Because of the inherent flexibility of this molecule and the r^{-6} dependence of the NOE, however, these NOE-derived time-averaged distances merely represent the minimum allowable internuclear distances. The conformer population with the shortest distance between a particular pair of protons will contribute a disproportionate amount to the internuclear relaxation.[28]

It appears that the conformation of 2′,5′-ddFU is closely related to the known conformations of other pyrimidine 2′-deoxynucleosides.[23,25] This similarity in conformation may partially account for its ready trans-2′,5′-dideoxyribosylation by thymidine phosphorylase despite the fact that it is not a natural substrate for this enzyme.

In summary, we developed an enzymatic method for the facile synthesis of 2′,5′-dideoxy-5-fluorouridine by a 2′,5′-dideoxyribosyl transfer reaction, which provides a new and attractive alternative to existing procedures for the synthesis of 2′,5′-ddFU and other modified nucleosides.

Experimental Section

General. The melting point is uncorrected. ^{1}H NMR and ^{19}F NMR spectra were obtained at ambient temperature at 500 MHz for ^{1}H and 470 MHz for ^{19}F. The DMSO-d_5 peak in the NMR solvent was used as the internal reference for all the ^{1}H NMR spectra and was referenced at 2.49 ppm relative to TMS. The chemical shifts for ^{19}F NMR were measured relative to external trifluoroacetic acid. The 2-D NOE spectra were obtained on approximately 5 mg of material and were recorded in the phase-sensitive absorption mode using the hypercomplex method.[29] The sweep width was set to 4000 Hz in both dimensions; 300–350 increments were acquired in the t_1 dimension with eight transients for each FID, and 2048 points were collected in the t_2 dimension. The recycle time was 5 s, and the mixing times were 500 and 700 ms. For data processing, zero-filling to 2K by 2K was carried out, and base-line corrections and sine-bell windows were used in both dimensions. The fast atom bombardment (FAB) mass spectral data were obtained in DTT/DTE (dithiothreitol:dithioerythritol = 3:1) as the sample matrix.

Analytical HPLC utilized an Alltech Econosphere RP-C18 (150 × 4.6 mm, 3 μm) column, eluted at 1 mL/min with a linear gradient of 4–10% CH_3CN in 50 mM $HCOONH_4$, for 5 min. Preparative HPLC was done on an Alltech Econosphere RP-C18 (250 × 22.5 mm, 10 μm) column, eluted at 5 mL/min with a mobile phase of 15% CH_3CN in water isocratically.

Molecular modeling studies on 2′,5′-ddFU were carried out using the program QUANTA (v 3.0, Polygen Corp.). Energy minimizations were done with the standard CHARMM minimizers (steepest descents and adopted-basis Newton–Raphson methods) within QUANTA. The standard force-field parameter set supplied with the program was employed. A distance-dependent dielectric constant was used to mimic solvent effects, since the solvent was not explicitly included.

Enzymatic Synthesis of 2′,5′-Dideoxy-5-fluorouridine. A solution of 39 mg (0.3 mmol) of 5-fluorouracil (Sigma Chemical Co.) and 22.6 mg (0.1 mmol) of 2′,5′-dideoxythymidine (Sigma Chemical Co.) in 5 mL of 5 mM sodium phosphate buffer, pH 7.4 (D_2O:H_2O = 3:1) was prepared. To this solution was added 23.8 units of thymidine phosphorylase from *E. coli* (Sigma Chemical Co.). A part of this solution (0.7 mL) was taken in an NMR tube for ^{19}F NMR monitoring at 20 °C for 8 h. The rest was analyzed simultaneously by HPLC. After 8 h of reaction at room temperature, the reaction mixture was filtered through an Amicon filter to remove the enzyme and to stop the reaction. The filtrate was loaded on a preparative HPLC column by consecutive injections of 1.0 mL each. The fractions corresponding to 2′,5′-dideoxy-5-fluorouridine were collected, combined, and finally freeze-dried, yielding 13.5 mg (0.059 mmol, 59%) of 2′,5′-dideoxy-5-fluorouridine as a white powder: mp 168 °C (lit.[7] mp 171–173 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.825 (H_6, 1 H, $^3J_{HF}$ = 7.0 Hz), 6.057 ($H_{1'}$, td, 1 H, $^3J_{1'2'\alpha}$ = $^3J_{1'2'\beta}$ = 6.7 Hz, $^5J_{1'5F}$ = 1.8 Hz), 3.943 ($H_{3'}$, dt, 1 H, $^3J_{3'2'\beta}$ = 6.7 Hz, $^3J_{3'2'\alpha}$ = $^3J_{3'4'}$ = 4.1 Hz), 3.765 ($H_{4'}$, qd, 1 H, $^3J_{4'5'}$ = 6.4 Hz, $^3J_{4'3'}$ = 4.1 Hz), 2.191 ($H_{2'\beta}$, dt, 1 H, $^2J_{2'\beta2'\alpha}$ = 13.5 Hz, $^3J_{2'\beta1'}$ = $^3J_{2'\beta3'}$ = 6.7 Hz), 2.039 ($H_{2'\alpha}$, ddd, 1 H, $^2J_{2'\alpha2'\beta}$ = 13.5 Hz, $^3J_{2'\alpha1'}$ = 6.7, $^3J_{2'\alpha3'}$ = 4.1 Hz), 1.233 ($H_{5'}$, d, 3 H, $^3J_{5'4'}$ = 6.4 Hz); ^{19}F NMR (470 MHz, D_2O:H_2O = 3:1) δ 89.847 (d, 1 F, $^3J_{5FH}$ = 7.0 Hz); FAB–MS *m/z* (relative intensity) 231.0766 (231.0781, calcd for $C_9H_{11}N_2O_4F$; MH^+, 49) and 131 (BH^+, 100).

Cytotoxicity Assay. The cytotoxicity assay using the human solid tumor cell line systems, following the microculture tetrazolium assay method,[30] was performed at the Purdue Cell Culture Laboratory. The target cells were HT-29 (human colon carcinoma), A-549 (human lung adenocarcinoma), and MCF-7 (human breast adenocarcinoma) cells.

Acknowledgment. We are grateful for the support of the National Cancer Institute (R 01 CA 44416).

Registry No. 1, 51-21-8; 2, 61168-97-6; 5′-deoxythymidine, 3458-14-8; thymine, 65-71-4; thymidine phosphorylase, 9030-23-3.

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(30) Alley, M. C.; Scudiero, D. A.; Monks, A.; Hursey, M. L.; Czerwinski, M. J.; Fine, D. L.; Abott, B. J.; Mayo, J. G.; Shoemaker, R. H.; Boyd, M. R. *Cancer Res.* **1988**, *48*, 589.

Chirality as a Probe in β-Keto Ester Tautomerism[1]

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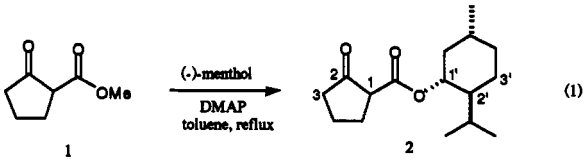
Over the past two decades, significant advances in the development of asymmetric synthetic methods have been achieved.[2] A direct consequence of these advances is a substantial increase in our understanding of reaction pathways at a very fundamental level. In this paper, the use of chirality as a probe to study equilibria in chiral β-keto esters is detailed. This analysis provides a direct method to study keto–enol tautomerism[3] utilizing NMR spectroscopy and details a ramification of having remote chiral centers in readily enolizable systems.

In a related investigation, we required a quantity of chiral keto ester **2**. As outlined in eq 1, (−)-menthyl 2-



1 2 (1)

oxocyclopentanecarboxylate (**2**) was prepared in 55% yield from **1**, following the method of Taber.[4,5] While an unequal mixture of epimers at C1 was expected, we were intrigued to find that the ^{1}H and ^{13}C NMR spectra indicated a *single diastereomer* of **2** was present in $CDCl_3$ solution at 20 °C (enol undetected by NMR). When **2** was analyzed in C_6D_6 at different times following dissolution, the emergence of a second product (an epimer at C1) was observed. Figure 1 is a composite of ^{1}H NMR spectra of **2** (in C_6D_6) in the region of 1.8 to 5 ppm,[6] taken over 5 h. The dd at 2.78 and the ddd at 4.90 ppm were identified as the protons on C1 (α-enolizable H) and C1′, respectively. Note that a second overlapping dd appears at 2.78 and that

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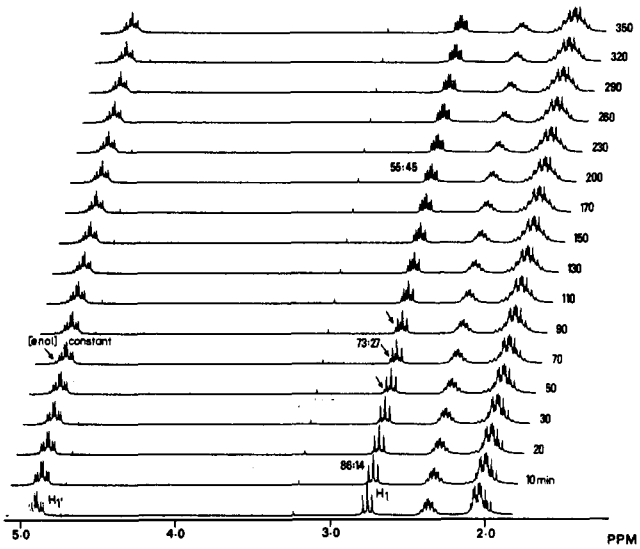


Figure 1. 300-MHz ^1H NMR spectra of **2** in C_6D_6 vs time.

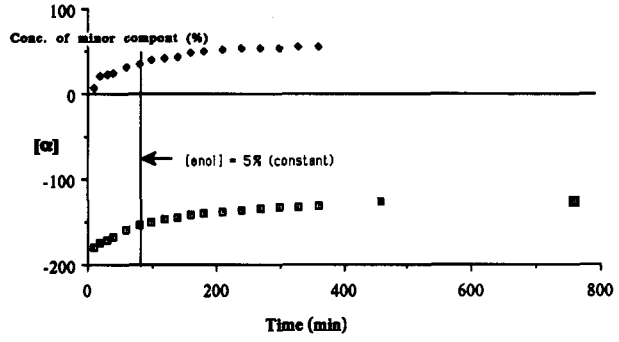
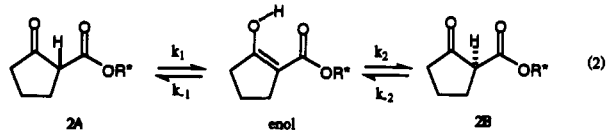


Figure 2. Rotation and NMR data vs time.

the ddd at 4.90 becomes more complex as a function of time. In addition, a shoulder ddd at 5.01 (corresponding to the C1′ enol form) also appears, which approaches constant concentration at approximately 70 min. Beyond 350 min (and up to 920 min) no further change was observed in 60-min interval spectra, indicating that the system had reached equilibrium at a 1:1 concentration of diastereomers. These spectra provide a detailed molecular picture of the tautomerization (eq 2).[7] The equilibrated



(2)

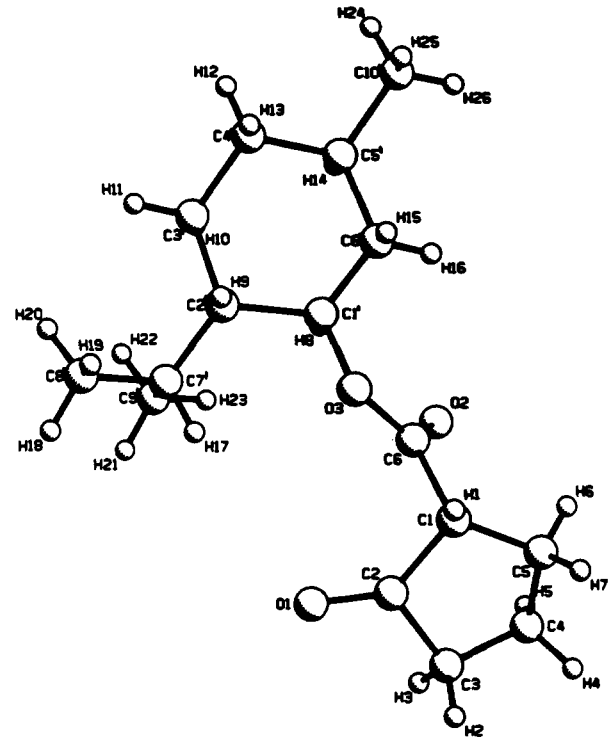


Figure 3. PLUTO structure generated from the single-crystal X-ray analysis of **2**.

mixture could be transformed back to the starting single diastereomer simply by stripping off the solvent using a rotary evaporator (as shown by ^1H NMR analysis in $CDCl_3$). This phenomenon has been described in related systems as a crystallization induced second-order asymmetric transformation.[8]

Figure 2 depicts the rate of isomerization of C1 as a function of time. While it is possible to calculate a k for this process, the change in enol concentration (in the first 70 min) complicates the kinetics making the usual first-order simplifications inappropriate.[9]

The absolute configuration of C1 was established as *R*, based on an X-ray single-crystal structure analysis (Figure 3).[10] The PLUTO diagram in Figure 3 illustrates that the C1-*R* configuration allows the molecule to adopt a relatively planar conformation, which may facilitate lower energy crystal packing.

It is interesting to note the large difference in the rate of equilibration of **2** in $CDCl_3$ versus C_6D_6. The NMR of chiral β-keto ester **2** in $CDCl_3$ was essentially unchanged over 2 weeks (i.e., one diastereomer in solution) which may be attributed to the hydrogen-bonding ability of this solvent, which disfavors enolization.[11,12] The chiral ester

(1) Dedicated to Professor Elias J. Corey, 1990 Nobel Prize winner in chemistry.

(2) Morrison, J. D., Ed. *Asymmetric Synthesis*; Academic Press: New York, 1983–85, Vols. 1–5. Nogradi, M. *Stereoselective Synthesis*; VCH: Weinheim, 1987. Tomioka, K. *Synthesis* **1990**, 541. Bosnich, B. *Asymmetric Catalysis*; NATO ASI Series 6, 103, Martinus Nijhoff: Dordecht, 1986. ApSimon, J. W.; Collier, T. L. *Tetrahedron* **1986**, *42*, 5157. Kagan, H. B.; Fiaud, J. C. *Top. Stereochem.* **1988**, *18*, 249. Brunner, H. *Synthesis* **1988**, 645.

(3) For recent contributions in the study of keto–enol tautomerism, see: Eldin, S.; Pollack, R. M.; Whalen, D. L. *J. Am. Chem. Soc.* **1991**, *113*, 1344 and references therein.

(4) Taber, D. F.; Amedio, J. C.; Patel, Y. K. *J. Org. Chem.* **1985**, *50*, 3618.

(5) This reaction has been proposed to proceed through a ketene intermediate, see: Witzman, J. S.; Nottingham, W. D. *J. Org. Chem.* **1991**, *56*, 1713. Witzman, J. S. *Tetrahedron Lett.* **1990**, *31*, 1401. Campbell, D. S.; Lawrie, C. W. *J. Chem. Soc., Chem. Commun.* **1971**, 355.

(6) The region from 1.7 to 0 ppm was omitted for clarity. New doublets representing the emerging diastereomer for the methyl attached to C5′ and the isopropyl group were also observed at 0.7 and 0.9 ppm, respectively.

(7) The isomerization of **2** in benzene at 22 °C was also followed by observing the $\Delta[\alpha]^{22}_{436}$ of **2** as a function of time; $[\alpha]^{22}_{436} = -185°$ initially to a constant value of −131° after 5 h (c = 0.43, C_6H_6).

(8) For related examples of crystallization-induced asymmetric transformations in menthyl half esters of malonic acid, see: Ihara, M.; Takahashi, M.; Taniguchi, N.; Yasui, K.; Fukumoto, K.; Kametani, K. *J. Chem. Soc., Perkin Trans. 1* **1989**, 897. Ihara, M.; Takahashi, M.; Taniguchi, N.; Fukumoto, K.; Kametani, T. *J. Chem. Soc., Chem. Commun.* **1987**, 619. In aminobenzodiazepinones, see: Reider, P. J.; Davis, P.; Hughes, E.; Grabowski, E. J. J. *J. Org. Chem.* **1987**, *52*, 957. In general, see: Jaques, J.; Collet, A.; Willen, S. H. *Enantiomers, Racemates and Resolutions*; Wiley: New York, 1981; and references cited therein.

(9) Since the equilibrium concentrations of **2A** and **2B** are 1:1, the simplification that $k_2 \ll k_{-1}$ or that $k_2 \gg k_{-1}$ (which would simplify the kinetics to a first-order treatment) would not necessarily be valid. A k for this process was not calculated.

(10) Compound **2** was sublimed at 45 °C at 0.1 mmHg to give colorless X-ray-quality crystals. X-ray data for this structure will be published separately.

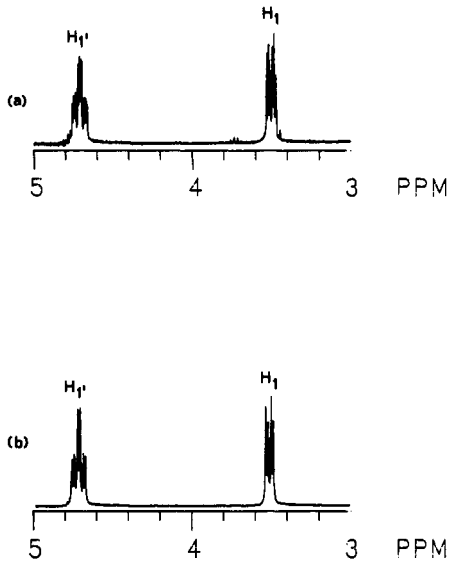
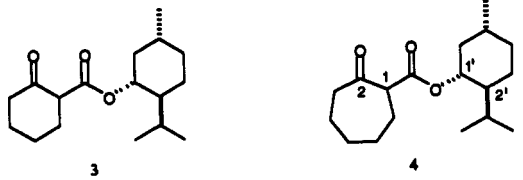


Figure 4. 300-MHz ^1H NMR spectrum of 4 (a) before and (b) after crystallization.

2 behaves similarly in CD_2Cl_2, with a complete absence of any enol detected by ^1H NMR and preponderance of one diastereomer as a function of time. When 2 is dissolved in CD_3OD, a 1:1 equilibrium (C1 epimers) is achieved in less than 20 min as observed by ^1H NMR, with essentially complete deuterium incorporation at C1. This rapid tautomerization is postulated to be the result of an acid–base equilibrium between the enolizable β-keto ester and relatively acidic H (D) of methanol.

To examine the generality of the crystallization induced asymmetric transformation in other chiral cyclic β-keto esters, compounds 3 and 4 were prepared as described for 2. The rate of formation of 3 from the corresponding methyl ester using standard conditions proved sluggish, and the reaction was accelerated by addition of 4A molecular sieves. Purification of 3 by SiO_2 chromatography gave an oil that was shown by NMR to be an 88:12 mixture of enol to keto products in $CDCl_3$. The keto product was a 1:1 mixture of diastereomers (epimers at C1) as determined from the integration of the two sets of dd's at 3.38 and 3.36 ppm corresponding to the C1 epimers.



3 4

Menthyl 2-oxocycloheptanecarboxylate (4) was produced in 70% yield following Taber's procedure. Initial purification by chromatography gave 4 as an oil following solvent removal and was shown by ^1H NMR to be a 1:1 mixture of diastereomers (epimers at C1). Upon storage at 5 °C, 4 crystallized over a period of 1 week. NMR analysis of this crystalline material (4) in $CDCl_3$, revealed the presence of a 9:1 mixture of diastereomers (Figure 4) indicating that a crystallization-induced second-order asymmetric transformation had occurred in the seven-membered ring menthyl keto ester as well. Kinetic analysis of the pure diastereomer 4 in C_6D_6 (as described for 2) showed a much slower rate of epimerization than that observed for 2,[13] which was attributed to a much slower rate of enolization in benzene than for compound 2.

In conclusion, it was shown that asymmetric crystallization-induced transformations occur in two cyclic chiral β-keto ester systems. It has been demonstrated that chirality can be used to probe β-keto ester tautomerism and that the rate of epimerization is suppressed in aprotic H-bonding solvents. The ability to fix the absolute configuration of C1 through a simple esterification reaction and recrystallization allows one to obtain a single optical isomer, which constitutes a valuable source of functionalized chiral starting material. We are presently investigating the utility of these chiral ester synthons in natural products synthesis.

Experimental Section

Melting points are uncorrected. IR spectra were recorded as thin films from CH_2Cl_2 on KBr plates. ^1H and ^{13}C NMR spectra were taken at 300 and 75 MHz, respectively, in the solvents indicated. Mass spectra were recorded at 70 eV using a direct inlet system. $CDCl_3$, CD_2Cl_2, and C_6D_6 were predried over anhydrous K_2CO_3 and distilled before use.

(1*R*,2*S*,5*R*)-(−)-Menthyl (1*R*)-2-Oxocyclopentanecarboxylate (2). A flame-dried two-necked flask equipped with a condensor and gas purge was flushed with N_2 and charged with (1*R*,2*S*,5*R*)-(−)-menthol (3.0 g, 19.2 mmol), DMAP (0.7 g, 5.8 mmol), and 50 mL of toluene. The mixture was stirred until complete dissolution of the solids followed by addition of methyl 2-oxocyclopentanecarboxylate (5.96 mL, 48 mmol) and reflux for 30 h. The homogeneous solution was then cooled to ambient temperature and slowly quenched with 40 mL of saturated aqueous NH_4Cl. The organic layer was separated, and the aqueous phase was further extracted with ether (3 × 30 mL). The combined organic phase was then dried over $MgSO_4$. The volatiles were removed by rotary evaporation, and the crude solid was purified by flash chromatography (SiO_2) using 20% ethyl acetate/hexane to give 2.72 g (55%) of a white solid. The solid was sublimed at 45 °C at 1 mmHg to give colorless X-ray quality crystals: $[\alpha]_{436}^{22} = -226°$ (c = 0.27, $CHCl_3$); mp 63.0–64.0 °C; IR (CCl_4) ν 2953, 2871, 1757, 1723 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.75 (d, J = 6.9 Hz, 3 H), 0.90 (d, J = 7.0 Hz, 3 H), 0.91 (d, J = 7.0 Hz, 3 H), 1.0 (m, 2 H), 1.4 (m, 2 H), 1.62 (m, 2 H), 1.85 (m, 1 H), 2.0 (m, 2 H), 2.1 (m, 2 H), 2.3 (m, 4 H), 3.13 (dd, J = 9.0, 9.0 Hz, 1 H), 4.71 (ddd, J = 10.9, 10.9, 4.4 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ATP 16.0 (−), 20.8 (−), 21.0, 22.0 (−), 23.1, 25.7 (−), 27.3, 31.4 (−), 34.2, 38.0, 40.7, 46.9 (−), 55.1 (−), 75.3 (−), 169.0, 212.4; MS m/e 266 (M^+, 2), 138 (100); exact mass calcd for $C_{16}H_{26}O_3$ 266.1882, found 266.1885.

(1*R*,2*S*,5*R*)-(−)-Menthyl 2-Oxocyclohexanecarboxylate (3). Procedure as described above; (−)-menthol (0.92 g, 5.88 mmol), DMAP (0.36 g, 2.94 mmol), ethyl 2-oxocyclohexanecarboxylate (1.0 g, 5.88 mmol), and 1 g of activated 4A molecular sieves in 40 mL of toluene were heated to reflux for 72 h. Workup as described above. The crude material was purified by SiO_2 flash chromatography using 10% ether/hexane to give 0.94 g (56%) colorless oil that did not crystallize on cooling to 0 °C: IR (thin film) ν 3390–3300 (br), 2935, 2868, 1717 (w), 1652 (s), 1617 (w), 1298 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.76 (d, J = 6.9 Hz, 3 H), 0.9 (d, J = 7.2 Hz, 3 H), 0.91 (d, J = 6.3 Hz, 3 H), 1.15–0.95 (m, 3 H), 1.55–1.35 (m, 3 H), 1.75–1.55 (m, 4 H), 1.95–1.80 (m, 1 H), 2.1–2.0 (m, 1 H), 2.3–2.15 (m, 4 H), 3.28 (m, 1 H, enol), 4.75 (ddd, J = 4.5, 6.6, 11.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ enol 16.4, 20.7, 22.0, 22.4, 23.3, 23.5, 26.3, 27.1, 29.1, 31.4, 34.2, 41.0, 41.5, 47.0, 73.9, 97.9, 170.0, 171.8; keto (minor diastereomer in parentheses) 16.1 (15.8), 21.9, 22.0, 23.0, 23.3 (23.2), 25.8, 26.1, 29.9 (30.0), 40.7 (40.6), 57.5 (57.2), 75.0, 172.3, 206.3 (206.4); EIMS m/e 280 (M^+, not observed), 142 ($M^+ - C_{10}H_{18}$, 25), 138 (69); exact mass calcd for $C_7H_{10}O_3$ 142.0629, found 142.0617.

(1*R*,2*S*,5*R*)-(−)-Menthyl 2-Oxocycloheptanecarboxylate (4). Procedure as described for 2; (−)-menthol (0.46 g, 3.0 mmol),

(11) A solution of 2 in $CHCl_3$ also gave a constant rotation of $[\alpha]_{436}^{22} = -226°$ (c = 0.27, $CHCl_3$) over a period of 2 weeks.

(12) Meyer, K.; Kappelmeier, K. *Ann. Chim.* 1911, *380*, 212. Gero, A. *J. Org. Chem.* 1954, *19*, 1960.

(13) After 24 h, a 4:1 mixture of C1 epimers was observed in C_6D_6.

DMAP (0.11 g, 0.9 mmol), and methyl 2-oxocycloheptanecarboxylate (1.0 g, 5.9 mmol) were heated to reflux in 7 mL of toluene for 30 h. Workup as described for 2. Purification by SiO_2 chromatography gave 635 mg of a colorless oil (72%) that crystallized on standing at 5 °C: $[\alpha]_{436}^{22} = 45°$ (c = 0.28, $CHCl_3$); mp 65.0–66.0 °C; IR (thin film) ν 2931, 2868, 1737, 1707 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.75 (d, J = 6.9 Hz, 3 H), 0.88 (d, J = 6.9 Hz, 3 H), 0.91 (d, J = 6.6 Hz, 3 H), 0.95 (m, 1 H), 1.0 (m, 2 H), 1.4 (m, 4 H), 1.65 (m, 4 H), 1.9 (m, 4 H), 2.1 (m, 2 H), 2.6 (m, 2 H), 3.51 (dd, J = 3.9, 10.2 Hz, 1 H), 4.71 (ddd, J = 4.5, 6.6, 11.1 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ATP 16.1 (–), 20.7 (–), 22.0 (–), 23.2, 24.4, 26.0 (–), 27.7, 27.9, 24.7, 31.3, 34.2, 40.5, 43.1, 46.8 (–), 59.0 (–), 75.0 (–), 170.1, 209.1; EIMS m/e 294 (M^+, not observed), 156 ($M^+ - C_{10}H_{18}$, 8), 138 (47), 55 (100); exact mass calcd for $C_8H_{12}O_3$ 156.0786, found 156.0786.

Acknowledgment. C.P.D. acknowledges financial support from the Natural Sciences and Engineering Research Council of Canada (NSERC) and MUN. R.N.B. acknowledges NSERC for a summer student scholarship. Professors L. Weiler and J. Burnell for valuable suggestions, C. Jablonski and N. Burnet for assistance in the kinetic NMR data acquisition, and J. Bridson for the X-ray analysis are also gratefully acknowledged.

Supplementary Material Available: NMR spectra of 4 (2 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Synthesis and Characteristics of Bis(5-carbomethoxy-4-(methylthio)-3-phenyl-2-thiazolinylidene)

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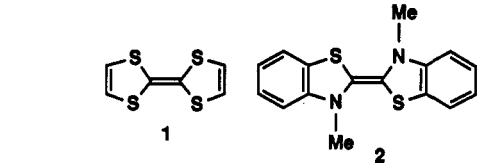
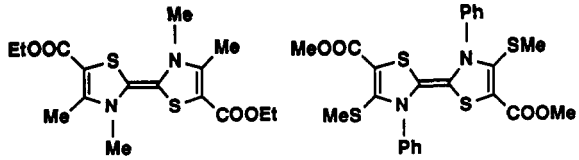
Received July 8, 1991

The chemistry of tetrathiafulvalene (TTF, 1) and its derivatives has been studied intensely for more than 15 years,[1] in view of their utility as starting materials for conducting organic metals. By replacing two of the sulfur



1 2



3 4

atoms in a TTF moiety by nitrogen, one can change the electron density of the molecule and considerably increase its donor ability. Although the first compound of this series, the benzannelated derivative 2, was reported in 1964 by Metzger and co-workers,[2] little progress in the synthesis of other such compounds has been achieved to date.

Bordwell and Satish recently detected several simple alkyl-substituted bis(thiazolinylidines) electrochemically,

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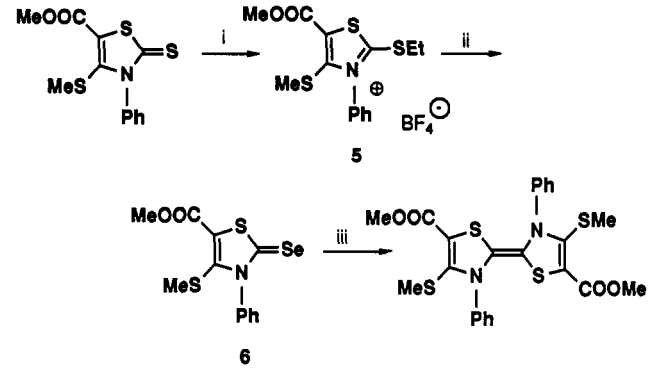
Scheme I[a]



[a] (i) $HC(OEt)_3$, $Et_2O{\cdot}BF_3$, $CHCl_3$, 100%; (ii) NaHSe, EtOH, 85%; (iii) $P(OMe_3)$, 100 °C, 100%.

but an attempt to isolate one of these led only to oxidation products.[3] Similarly, Thummel et al. observed the two-electron electrochemical reduction of a bridged 2,2′-bithiazolium salt, but a stable reduction product was not obtained.[4] The only compound of this type heretofore reported is the diester 3, isolated by Doughty as an oxygen-sensitive, light red oil.[5]

In this paper, we report the synthesis and some properties of the first noncondensed crystalline bis(thiazolinylidine) 4. In view of the expected ease of oxidation of such a compound, we chose a synthetic approach different from that employed by Metzger[2] and explored by others (Scheme I).[3,5] Our synthetic route is illustrated in Scheme I. The title compound was prepared in the last step in a quantitative yield.

The synthesis and properties of the starting 1,3-thiazoline-2-thione have been reported by us recently.[6] Conversion to the 2-(alkylthio)-1,3-thiazolium salt 5 and to the corresponding selone 6 in 85% overall yield was carried out by analogy with procedures employed in the 1,3-dithiole series.[7]

The cyclic voltammogram of 4 measured in dichloroethane solution shows two reversible peaks at 0.00 and 0.48 V in accord with the redox system shown in Scheme II.

Dication 7 was isolated as its diperchlorate by treatment of the neutral form 4 with phenyliodoso diacetate in the presence of perchloric acid in dioxane (Scheme III). The cyclic voltammogram obtained for the salt 7 is identical to that of 4 under the same conditions.

The mass spectral data obtained for the dimer 4 are in good agreement with the expected structure, the most prominent peaks being the molecular ion (84%) and the base peak corresponding to the loss of one phenyl group.

The ^1H NMR data obtained in $CDCl_3$ solution for the dimer 4 shows, besides phenyl protons in the region 7.51–7.28 ppm, two methyl singlets at δ 2.12 and 2.19 (SMe) and two others at 3.79 and 3.83 (OMe) ppm in ratios of 1:1. Although for the dimer 2 the E configuration was assumed,[2,3] our results testify to the existence of both E and Z isomers in $CDCl_3$ solution. The doubling of the

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