tered solution, and the residue was extracted with boiling acetone, from which on cooling the product crystallized.

F. 2-Bromo-6-chloro-1-methylnaphthalene (9a). K (1 g) was dissolved in *t*-BuOH (25 ml), and the solution was cooled in ice–water. **6a** (4 g) was added followed by bromoform (8 g). The solution was stirred in the cold for 2 hr and diluted with water. The precipitated solid was collected, yield 1 g.

Acknowledgments. The authors wish to thank Dr. William J. Welstead, Jr., and Mr. Ashby F. Johnson, A. H. Robins Company, Inc., Richmond, Va., for NMR spectra.

Registry No.—**1a,** 21133-98-2; **1b,** 55058-75-8; **2a,** 55058-76-9; **3a,** 5292-23-9; **3b,** 55058-77-0; **4a,** 54795-05-0; **4b,** 55058-78-1; **5a,** 55058-79-2; **5b,** 55058-80-5; **6a,** 55058-81-6; **6b,** 55058-82-7; **7a,** 55058-83-8; **7b,** 55058-84-9; **8b,** 55058-85-0; **9a,** 55058-86-1.

References and Notes

(1) The work described in this paper was performed under Contract DADA-17-72-C-2078 with the U.S. Army Medical Research and Development Command. This is Contribution No. 1281 from the Army Research Program on Malaria.
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(9) The isomerization was followed by NMR. For 4,6-dichloro-1-methylindene (**6b**) in $CDCl_3$: δ 7.27 (2 H, s, phenyl), 6.88 (1 H, d of d, J_{12} = 2 Hz, =CH), 6.52 (1 H, d of d, J_{23} = 6 Hz, =CH), 3.53 (1 H, broad q, $J_{1\,CH_3}$ = 8 Hz, CH_3CH), 1.28 (3 H, d, J_{13} = 2 Hz, CH_3). For 5,7-dichloro-3-methylindene (**8b**) in $CDCl_3$ with a trace of C_6D_5N: δ 7.17 (2 H, s, phenyl), 6.23 (1 H, m, J_{12} = 2, J_{13} = 2 Hz, =CH), 3.20 (2 H, m, J_{2CH_3} = 2 Hz, CH_2), 2.03 (3 H, m, CH_3).
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Ylidenemalononitriles in Thiophene Ring Annelations

S. W. Schneller* and D. R. Moore

Department of Chemistry, University of South Florida, Tampa, Florida 33620

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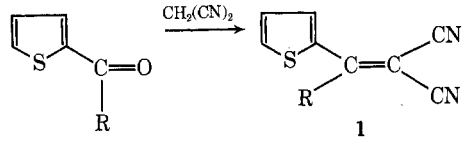
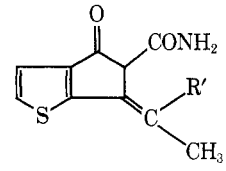
Synthetic methods available for the construction of rings fused to heterocyclic molecules are limited owing to the vulnerability of the heteroatom to the well-established conditions of carbocyclic chemistry. Acid-mediated cyclizations of ylidenemalononitriles[1,2] to form fused keto amides appeared to present a valuable potential for this problem. This has now proven successful in the thiophene series.

The thiophene ylidenemalononitriles (1) were readily obtained by a Knoevenagel reaction between the corresponding precursor[3] and malononitrile.



1

Treatment of **1** (R = C_2H_5) and **1** (R = *i*-C_3H_7) with polyphosphoric acid produced the ring-cyclized products **2**. The structural assignments for **2** were based on spectral data. The ir spectrum (KBr) of **2** (R′ = H) has NH absorption at 3.00 and 3.15 μ, ketone carbonyl at 5.91 μ, and



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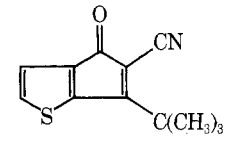

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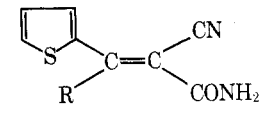


4

amide carbonyl at 6.02 μ, while **2** (R′ = CH_3) has similar peaks at 2.98, 3.14, 5.90, and 6.02 μ which is in agreement with similar ring systems in the benzene series.[6] The NMR spectrum (DMSO-d_6) also supports structure **2** by displaying a simple two-proton thiophene absorption with doublets at δ 7.19 (J = 5 Hz) and 7.70 (J = 5 Hz), methine (proton α to amide and ketone carbonyls) absorption at δ 4.32, vinyl quartet absorption (for **2**, R′ = H) at δ 5.75 (J = 7 Hz), and methyl singlets at δ 1.80 and 1.97 for **2** (R′ = CH_3) and a methyl doublet at δ 1.93 (J = 7 Hz) for **2** (R′ = H). The above data is clearly in accord with the bicyclic systems **2** possessing the exocyclic double bond.[7]

On the other hand, when **1** (R = *t*-C_4H_9) was subjected to polyphosphoric acid the anticipated endocyclic fused system (**3**) resulted. The structural assignment for **3** was based on the ir spectrum (KBr) (nitrile absorption at 4.52 μ and a carbonyl band at 5.80 μ) and the NMR spectrum (DMSO-d_6) [two-proton thiophene doublets at δ 7.20 (J = 5 Hz) and 7.62 (J = 5 Hz) and a nine-proton methyl singlet at δ 1.54]. Thus far it has not been possible to hydrolyze the nitrile functionality of **3** to the corresponding carboxamido group.

To complete the series, **1** (R = H and CH_3) was studied under the cyclization conditions and found to yield only (by TLC) **4**. Confirmation of the product formation was obtained when products identical (by melting point and TLC) with **4** were realized from the reactions of thiophenecarboxaldehyde and methyl 2-thienyl ketone with cyanoacetamide.[1,8]

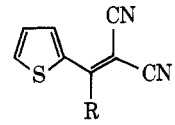
These results suggest that the fusion of a functionalized five-membered ring to a thiophene ring is possible via ylidenemalononitriles which possess at least a secondary γ carbon.[9] If the γ carbon possesses at least one hydrogen the exocyclic products (**2**) are realized as a means of relieving the steric strain which would result with the endocyclic isomer. When the γ carbon is quaternary, the endocyclic isomer (**3**) is the only structure possible and it forms, but in considerably diminished yields compared to **2**.

Experimental Section[10]

Preparation of the Ylidenemalononitriles. A solution of 0.3 mol of the carbonyl agent,[3] 0.5 mol of malononitrile, 12.0 g of ammonium acetate, and 24 ml of glacial acetic acid in 200 ml of toluene was refluxed with the aid of a Dean-Stark trap until the amount of water collected in the trap remained constant (4–24 hr, the sterically hindered ketones requiring the longer reflux time). Following the reflux period, the solution was cooled and decanted from a malononitrile polymer. The polymeric gum was washed with toluene (50 ml) and the combined toluene fractions were washed with water (2 × 50 ml), dried over anhydrous magnesium sulfate, and concentrated to yield the crude product, whose properties are listed in Table I. In the case of **1** (R = *i*-C_3H_7) and **1** (R = *t*-C_4H_9) it was necessary to remove the unreacted ketone (via vacuum distillation) from the crude product mixture to realize the desired ylidenemalononitrile.

Treatment of Ylidenemalononitriles (1) with Polyphosphoric Acid. After 200 g of polyphosphoric acid was warmed to the temperature required for reaction, 2.0 g of **1** was added slowly

Table I
Properties of Thiophene Ylidenemalononitriles



Registry no.	R	Yield, %	Mp, °C	Purification method[a,b]	Anal. calcd (found), %	Ir (ν_{CN}), cm^{-1}	Proton NMR,[c-e] δ ppm
28162-32-5	H[f]	86	95–96	S, C, A	C, 59.98 (60.15) H, 2.52 (2.77)	2220	7.38 (t, 4-H) 7.85 (m, =CH, 3-H and 5-H)
10432-44-7	CH_3	77	85	S, C	C, 62.05 (62.23) H, 3.47 (3.56)	2215	2.74 (s, CH_3) 7.26 (t, 4-H) 7.83 (d of d, 5-H) 8.03 (d of d, 3-H)
54688-90-3	C_2H_5	44	31	A	C, 63.82 (63.77) H, 4.26 (4.30)	2220	1.35 (t, CH_3) 3.04 (q, CH_2) 7.36 (t, 4-H) 7.98 (d of d, 5-H) 8.18 (d of d, 3-H)
54688-91-4	i-C_3H_7	25	56	E	C, 65.32 (65.18) H, 4.98 (5.12)	2220	1.34 (d, 2 CH_3) 3.50 (sp, CH) 7.08 (t, 4-H) 7.70 (d, 3-H and 5-H)
54688-92-5	t-C_4H_9	14	103–104	A	C, 66.63 (66.43) H, 5.59 (5.46)	2230	1.36 (s, 3 CH_3) 7.00 (m, 4-H and 3-H or 5-H) 7.45 (d of d, 3-H or 5-H)

[a] S = sublimation in vacuo; C = chloroform–hexane; A = aqueous ethanol; E = 95% ethanol. [b] All ylidenemalononitriles reported herein are colorless. [c] All spectra were recorded in $CDCl_3$. Chemical shifts are in parts per million from internal Me_4Si. [d] Multiplicity indicated paranthetically by the following abbreviations: s, singlet; d, doublet; t, triplet; sp, septuplet; m, multiplet. [e] Assignments based on spectral integrations. [f] K. Friedrich and W. Ertel [German Patent 1,936,047; *Chem Abstr.*, 74, 76197 (1971)] report this compound but make no mention of its properties.

Table II
Products from Acid Treatment of Thiophene Ylidenemalononitriles

Registry no.	Compd	Yield, %	Mp, °C	Purification method[a]	Anal. calcd (found), %
54738-97-5	**2** (R′ = H)[b]	58	210–211	E	C, 57.95 (58.04) H, 4.38 (4.24)
54688-93-6	**2** (R′ = CH_3)[b]	59	221–223	E	C, 59.73 (59.52) H, 4.98 (5.12)
54688-94-7	**3**[c]	33	142–144	A	C, 66.33 (65.96) H, 5.10 (5.39)
54688-95-8	**4** (R = H)[d,f]	93	166	D	C, 53.92 (53.80) H, 3.39 (3.51)
54688-96-9	**4** (R = CH_3)[e,g]	86	150–151	C	C, 56.23 (55.97) H, 4.19 (4.11)

[a] E = 95% ethanol; A = aqueous ethanol; D = dimethyl sulfoxide–water; C = chloroform–hexane. [b] Colorless crystals. [c] Red crystals. [d] Light gray crystals. [e] Tan crystals. [f] ^1H NMR (dimethyl sulfoxide-d_6) δ 4.50 (br, NH_2), 7.24 (t, 4-H), 7.89 (m, 3-H and 5-H), 8.39 (s, =CH). [g] ^1H NMR (dimethyl sulfoxide-d_6) δ 2.58 (s, CH_3), 7.23 (t, 4-H), 8.00 (m, 3-H and 5-H); no NH_2 could be discerned.

under mechanical stirring. The resulting mixture was heated at 85–95° for 3 hr (R = H), 85° for 2 hr (R = CH_3), 50° for 2 hr (R = C_2H_5), 90° for 3 hr (R = i-C_3H_7), and 90° for 6 hr (R = t-C_4H_9) and then cooled and poured over 500 ml of ice water with vigorous stirring. After standing overnight the aqueous solution was filtered and the isolated product was air dried and purified to yield the products summarized in Table II.

Condensation of Thiophenecarboxaldehyde and Methyl 2-Thienyl Ketone with Cyanoacetamide. A 100-ml absolute ethanolic solution of 0.2 mol of the alkehyde or ketone, 0.2 mol of cyanoacetamide, 0.5 g of ammonium acetate, and 2.0 g of glacial acetic acid was refluxed for 6 hr. Upon cooling the cyanoacetamide (4) precipitated and was purified by recrystallization (R = H, 93% yield; R = CH_3, 86% yield). These products were identical (by mixture melting point and TLC in chloroform) with that obtained from the polyphosphoric acid treatment of 1 (R = H and CH_3) as characterized in Table II.

Acknowledgment. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the

American Chemical Society, for their support of this research.

Registry No.—2-Thiophenecarboxaldehyde, 98-03-3; methyl 2-thienyl ketone, 88-15-3; ethyl 2-thienyl ketone, 13679-75-9; isopropyl 2-thienyl ketone, 36448-60-9; *tert*-butyl 2-thienyl ketone, 20409-48-7; malononitrile, 109-77-3.

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(2) S. W. Schneller and F. W. Clough, *J. Heterocycl. Chem.*, **10**, 131 (1973); S. W. Schneller and D. R. Moore, *J. Org. Chem.*, **39**, 1433 (1974).
(3) Thiophenecarboxaldehyde, methyl 2-thienyl ketone, and phenyl 2-thienyl ketone were available from Aldrich Chemical Co., whereas ethyl 2-thienyl ketone was obtained from Columbia Organic Chemicals Co. Isopropyl 2-thienyl ketone[4] and *tert*-butyl 2-thienyl ketone[5] were prepared by the method of J. R. Johnson and G. E. May, "Organic Syntheses", Collect. Vol. II, Wiley, New York, N.Y., 1943, p 8.
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(6) D. A. Templer, Ph.D. Thesis, Indiana University, Bloomington, Ind., Aug 1968.
(7) Compound **2** (R′ = H) was a single isomer by TLC. However, to date it has not been possible to assign the exact geometrical stereochemistry for **2** (R′ = H) and the representation given here is arbitrary but is believed to be correct based on data accrued in ref 6 for a similar benzene system.
(8) The stereochemistry of **4** (obtained as a single isomer by TLC) was not crucial to this aspect of the problem and has not been established. However, the condensation between thiophenecarboxaldehyde and methyl 2-thienyl ketone and cyanoacetamide is apparently stereospecific, since only the product (by TLC) corresponding to **4** was produced in quantitative yield.
(9) Several less functionalized, and therefore less versatile, derivatives of the cyclopenta[*b*]thiophene ring system have been reported. For example, see (a) O. Meth-Conn and S. Gronowitz, *Acta Chem. Scand.*, **20**, 1577 (1966); (b) K. Aparajithan, A. C. Thompson, and J. Sam, *J. Heterocycl. Chem.*, **3**, 466 (1966); (c) J. Skramstad, *Acta Chem. Scand.*, **25**, 1287 (1971).
(10) Melting points were taken on a Mel-Temp capillary melting point apparatus and are uncorrected. The NMR spectra were obtained on a Varian A-60 spectrometer using Me_4Si as an internal standard. Ir spectra were recorded on a Perkin-Elmer Model 337 spectrophotometer. The microanalyses were performed by Het-Chem-Co., Harrisonville, Mo.

Stereochemical Course of Sulfolane Fragmentation

William L. Mock,* Indu Mehrotra, and Joseph A. Anderko

Department of Chemistry, University of Illinois at Chicago Circle, Chicago, Illinois 60680

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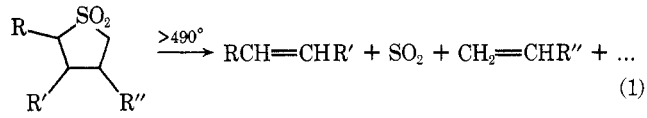
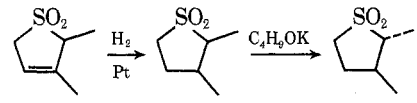
At elevated temperatures, simple sulfolanes (tetrahydrothiophene 1,1-dioxides) are pyrolyzed to sulfur dioxide and olefins (eq 1: R, R′, R″ = H; R = CH_3, R′, R″ = H; R′ = CH_3, R, R″ = H; R′, R″ = CH_3, R = H; R, R″ = CH_3, R′ = H, etc).[1] We have now examined the stereochemistry of this reaction (R, R′ = CH_3; R″ = H), with a view to detecting possible concertedness.



(1)

Results

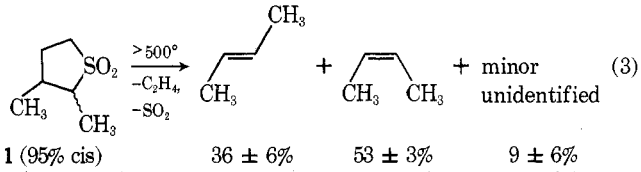
The requisite sulfones were obtained (eq 2) via 2,3-dimethylsulfolene (adduct from 3-methyl-1,3-pentadiene plus SO_2).[2] Catalytic hydrogenation (PtO_2) gave an inseparable mixture of sulfolanes (ca. 95:5) of which the major isomer was assigned the cis configuration (**1**) on the basis of steric considerations and subsequent results. Epimerization of this mixture with potassium *tert*-butylate in *tert*-butyl alcohol (eq 2) gave a new mixture (ca. 10:90), enriched in the trans isomer (**2**). Isomer ratios were estimated by NMR analysis.



(2)

1 **2**

Thermolyses were carried out by injection of the enriched mixtures of **1** and **2** into a hot (>500°) bed of silicon carbide chips. The effluent gases were collected in a cold trap, and the butenes were subsequently analyzed by GLC. The results are summarized in eq 3.



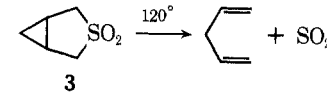
(3)

1 (95% cis)	36 ± 6%	53 ± 3%	9 ± 6%
2 (90% trans)	51 ± 6%	40 ± 3%	9 ± 6%

In the appropriate control experiments, it was found that from a partial pyrolysis **1** could be recovered unchanged (no appreciable epimerization to **2**). Furthermore, authentic *cis*-2-butene when passed through the reactor suffered less than 2% isomerization to *trans*-2-butene. In view of the substantial crossover in the thermolysis of **1** and **2** it was felt that attempts to refine the experiment by further purification of **1** and **2** or by improving the GLC resolution of the products were unwarranted.

Discussion

It has previously been demonstrated that pericyclic [$_\sigma 2_s + {}_\sigma 2_s + {}_\sigma 2_s$] fragmentation in the strained system **3** (eq 4)



(4)

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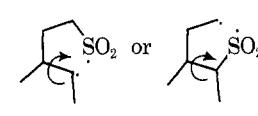
proceeds concertedly by tests of stereospecificity and kinetic facility.[3] Although equivalent thermolysis of simple sulfolanes requires temperatures more than 200° higher than for **3**, it was considered plausible that **1** and **2** might dissociate with retention of methyl group stereochemistry in view of the fully synchronous nature of the *sulfolene* reaction.[4] The experimental results indicate otherwise. From either sulfolane (**1** or **2**) mixtures of 2-butenes were obtained (uncorrected trans/cis ratios 0.7 *E*:1.0 *Z* and 1.0 *E*:0.8 *Z*, respectively). We suggest that the results are best accommodated by a multistep mechanism, in which diradical (or zwitterionic) intermediates exist for appreciable lifetimes. It is sufficient that internal rotation within such an intermediate (**4**) be competitive with bond scission. In



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spite of our control experiments the possibility cannot rigorously be excluded that fragmentation is in fact concerted, but that isomerization occurs subsequently (SO_2 catalysis). However, it is difficult to envision such a latter mechanism which would not in actuality be available to the incipient reaction products in the primary step.

The low residual stereospecificity is reminiscent of other recently reported extrusion reactions.[5] We would only comment that concepts of diradical chemistry should be adjusted to accommodate what appears to be a pattern of partial stereochemical retention.