.45–2.47 (m, 6 H). **6b**: IR ($CHCl_3$) 1675 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 7.30 (m, Ph), 5.66–6.07 (m, C*H*=CH_2), 5.17 (d, *J* = 15 Hz, C*H*Ph), 4.91–5.31 (m, HC=CH_2), 3.91 (d, *J* = 15 Hz, C*H*Ph); 3.54 (d, *J* = 6 Hz, NCH), 2.56 (m, COCH), 1.35–2.47 (m, 7 H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 175.3 (s), 140.4 (d), 136.3 (s), 127.6 (d), 127.0 (d), 126.4 (d), 113.7 (t), 58.0 (d), 44.6 (t), 41.1 (d), 39.6 (d), 37.6 (t), 24.2 (t), 23.1 (t). **6d**: IR ($CHCl_3$) 1665 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 7.32 (m, Ph), 5.49–5.90 (m, C*H*=CH_2), 4.85–5.18 (m, CH=CH_2), 5.04 (d, *J* = 15 Hz, C*H*Ph), 3.96 (d, *J* = 15 Hz, C*H*Ph), 3.49 (dd, *J* = 7, 1.5 Hz, NCH), 1.16–2.77 (m, 10 H); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 176.9 (s), 139.5 (d), 136.4 (s), 128.3 (d), 127.8 (d), 127.2 (d), 114.6 (t), 60.1 (d), 43.5 (t), 42.0 (d), 41.2 (d), 31.7 (t), 29.7 (t), 26.5 (t), 21.7 (t). **6f**: IR ($CHCl_3$) 1955, 1640 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.33 (m, Ph), 5.15 (d, *J* = 15 Hz, C*H*Ph), 4.62 (m, C=CH_2), 4.11 (d, *J* = 15 Hz, C*H*Ph), 3.98 (m, NCH), 2.88 (m, COCH), 1.56–2.70 (m, 8 H). **6gh**: IR ($CHCl_3$) 1635 cm^{-1}. **6i**: IR ($CHCl_3$) 1955, 1630 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.32 (m, Ph), 5.40 (d, *J* = 15 Hz, C*H*Ph), 4.62 (m, C=CH_2), 4.08 (m, NCH), 3.78 (d, *J* = 15 Hz, C*H*Ph), 2.92 (m, COCH), 1.10–2.50 (m, 10 H). **7a**: IR ($CHCl_3$) 3365, 1725 cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 5.80–6.21 (m, *H*C=CH_2), 5.04–5.30 (m, HC=CH_2), 4.14 (q, *J* = 7 Hz, OCH_2CH_3), 2.84 (dt, *J* = 11, 4 Hz, *H*CNH$_2$), 2.23–2.60 (m, *H*CCO$_2$Et, *H*CCH=CH_2) 1.34–2.02 (m, 6 H), 1.28 (s, NH_2), 1.26 (t, *J* = 7 Hz, OCH_2CH_3).

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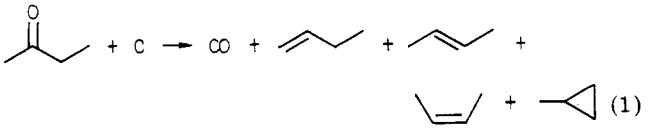
Intramolecular Trapping of an Intermediate in the Deoxygenation of a Carbonyl Compound by Atomic Carbon

Summary: Deoxygenation of 2,3-butanedione by atomic carbon generates acetylethylidene, CO, CO_2, 2-butyne, and 1,2-butadiene.

Sir: The high energy of atomic carbon renders many otherwise difficult reaction pathways accessible.[1] An interesting example is the deoxygenation of carbonyl compounds, which generates carbon monoxide and a carbene. Thus, 2-butanone is deoxygenated to the products in eq 1.[2,3]



(1)

We have recently used MNDO calculations to investigate the reaction coordinate for the deoxygenation of 2-

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