mp 132–133°,¹³ [α]D (ether) +26°, λ_{max} (ether) 264 nm (20,200), and on treatment with iodine underwent smooth isomerization attended by spectral changes $[\lambda_{max} 270 \text{ nm} (20,000)]$ completely analogous to those accompanying the conversion of vitamin D_3 into 5,6trans-vitamin D₃.¹⁴ The pmr spectrum of 2b showed the 6 and 7 protons as an AB quartet ($J_{AB} = 11.5 \text{ Hz}$) centered at δ 6.20 while the 19 protons appeared as a pair of one-proton multiplets at δ 4.85 and 5.30. These spectral parameters are completely analogous to those observed for vitamin D_3 itself and are not compatible with any of the other triene isomers encountered in the vitamin D series.

We have found that 1α -hydroxy-vitamin D₃ possesses potent vitamin D activity and in particular is associated with an onset of activity fully as rapid as that observed for the natural polar metabolite 1 of D₃.¹⁵ The important implications of this biological activity to vitamin D biochemistry and therapy will be discussed fully in a subsequent paper.¹⁷⁻¹⁹

(13) The cited melting point was obtained by placing the specimen on the hot stage preheated to 100° and increasing the temperature at the rate of 1°/4 sec (the block thermometer and specimen are in reasonable equilibrium at this rate).

(14) A. Verloop, A. L. Koevoet, and E. Havinga, Recl. Trav. Chim. Pays-Bas, 74, 1125 (1955).

(15) 1 α -Hydroxy-vitamin D₃ was >10 times as effective as vitamin D3 in raising the serum calcium of thyroidectomized-parathyroidectomized rats. A direct comparison between 1a-hydroxy-vitamin D₃ and biosynthetic 1,25-dihydroxy-vitamin D3 demonstrated that the former was fully as effective as the latter in stimulating calcium transport across the chick intestines.^{16,17} Essentially identical time courses were observed.

(16) M. E. Coates and E. S. Holdsworth, Brit. J. Nutr., 15, 131 (1961). (17) In collaboration with M. R. Haussler whom we thank for preliminary biological data in the chick assay.

(18) All new compounds exhibited appropriate and expected spectral characteristics and (with the exception of 7a) were of the required composition as established by microanalysis.

(19) NOTE ADDED IN PROOF. Application of the synthesis reported in this paper to 25-hydroxycholesterol has led to 1α ,25-dihydroxycholecalciferol (1). The details will comprise a future communication.

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The Thieno[3,4-c]pyrrole System, a "Tetravalent Sulfur" Heterocycle Showing Both Azomethine Ylide and Thiocarbonyl Yiide Dipolar Characteristics

Sir:

The title ring system 4 is one of several 10π -electron heterocyclic systems containing "tetravalent sulfur" atoms that have been reported recently in the literature.^{1,2} Described as a bright red powder, it formed a 1:1 adduct with dimethyl acetylenedicarboxylate, shown to be 8 ($R = COOCH_3$) by its oxidation to the benzo[c]thiophene (9) ($R = COOCH_3$).

We wish to report a very convenient synthesis of 4 which now makes it readily available in quantities sufficient to study a variety of cycloaddition reactions. Utilizing cycloaddition reactions³ as a route to the penultimate product of 4, N-benzoyl- α -phenylsarcosine⁴

(1972).
(2) M. P. Cava and M. A. Sprecker, *ibid.*, 94, 6214 (1972).
(3) For earlier references, see K. T. Potts, A. J. Elliott, and M. Sorm,

(1) was treated with dibenzoylacetylene in the presence of acetic anhydride, affording⁵ a 63% yield of 3,4-dibenzoyl-2,5-diphenyl-1-methylpyrrole (3) as colorless, matted needles from ethanol, mp 200-202° (vco 1655, 1635 cm⁻¹; nmr (CDCl₃) τ 6.62 (s, 3, NCH₃), 3.15-2.36 (m, 20, aromatic); $M \cdot + 441$ (55)). The mesoionic anhydro-2,4-diphenyl-5-hydroxy-3-methyloxazolium hydroxide (2) was undoubtedly the intermediate in this reaction which may be utilized for the synthesis of a variety of 1,2,5-substituted pyrroles.^{4,6} Treatment of 3 with P_2S_5 in refluxing pyridine over 5 hr, followed by quenching the reaction mixture in 10% sodium hydroxide solution, gave 5-methyl-1,3,4,6-tetraphenylthieno[3,4-c]pyrrole (4) in 60% yield as small, brilliant



red needles, mp 110–112° ($\lambda_{max}^{CHCl_2}$ 256 nm (log ϵ 4.41), 533 (3.15); M·+ 441 (61), M²⁺ 220.5 (15), PhC=S⁺ m/e 121 (37), Ph⁺ m/e 77 (100)).

In the crystalline state the thienopyrrole 4 is quite stable. In solution or on a tlc plate its color is rapidly bleached by light which, together with its poor solubility, precludes successful recrystallization.

We have found that the substitution pattern of the pyrrole moiety is critical for the formation of this ring system by the action of P_2S_5 , those pyrroles with 1methyl-2-phenyl or 1,2-diphenyl substituents being converted into the corresponding 3,4-dithiobenzoyl products.

The ring system 4 is a reactive substrate for cycloadditions, behaving both as an azomethine ylide 4a and a thiocarbonyl ylide 4b, depending on the reaction conditions. Olefinic dipolarophiles exhibited a temperature-dependent mode of addition to 4. Fumaronitrile in refluxing toluene (12 hr) formed the primary 1:1 cycloadduct 5 in 67 % yield, colorless needles from acetonitrile, mp 244-245° (dec) ($\lambda_{max}^{CH_{2}OH}$ 278 nm, log ϵ 4.06; $\nu_{\rm CN}$ 2250 cm⁻¹; nmr (CDCl₃) τ 6.87 (s, 3, NCH₃), 5.88 (d, 1, J = 3.9 Hz, H₃), 5.42 (d, 1, J = 3.9 Hz, H₂), 3.34–2.40 (m, 20, aromatic); M + 519 (2)), together with the isoindole 6(5%) which also crystallized from acetonitrile forming yellow needles, mp 332-334° ($\lambda_{\max}^{CHCl_3}$ 245 nm (log ϵ 4.58), 269 (4.51), 408 (3.31); ν_{CN} 2225 cm⁻¹; nmr (CDCl₃) τ 6.54 (s, 3, NCH₃), 3.28-2.65 (m, 20, aromatic); M·+ 485 (100)). In refluxing xylene, the yield of the cycloadduct 5 decreased to 10%with an accompanying increase in the yield of 6 to 53%, suggesting the formation of 6 from 5 by the thermal elimination of the elements of H₂S. The conversion could also be effected in quantitative yield by

⁽¹⁾ K. T. Potts and D. McKeough, J. Amer. Chem. Soc., 94, 6215

⁽⁴⁾ H. O. Bayer, R. Huisgen, R. Knorr, and F. C. Schaefer, Chem. Ber., 103, 2581 (1970).

⁽⁵⁾ All products described gave satisfactory analytical data. (6) K. T. Potts and U. P. Singh, Chem. Commun., 66 (1969).

treatment of 5 with sodium methoxide in methanol at room temperature.

In contrast to the above addition across the thiocarbonyl ylide system, reaction of 4 with fumaronitrile in refluxing benzene gave an exclusive 1:1 cycloadduct 7 as colorless irregular prisms, mp 231-234° (dec), in which addition had occurred across the azomethine ylide system ($\lambda_{max}^{CHCl_{4}}$ 288 nm, log ϵ 4.27; ν_{CN} 2245 cm⁻¹; nmr (CF₃COOD) τ 7.07 (s, 3, NCH₃), 5.20 $(d, 1, J = 3.7 \text{ Hz}, H_3), 4.53 (d, 1, J = 3.7 \text{ Hz}, H_2),$ 3.17-2.27 (m, 20, aromatic)). On attempted dissolution in warm solvents, the adduct 7 underwent a ready retro-Diels-Alder type reaction, also observed in the mass spectrometer. This thermal instability allowed the conversion of 7 into 6 (60%) with trace amounts of 5 by refluxing in xylene (14 hr). These data show the greater reactivity of the azomethine ylide over the thiocarbonyl ylide dipole and the greater thermodynamic stability of the cycloadducts from the latter.

As was shown earlier² with dimethyl acetylenedicarboxylate, dibenzoylacetylene in refluxing benzene (15 hr) gave a cycloadduct 8 (R = COPh) in which addition had occurred across the azomethine ylide system. Formed in 66% yield, it crystallized from acetonitrile as pale yellow needles, mp 247-249° (dec) (λ_{max}^{CHCls} 264 nm (log ϵ 4.54), 273 sh (4.48), 284 sh (4.45); ν_{CO} 1670, 1650 cm⁻¹; nmr (CDCl₃) τ 7.98 (s, 3, NCH₃), 3.20-2.30 (m, 30, aromatic); M·+ 675 (1)). This adduct could be oxidized to the benzo[c]thiophene derivative 9 (R = COPh) with *m*-chloroperbenzoic acid.^{2,7} In



refluxing xylene (48 hr) addition also occurred across the azomethine ylide system giving 8 in 31% yield along with a 17% yield of 9. It is thought that 9 resulted from the slow oxidation of 8 rather than from the elimination of methyl nitrene and that the insensitivity of the acetylene cycloadditions to temperature is due to the stability of the azomethine ylide cycloadducts.

The above manifestations of ylide chemistry were observed with a variety of olefinic dipolarophiles and these results will be described in the full publication.

(7) K. T. Potts and D. McKeough, J. Amer. Chem. Soc., 95, 2750 (1973).

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The Thieno[3,4-f]benzo[c]thiophene System, a Nonclassical 14π -Electron Heterocycle

Sir:

The thieno[3,4-c]thiophene ring system (3), first reported ¹ in 1967, was the initial bicyclic heterocycle containing 10 π electrons and a "tetravalent sulfur" atom. Other representatives of this class of compound have since been described,² but the original system still re-

Scheme I



M. P. Cava and N. M. Pollack, J. Amer. Chem. Soc., 89, 3639 (1967);
 M. P. Cava and G. E. M. Husbands, *ibid.*, 91, 3952 (1969).
 (2) (a) R. H. Schlessinger and J. D. Bower, *ibid.*, 91, 6891 (1969);
 (b) M. P. Cava and M. A. Sprecker, *ibid.*, 94, 6215 (1972);
 (c) K. T. Potts and D. McKeough, *ibid.*, 94, 6215 (1972).