equilibrium isotope effect is understandable in terms of n-σ^* hyperconjugation (no-bond resonance) of a type which is also responsible, in large part,[2] for the anomeric effect.[3] The latter is a stabilization of an axial vs. an equatorial electronegative substituent, as in II. The bond to the axial substituent is weakened and lengthened, whereas the adjacent C-O bond is changed in an opposite fashion.[4] The weakening of the axial bond, albeit in reduced form, should exist even when X = H in II. The anomeric effect is responsible for stereoselective reactions in carbohydrates,[3] and, more generally, in ketals.[5] The same electronic feature is responsible also for the conformational dependence of the α C-H stretching frequencies in ethers.[6]

The 1,3-dioxane structure is well suited for the purpose of detecting a deuterium isotope perturbation originating from an anomeric effect, since a CHD group in the 2-position is flanked by two oxygens, thus doubling the energy difference of the effect. Also, such compounds are easy to synthesize and their conformational properties are well established.[7]

We chose the 5,5-dimethyl derivative of 1,3-dioxane since the methyl groups are sufficiently well isolated from the C-2 position so that intrinsic isotope effects[8] can be safely neglected in applying Saunders' isotopic perturbation method.[9] The 500-MHz ^{1}H NMR spectrum of I showed a 1:1 doublet with a separation of 0.0194 ppm for the methyl groups. Taken together with the methyl axial-equatorial chemical shift difference of 0.470 ppm,[10] this gives a $|\Delta G°|$ value of 49 ± 3 cal/mol for the isotope effect at room temperature. The isotope effect is so large that direct integration of the two peaks for the C-2 proton of I under slow inversion conditions (-70 °C) can be used.[11] The ratio of the integrals was measured to be 0.88 ± 0.02 with the axial site more populated than the equatorial site. This corresponds to deuterium favoring the equatorial position by a $\Delta G°$ of 52 ± 10 cal/mol at -70 °C, in agreement with the isotopic perturbation value and with the expected near-zero entropy contribution to $\Delta G°$.

The CH stretching frequencies in 1,3-dioxane-2,4,4,5,5,6,6-d_7 (III) are reported to be 2828 and 2990 cm^{-1},[7] giving a zero point energy (ZPE) contribution of 65 cal/mol to $\Delta G°$ in that compound. In I itself, the C-D stretching bands in the infrared occur at 2081 and 2131 cm^{-1}, corresponding to a slightly higher ZPE contribution of 85 cal/mol. Additionally, bending vibrations must be considered. In cyclohexane-d_1,[1] it appears that the angle bending force constants are the same for axial and equatorial CH bonds but that the bending frequencies are a little higher for the axial than for the equatorial CH bond because of differences in the 1,4 and 1,5 non-bonded interactions for the two types of protons. Thus, in cyclohexane-d_1, bending contributions (-6 cal/mol) partially cancel the stretching contributions (12 cal/mol).[1] In the 1,3-dioxane system, the ZPE contribution from bond stretching is also larger than the observed isotope effect, and thus a bending contribution of about -30 cal/mol is needed.[12]

Previously observed, but puzzling and unexplained, deuterium isotope chemical shift effects in some cyclic ethers are most probably of an equilibrium type resulting from conformational differences in C-H bond strengths α to an oxygen atom.[13]

Further calculations on I and the parent 1,3-dioxane using molecular mechanics calculations are in progress,[14] and deuterium equilibrium isotope effects in other 1,3-dioxanes and their isotopomers are under investigation.

Acknowledgment. The 500-MHz spectrometer was purchased through funds provided in part by the National Science Foundation.

(2) For a review, see: Wolfe, S.; Whangbo, M.-H.; Mitchell, D. J. *Carbohydr. Res.* **1979**, *69*, 1-26. Dipole-dipole interactions also play a role in the anomeric and related effects. See also: Cieplak, A. S. *J. Am. Chem. Soc.* **1981**, *103*, 4540-4552 and references therein.

(3) For reviews, see: (a) Lemieux, R. U. *Pure Appl. Chem.* **1971**, *25*, 527-548. (b) Eliel, E. L. *Acc. Chem. Res.* **1970**, *3*, 1-8. (c) Zefirinov, N. S.; Shektman, N. M. *Russ. Chem. Rev. (Engl. Transl.)* **1979**, *40*, 315-329. (d) "Anomeric Effect, Origin and Consequences"; *ACS Symp. Ser.* **1979**, *No 87*. (e) Kirby, A. J. *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*; Springer Verlag: Berlin, 1983. The effect in I, with deuterium as the substituent, is actually a reverse anomeric effect.

(4) (a) Romers, C.; Altona, C.; Buys, H. R.; Havinga, E. *Top. Stereochem.* **1969**, *4*, 39-97. (b) Allen, F. H.; Kirby, A. J. *J. Am. Chem. Soc.* **1984**, *106*, 6197-6200. (c) Briggs, A. J.; Glenn, R.; Jones, P. G.; Kirby, A. J.; Ramaswamy, P. *J. Am. Chem. Soc.* **1984**, *106*, 6200-6206. (d) Jones, P. G.; Kirby, A. J. *J. Am. Chem. Soc.* **1984**, *106*, 6207-6212. (e) Jeffrey, G. A. in ref 3d, p 50-62.

(5) Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Pergamon Press: Oxford, 1983.

(6) (a) Saur, O.; Janin, A.; Vallet, A.; Lavalley, J.-C. *J. Mol. Struct.* **1976**, *34*, 171-180. (b) Caillod, J.; Saur, O.; Lavalley, J.-C. *Spectrochim. Acta, Part A* **1980**, *36*, 185-191. (d) McKean, D. C. *J. Mol. Struct.* **1976**, *34*, 181-185.

(7) Riddell, F. G. *The Conformational Analysis of Heterocyclic Compounds*; Academic Press: New York, 1980. The deuterated compound, I, was prepared from 2-methoxy-5,5-dimethyl-1,3-dioxane (Eliel, E. L.; Nader, F. W. *J. Am. Chem. Soc.* **1970**, *92*, 584-590) by reduction with $LiAlD_4$-$AlCl_3$ according to the procedure of: Eliel, E. L.; Nader, F. W. *J. Am. Chem. Soc.* **1970**, *92*, 3045-3050.

(8) (a) Anet, F. A. L.; Dekmezian, A. H. *J. Am. Chem. Soc.* **1979**, *101*, 5449-5451. (b) Hansen, P. E. *Annu. Rep. NMR Spectrosc.* **1983**, *15*, 105-234.

(9) (a) Saunders, M.; Jaffe, M. H.; Vogel, P. *J. Am. Chem. Soc.* **1971**, *93*, 2558-2559. (b) Anet F. A. L.; Basus, V. J.; Hewitt, A. P. W.; Saunders, M. *J. Am. Chem. Soc.* **1980**, *102*, 3945-3946 and references therein.

(10) The methyl chemical shift difference in I was measured in the same solvent (CD_2Cl_2) at -60 to -90 °C and extrapolated to room temperature. Previous investigators have not reported any temperature dependence (and only a very small solvent dependence) for this chemical shift difference: (a) Friebolin, H.; Kabuss, S.; Maier, W.; Lüttringhaus, A. *Tetrahedron Lett.* **1962**, 683-690. (b) Anderson, J. E.; Brand, J. C. D. *Trans. Faraday Soc.* **1966**, *62*, 39-45. (c) Friebolin, H.; Schmid, H. G.; Kabuss, S.; Faisst, W. *Org. Magn. Reson.* **1969**, *1*, 67-86. (d) Coene, E.; Anteunis, M. *Bull. Soc. Chim. Belg.* **1970**, *79*, 37-43. (e) Binsch, G.; Eliel, E. L.; Mayer, S. *J. Org. Chem.* **1973**, *38*, 4079-4081. The free energy barrier to ring inversion in 5,5-dimethyl-1,3-dioxane is reported by the above workers to be about 10.7 kcal/mol.

(11) Direct determinations of equilibrium isotope effects by integration under slow exchange conditions have been made in a few cases: (a) Jensen, F. R.; Smith, L. A. *J. Am. Chem. Soc.* **1964**, *86*, 956-957. (b) Aydin, R.; Günther, H. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 985-986. (c) Biali, S. E.; Rappaport, Z.; Hull, W. E. *J. Am. Chem. Soc.* **1985**, *107*, 5450-5459. However, small differences can be difficult to measure reliably.[1]

(12) A similar situation holds for (positive) hyperconjugation in carbocations: (a) Sunko, D. E.; Hehre, W. J. *Prog. Phys. Org. Chem.* **1983**, *14*, 205-246. (b) Hout, R. F., Jr.; Levy, B. A.; Hehre, W. J. *J. Comput. Chem.* **1983**, *4*, 499-505.

(13) (a) Canuel, L.; St-Jacques, M. *Can. J. Chem.* **1974**, *52*, 3581-3588. (b) Canuel, L.; St.-Jacques, M. *J. Org. Chem.* **1976**, *41*, 1380-1384.

(14) Existing molecular-mechanics force fields for ether and ketal functions do not have conformationally different C-H stretching force constants required to explain the present results: Nørskov-Lauritsen, L.; Allinger, N. L. *J. Comput. Chem.* **1984**, *5*, 326-335 and references therein.

Photocyclization Strategy for the Synthesis of Antitumor Agent CC-1065. Synthesis of the B and C Unit Fragments

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The potent antitumor antibiotic CC-1065 (**1**), which is composed of three essentially planar benzo[1,2-*b*:4,3-*b*]dipyrrole units connected by amide bonds, has been the subject of a number of synthetic efforts in recent years.[1-4] Much of this research has

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(1) (a) Isolation and characterization: Chidester, C. G.; Krueger, W. C.; Mizsak, S. A.; Duchamp, D. J.; Martin, D. G. *J. Am. Chem. Soc.* **1981**, *103*, 1629 and reference cited therein. (b) DNA binding studies: Hurley, L. H.; Reynolds, V. L.; Swenson, D. H.; Petzold, G. L.; Scahill, T. A. *Science (Washington, D.C.)* **1984**, *226*, 843. Needham-Vandevanter, D. R.; Hurley, L. H.; Reynolds, V. L.; Theriault, N. Y.; Krueger, W. C.; Wierenga, W. *Nucleic Acids Res.* **1984**, *12*, 6159.

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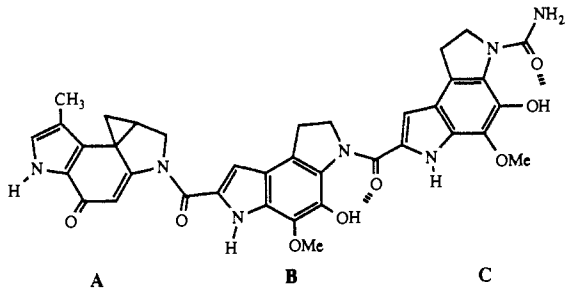
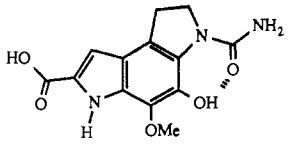
been directed toward the cyclopropane-containing A unit and has

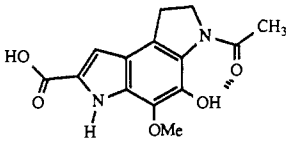


A B C

1: CC-1065



2: PDE-I



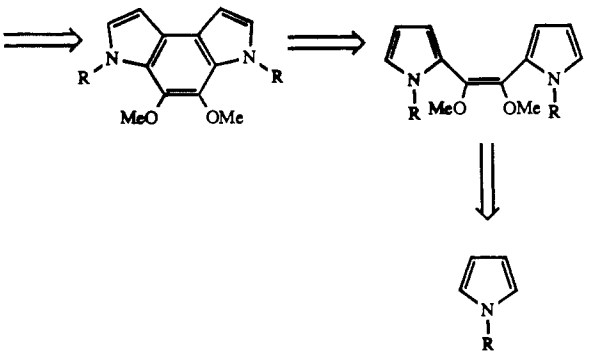
3; PDE-II

resulted in three clever, and conceptually different, syntheses.[2] The dioxygenated and essentially identical B and C units are like the natural products PDE-I (**2**) and PDE-II (**3**), which were isolated by Umezawa's group and shown to exhibit inhibitory activity against cyclic adenosine-3′,5′-monophosphate phosphodiesterase.[3] Furthermore, both PDE-I and PDE-II were found to have remarkably low toxicity, no signs of toxicity being visible even when high doses (200 mg/kg) were administered intraperitoneally into mice.[3a] Unlike in the case of unit A, relatively little work has been directed toward the synthesis of the structurally and biologically interesting B and C units.[4] Aside from Umezawa's classical syntheses, which began with isovanillin and served to confrim the structures of PDE-I and PDE-II, no other successful syntheses have been reported.[4d]

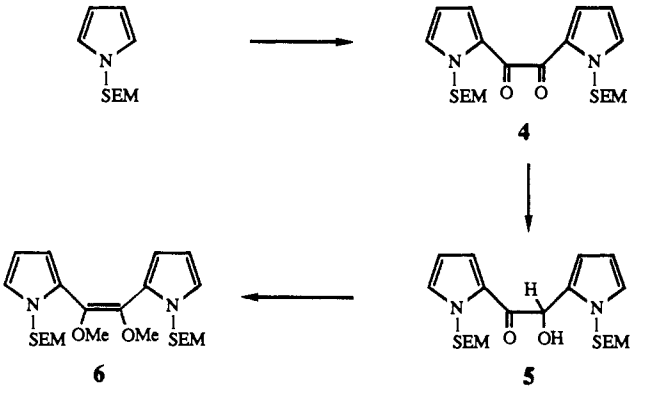
We have undertaken the development of a general, flexible strategy which should allow the rapid construction of not only the individual units of CC-1065, but also numerous other potentially active analogues.[5] We communicate here a successful implementation of this strategy in the syntheses of the B and C unit fragments of CC-1065, which is to say the methyl esters of PDE-I and PDE-II.

Our synthetic design unmasks the symmetry inherent in these units (Scheme I). In relatively few retrosynthetic steps—methylation, deacylation, aromatization, and decarboxylation—both PDE-I and PDE-II can be seen to arise from a common, phenanthrene-like precursor possessing a plane of symmetry. This tricyclic unit we envisioned as arising via a Mallory-type photocyclization[6] of an α,α'-dioxygenated stilbenoid system, using the Pd/C mediated photocyclization technology[5b] that we have developed specifically for constructing such electron-rich systems.

Scheme I



Scheme II



The starting material for the synthesis (Scheme II) was the simple heterocycle pyrrole, which was protected in high yield (90%) with the [2-(trimethylsilyl)ethoxy]methyl (SEM) group.[7] The two carbons and two oxygens required for the benzenoid portion were provided by oxalyl chloride[8] [$(COCl)_2$, pyr, CH_2Cl_2, −24 °C to room temperature, 75%], and the resulting diketone **4**[9] was reduced selectively to the benzoin-like hydroxy ketone **5** using sodium dithionite[10] ($Na_2S_2O_4$, $NaHCO_3$, DMF-H_2O, 100 °C, 1 h, 99%).

Conversion of hydroxy ketone **5** into a suitably protected enediol proved to be unexpectedly difficult. Success was achieved by extending the findings of Heine,[11] who has examined the C vs. O alkylation of benzoin with a variety of alkylating agents, and in different solvents, using aqueous sodium hydroxide. We found almost exclusive O-alkylation when a Me_2SO solution of **5** was treated with *t*-BuOK (5 equiv) in the presence of the hard alkylating agent methyl tosylate (5 equiv) and obtained in good yield (86%) the desired, light- and acid-sensitive stilbenoid **6**.

A cis–trans mixture of this enediol dimethyl ether **6** was photocyclized in good yield (82%), under anaerobic conditions, using the novel Pd/C protocol.[5b,12] Interestingly, addition of a small amount of silica gel to the reaction mixture prevented the formation of a thin, dark, resinous layer on the reactor wall and speeded up the reaction considerably. The cyclization product was lithiated[7] in DME at 0 °C, then chilled to −78 °C, and quenched with an excess of $ClCO_2Et$ to give the desired ester **8** (60%). Unfortunately, after numerous attempts, using a variety

(2) Studies directed toward unit A: (a) Wierenga, W. *J. Am Chem. Soc.* **1981**, *103*, 5621. (b) Magnus, P.; Or, Y.-S. *J. Chem. Soc. Chem. Commun.* **1983**, 26. (c) Kraus, G. A.; Yue, S. *J. Chem. Soc., Chem. Commun.* **1983**, 1198. (d) Magnus, P.; Gallager, T. *J. Chem. Soc., Chem. Commun.* **1984**, 389. (e) Kraus, G. A.; Yue, S.; Sy, J. *J. Org. Chem* **1985**, *50*, 284.

(3) PDE-I and PDE-II. Isolation: (a) Enomoto, Y.; Furutani, Y.; Naganawa, H.; Hamada, M.; Takeuchi, T.; Umezawa, H. *Agric. Biol. Chem.* **1978**, *42*, 1331. (b) Nakamura, H.; Enomoto, Y.; Takeuchi, T.; Umezawa, H.; and Litaka, Y. *Agric. Biol. Chem.* **1978**, *42*, 1337. Synthesis: (c) Komoto, N.; Enomoto, Y.; Miyagaki, M.; Tanaka, Y.; Nitanai, K.; Umezawa, H. *Agric. Biol. Chem.* **1979**, *43*, 555. (d) Komoto, N.; Enomoto, Y.; Tanaka, Y.; Nitanai, K.; Umezawa, H. *Agric. Biol. Chem.* **1979**, *43*, 559.

(4) Studies directed toward units B and C: (a) Boger, D. L.; Coleman, R. S. *J. Org. Chem.* **1984**, *49*, 2240. (b) Sundberg, R. J.; Pearce, B. C. *J. Org. Chem.* **1985**, *50*, 425. (c) Magnus, P.; Halazy, S. *Tetrahedron Lett.* **1985**, *26*, 2985. (d) **Note Added in Proof**: A new synthesis of PDE-I and PDE-II has now appeared: Bolton, R. E.; Moody, C. J.; Rees, C. W.; Tojo, G. *J. Chem. Soc., Chem. Commun.* **1985**, 1775.

(5) For previous work in this series, see: (a) Rawal, V. H.; Cava, M. P. *J. Chem. Soc., Chem. Commun.* **1984**, 1526. (b) Rawal, V. H.; Jones, R. J.; Cava, M. P. *Tetrahedron Lett.* **1985**, *25*, 2423.

(6) Mallory, F. B.; Mallory, C. W. *Org. React.* **1984**, *30*, 1.

(7) (a) Martin, E. P.; Ley, S. V.; Lister, S. G.; Palmer, B. D. *J. Chem. Soc., Chem. Commun.* **1983**, 630. (b) Muchowski, J. M.; Solas, D. R. *J. Org. Chem.* **1984**, *49*, 203.

(8) Bher, D.; Brandange, S.; Lindstrom, B. *Acta Chem. Scand.* **1973**, *27*, 2411.

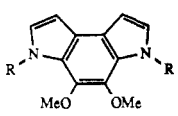
(9) Diketone **4** was also prepared by alkylating the disodium salt of dipyrrol-2-ylglyoxal[8] with SEM chloride (NaH, DMF, room temperature, 95%).

(10) Haddadin, M. J.; Zahr, G. E.; Rawdah, T. N.; Chelhot, N. C.; Issidorides, C. H. *Tetrahedron* **1974**, *30*, 659.

(11) Heine, H.-G. *Liebigs Ann. Chem.* **1970**, *735*, 56.

(12) To our knowledge there is no report of successful photocyclization of an α,α'-dialkoxy silbenoid.[6] The present case represents a particularly oxygen-sensitive substrate and serves to extend the utility of the Pd/C procedure.[5b]

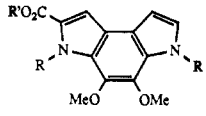
of fluoride sources, we were unable to remove both of the SEM groups from ester **8**. By contrast, removal of these groups from **7** proceeded smoothly in DMF at 85 °C using n-Bu_4NF, with ethylenediamine as the formaldehyde sponge (75%).[7b]



7: R=SEM

9: R=H

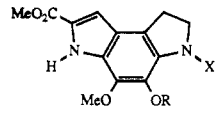
10; R=BOC



8: R=SEM; R'=Et

11; R=BOC; R'=Me

12; R=H; R'=Me



13; R=Me; X=H

14; R=Me; X=$CONH_2$

15; R=Me; X=$COCH_3$

16: R=H; X=$CONH_2$

17; R=H; X=$COCH_3$

To allow functionalization at the α-position, indole **9** mp 201-202 °C, was first blocked in quantitative yield with the *tert*-butyloxycarbonyl (BOC) group,[13] which is known to direct lithiation on indoles[14] and is easily removable under both acidic and basic conditions. The resulting protected indole **10**, mp 111-113 °C, was lithiated in THF with lithium 2,2,6,6-tetramethylpiperidide (-78 °C, 10 min) and, after cooling to -100 °C, treated with $ClCO_2Me$ to effect the desired homologation in 76% yield (88%, based on recovered starting material). Deprotection of the resulting ester **11** was accomplished most efficiently under thermolytic conditions (185 °C, oil bath temperature, 25 min),[15] affording **12** as a viscous liquid which slowly crystallized (mp 126-128 °C). As this substance was clean by both TLC and 250-MHz NMR, the next two steps were also carried out in the same flask. Thus reduction of **12** proceeded chemoselectively to indoline **13** (CH_3CO_2H, $NaCNBH_3$, 15-20 °C),[16] which upon quenching with aqueous KOCN and warming generated urea **14**, mp 186-188 °C (lit.[3a] 175-177 °C), in 92% yield from **11**.

Selective demethylation of **14**, on the side with the urea, was expected, since the resulting hydroxyl is strongly hydrogen bonded in both CC-1065 and the PDE's. By use of the dimethyl sulfide complex of BBr_3,[17] the demethylation was indeed selective but was accompanied by appreciable amounts of the didemethylated compound. The related BCl_3 complex[17] was milder and gave a good yield of urea **16** (85%, 70% conversion). An analogous sequence of reactions, using acetic anhydride instead of KOCN, afforded the amide **15**, which was demethylated to **17**.[18-20]

Since the deprotection, reduction, and acylation are all performed in one pot, our synthesis of the B and C units requires only 10 steps from pyrrole; the overall yield is in excess of 20% for both systems, making these compounds synthetically far more accessible than by the previous route.[21] Moreover, we are successfully applying this basic strategy to synthesize the A unit of CC-1065 as well as the thiophene analogues of both PDE-I and PDE-II.[22]

Acknowledgment. This work was supported by a grant from the National Institutes of Health (Grant NIH-CA 41995). V.H.R. thanks the University of Pennsylvania for partial support in the form of a Dean's Fellowship.

(13) Grehn, L.; Ragnarsson, U. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 296.

(14) (a) Hasan, I.; Marinelli, E. R.; Lin, L. C.; Fowler, F. W.; Levy, A. B. *J. Org. Chem.* **1981**, *46*, 157. (b) Kline, T. *J. Heterocycl. Chem.* **1985**, *22*, 505.

(15) This thermolytic deprotection procedure appears to be general: Rawal, V. H.; Cava, M. P. *Tetrahedron Lett.* **1985**, *26*, 6141.

(16) Gribbe, G. W.; Hoffman, J. *Synthesis* **1977**, 859.

(17) (a) Willard, P. G.; Fryhle, C. B. *Tetrahedron Lett.* **1980**, *21*, 3731. (b) Teitel, S.; O'Brien, J.; Brossi, A. *J. Org. Chem.* **1972**, *37*, 3368. (c) Barton, D. H. R.; Bould, L.; Clive, D. L. J.; Magnus, P. D.; Hase, T. *J. Chem. Soc. C* **1971**, 2204. (d) Dean, F. M.; Goodchild, J.; Houghton, L. E.; Martin, J. A.; Morton, R. B.; Parton, B.; Price, A. W.; Somvichien, N. *Tetrahedron Lett.* **1966**, 4153.

(18) Spectral data of selected intermediates. ^1H NMR (250 MHz, $CDCl_3$): **7**, δ -0.056 (s, 9 H, $SiMe_3$), 0.89 (t, 2 H, J = 8.3 Hz, CH_2Si), 3.50 (t, 2 H, J = 8.3 Hz, OCH_2), 4.04 (s, 3 H, OCH_3), 5.72 (s, 2 H, NCH_2O), 6.57 (d, 1 H, J = 3.2 Hz, Ar H), 7.10 (d, 1 H, J = 3.2 Hz, Ar H); **9**, δ 4.06 (s, 3 H, OCH_3), 6.73 (dd, 1 H, J = 2.3, 2.9 Hz, Ar H), 7.18 (t, J = 2.7 Hz, 1 H, Ar H), 8.38 (br s, 1 H, NH); **10**, δ 1.65 (s, 9 H, *t*-Bu), 3.96 (s, 3 H, OCH_3), 6.68 (d, 1 H, J = 3.6 Hz, Ar H), 7.53 (d, 1 H, J = 3.6 Hz, Ar H); **11**, δ 1.65 (s, 9 H, *t*-Bu), 1.69 (s, 9 H, *t*-Bu), 3.92 (s, 3 H, OCH_3), 3.93 (s, 3 H, OCH_3), 3.99 (s, 3 H, OCH_3), 6.71 (d, 1 H, J = 3.7 Hz, Ar H), 7.38 (s, 1 H, Ar H), 7.54 (d, 1 H, J = 3.7 Hz, Ar H); **12**, δ 3.94 (s, 3 H, OCH_3), 4.01 (s, 3 H, OCH_3), 4.08 (s, 3 H, OCH_3), 6.73 (dd, 1 H, J = 2.2, 2.9 Hz, Ar H), 7.17 (t, 1 H, J = 2.9 Hz, Ar H), 7.42 (d, 1 H, J = 2.2 Hz, Ar H), 8.62 (br s, 1 H, NH), 9.21 (br s, 1 H, NH); **15**, δ 2.27 (s, 3 H, $COCH_3$), 3.10 (t, 2 H, J = 7.5 Hz, Ar CH_C), 3.83 (s, 3 H, OCH_3), 3.95 (s, 3 H, OCH_3), 4.05 (s, 3 H, OCH_3), 4.34 (t, 2 H, J = 7.5 Hz, CH_2iN), 7.07 (d, 1 H, J = 2.1 Hz, Ar H), 9.00 (br s, 1 H, NH).

(19) Spectra (200 MHz NMR, IR, and MS) of compounds **14**, **16**, and **17** corresponded perfectly with those of the naturally derived materials.[3a,20]

(20) We thank Professor Umezawa for providing us spectra of PDE-I and PDE-II and some of their methyl derivatives.

(21) We had hoped to further shorten our synthesis by starting with the BOC analogue of diketone **4**. While this derivative is easily prepared, all attempts to convert it to the BOC analogue of the enol ether **6** led to loss of the BOC group. Details of these experiments and other variants in the synthesis will be described in the full publication.

(22) Jones, R. J.; Cava, M. P., unpublished results.

Alkali Metal Complexation by Thione Sulfur in *N*-Acyl Thioamides[1]

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Alkali-metal complexation by amide carbonyl oxygen is a well-established phenomenon which has been investigated by a number of techniques including NMR spectroscopy.[2-7] Complexation by thioamide sulfur, however, has not previously been investigated by these methods. This paper reports on experiments which demonstrate potassium ion chelation by *N*-acyl thioamides by monitoring perturbations in the equilibrium of diastereomers that differ in configuration (*E*,*Z*) at the thioamide partial double bond.

The *N*-acyl thioamides employed in this study, *N*-acetylthioacetamide (**1**, mp 59-61 °C, lit.[8] 61-62 °C), and *N*-propionylthiopropionamide (**2**, mp 42-45 °C), were prepared by treatment of the corresponding imides with Lawesson's reagent.[9] Although both mono- and dithiation have been reported for the reaction of Lawesson's reagent with cyclic imides,[10] the reaction of acyclic compounds, in our hands, produced only monothiated derivatives as isolable products. A similar observation has been noted for *N*-benzoylacetamide although *N*,*N*-diacetylaniline produced no isolable products other than thioacetanilide.[11]

The room temperature ^1H spectrum of *N*-acetylthioacetamide features two methyl singlets at δ 2.094 and 2.883 assigned to the acetyl and thioacetyl methyl groups, respectively. Similarly the ^{13}C spectrum features signals at δ 166.6 (carbonyl), 211.2

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