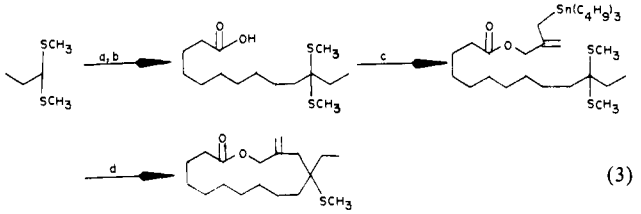
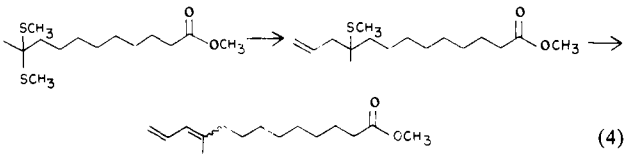


(3)

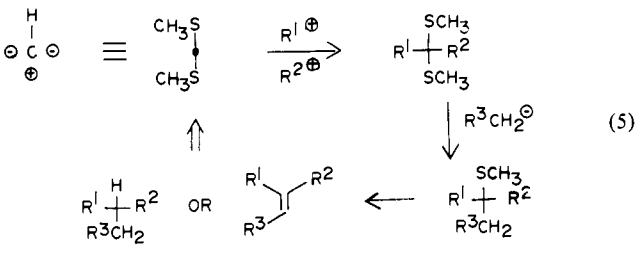
(a) nC_4H_9Li, THF, $Br(CH_2)_8Br$. (b) $LiCH_2CO_2Li$, THF. (c) $(Im)_2CO$, THF $(C_4H_9)_3SnCH_2(C{=}CH_2)CH_2OH$. (d) DMTSF, CH_2Cl_2.

alkylation of a carbonyl group. The ease of elimination by oxidation ($NaIO_4$, CH_3OH, H_2O, room temperature, 87%) and thermolysis ($PhCH_3$, $CaCO_3$, reflux, 97%) as in eq 4 makes the



(4)

overall reaction a convenient procedure for alkylation–elimination. Combined with the ready availability of thioacetals and thioketals by alkylation of lithiated bis(methylthio)methane, the direct and selective DMTSF-induced reactions of the thioketals and -acetals streamlines their application in synthesis (see eq 5).



(5)

Acknowledgment. We thank the National Science Foundation for their generous support of our programs.

Registry No. 3, 75920-72-8; **4**, 94202-85-4; **5**, 94203-00-6; 7,7-bis(methylthio)-2-octyne, 94202-84-3; 3,3-bis(methylthio)-1-phenyl, 94202-86-5; 11,11-bis(methylthio)-2-dodecanone, 94202-87-6; methyl 10,10-bis(methylthio)undecanoate, 94202-88-7; 11,11-bis(methylthio)-12-methyl-1-tridecene, 94202-89-8; 3,3-bis(methylthio)-5α-androst-17-one, 56253-73-7; 1,1-bis(methylthio)hexane, 82726-67-8; α,α-bis(methylthio)toluene, 14252-44-9; tributylallylstannane, 24850-33-7; tributylmethylallylstannane, 67883-62-9; (*E*)-tributyl-2-butenylstannane, 35998-93-7; (*Z*)-tributyl-2-butenylstannane, 35998-94-8; 4-methyl-4-(methylthio)-1-nonene, 94202-90-1; 2,4-dimethyl-4-(methylthio)-1-nonene, 94202-91-2; 3,4-dimethyl-4-(methylthio)-1-nonene (isomer 1), 94202-92-3; 3,4-dimethyl-4-(methylthio)-1-nonene (isomer 2), 94202-93-4; 7-methyl-(methylthio)-2-decyn-9-ene, 94202-94-5; 4-propyl-4-(methylthio)-3-methyl-1-heptene, 94202-95-6; 4-methyl-4-(methylthio)-6-phenyl-1-hexene, 94202-96-7; 11-methyl-11-(methylthio)-13-tetradecen-2-one, 94202-97-8; methyl 10-methyl-10-(methylthio)-12-tridecenoate, 94202-98-9; 4-isopropyl-4-(methylthio)-1,13-tetradecadiene, 94202-99-0; 4-(methylthio)-1-nonene, 94203-01-7; 1-phenyl-1-(methylthio)-3-butene, 63297-72-3; allyltrimethylsilane, 762-72-1; 2-[(tributylstannane)methyl]-2-propenyl 10,10-bis(methylthio)undecanoate, 94203-02-8; 1-oxa-2-oxo-11-methyl-11-(methylthio)-13-methylenecyclotetradecane, 94203-03-9; 1,1-bis(methylthio)propane, 57093-94-4; 11,11-bis(methylthio)tridecanoic acid, 94203-04-0; 2-[(tributylstannane)methyl]-2-propenyl] 11,11-bis(methylthio)tridecanoate, 94203-05-1; 1-oxa-2-oxo-11-ethyl-11-(methylthio)-13-methylenecyclopentadecane, 94234-88-5; 1,8-dibromooctane, 4549-32-0; lithium lithioacetate, 60419-47-8; methyl 10-methyl-10,12-tridecadienoate, 94203-07-3; 4-allyl-4-(methylthio)heptane, 94203-08-4; DMTSF, 5799-67-7; $(C_4H_9)_3SnCH_2(C{=}CH_2)CH_2OH$, 94203-06-2.

Supplementary Material Available: Detailed experimental procedure for entries 8 and 10 in Table I (1 page). Ordering information appears on any current masthead page.

Chemoselectivity in Palladium-Mediated Cycloadditions of Substituted Trimethylenemethanes

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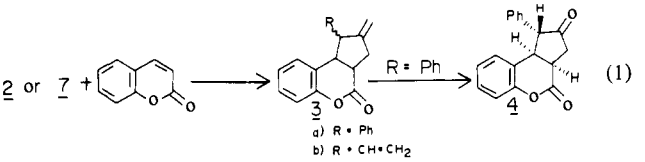
Received August 20, 1984

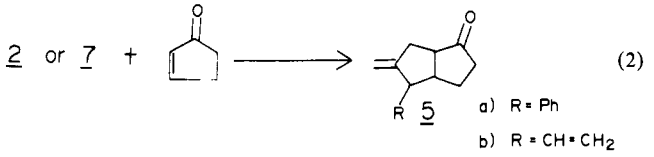
The utility of cycloadditions depends upon the acceptability of diverse substituents on both reaction partners. For Pd-mediated [3 + 2] cycloadditions, we have established a broad base of acceptors.[1,2] The compatibility of functional groups on the donor, i.e., on the trimethylenemethane (TMM) conjunctive reagent, would represent a significant development in the applicability of this strategy in complex synthesis.[3] Because of the established nucleophilic nature of the TMM–Pd complex, we were especially interested in substituents possessing functional groups such as a carbonyl or cyano group which offers an alternative reactivity profile such as self-condensation. In addition, unsymmetrical TMM systems raise the spectre of regioselectivity problems. We wish to report the remarkably diverse array of substituents on the TMM unit cannot only be tolerated but also give highly selective cycloadditions.

2-(Trimethylsilyl)methacrolein[4] (**1**) allows ready access to a wide variety of substituted TMM precursors ranging from cyano to acetoxy as summarized in Scheme I. Initial work focused on the phenyl analogue **2**, which undergoes cycloaddition to coumarin under our usual conditions[1] [9 mol % $(Ph_3P)_4Pd$, $PhCH_3$, 110 °C, 76% yield] to form a 70:30 mixture of cycloadducts **3a**[5] (see eq 1). That the cycloadducts differ only in the stereochemistry of



(1)

the phenyl ring is established by ozonolysis, which gives an isomeric mixture of products. Purification by TLC effects equilibration to a single regio- and stereoisomer **4**[5], mp 174–177 °C, in 98% yield. The structure of **4** is unambiguously established by X-ray crystallography.[6] In employing cyclopentenone as a trap (eq 2),



(2)

a somewhat improved yield arises when the catalyst is switched

(1) Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1983**, *105*, 2315, 2326.

(2) For some other recent [3 + 2] cycloadditions, see: Binger, P.; Brinkmann, A.; Richter, W. J. *Tetrahedron Lett.* **1983**, *24*, 3599. Noyori, R.; Yamakawa, M.; Takaya, H. *Ibid.* **1978**, 4823. Little, R. D.; Stone, K. J. *J. Am. Chem. Soc.* **1983**, *105*, 6976. Fierz, G.; Chidgey, R.; Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 410. Danheiser, R. L.; Carini, D. J.; Basak, A. *J. Am. Chem. Soc.* **1981**, *103*, 1604. Boger, D. L.; Brotherton, C. E. *J. Am. Chem. Soc.* **1984**, *106*, 805.

(3) For reviews, see: Trost, B. M. *Chem. Soc. Rev.* **1982**, *11*, 141. Paquette, L. A. *Top. Curr. Chem.* **1984**, *119*, 1.

(4) (a) Prepared in 71% yield by swern oxidation of 2-[(trimethylsilyl)methyl]allyl alcohol [Trost, B. M.; Chan, D. M. T.; Nanninga, T. N. *Org. Synth.* **1984**, *62*, 58]. (b) See: Chan, D. M. T. Ph.D. Thesis, University of Wisconsin, Madison, 1982.

(5) All new compounds have been fully characterized spectrally and elemental composition determined by combustion analysis and/or high-resolution mass spectroscopy.

(6) We thank Dr. Ken Haller for aid in this determination.

(7) We assume n = 2, 3, or 4 so that 5–7 equiv of triisopropyl phosphite relative to palladium acetate is employed.

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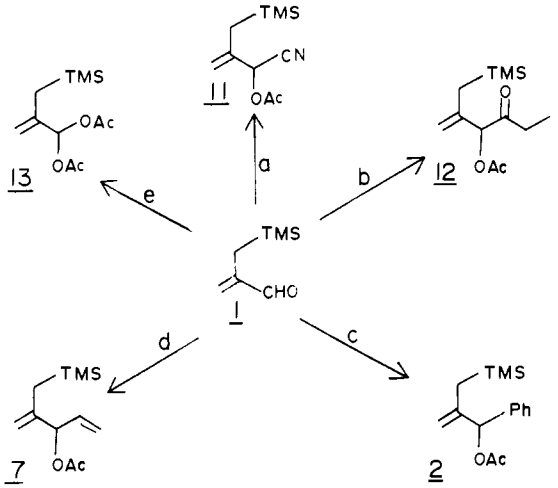
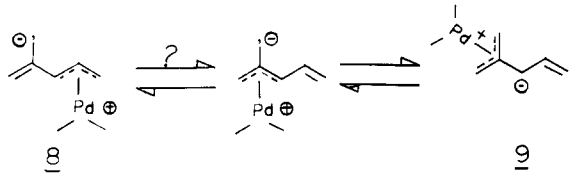
Scheme I. Synthesis of Substituted TMM-Pd Precursors[a,b]



[a] (a) (i) TMSCN, ZnI_2, neat, 83%; (ii) Ac_2O, 9 mol % $FeCl_3$, 0 °C, neat 81%. (b) (i) $C_2H_5CH(SCH_3)_2$, *n*-C_4H_9Li, THF, −78 to 0 °C, 65%; (ii) Ac_2O, C_5H_5N, DMAP, room temperature, 95%; (iii) $AgNO_3$, 95% C_2H_5OH, 50 °C, 83%. (c) (i) PhLi, ether, −78 to 20 °C, 82%; (ii) AcCl, C_5H_5N, DMAP, CH_2Cl_2, 90%. (d) (i) CH_2=CHLi, ether, −60 to 20 °C; (ii) AcCl, C_5H_5N, DMAP, CH_2Cl_2, 73% overall. (e) Ac_2O, 5 mol % $FeCl_3$, neat, 0 °C, 71%. [b] Reference 5.

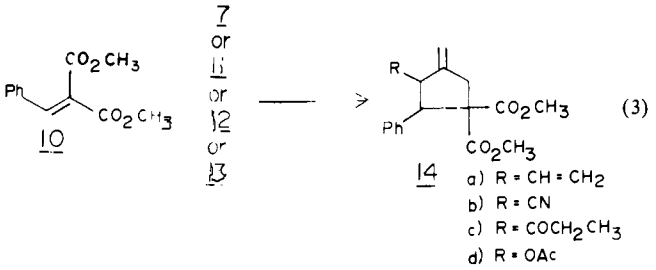
from $(Ph_3P)_4Pd$ (50% yield of **5a**)[5] to an in situ prepared catalyst derived by reacting triisopropyl phosphite with palladium acetate either in the presence of a reductant such as *n*-butyllithium or 1-hexene or without any additional reductant where the phosphite may serve as such (60% yield of **5a**).[8] The latter catalyst [$((i\text{-}C_3H_7O)_3P)_nPd$ (**6**)] was employed in all subsequent runs except one (vide infra).

The vinyl derivative **7** allows participation of the conjugating substituent which should preferentially coordinate with Pd(0).[9] Thus, an alternative zwitterion **8** may preferentially form which



might lead to non-cyclopentane products. Of course, formation of **8** does not preclude reaction via **9** by palladium migrations. In the event, reaction of **7** and coumarin at 90 °C in toluene gives the desired methylenecyclopentane **3b**[5] (eq 1) in 61% yield. The effect of the catalyst is particularly noteworthy here where only a 6% yield of **3b** is obtained with $(Ph_3P)_4Pd$.[4b] The NMR spectrum cleanly establishes the regiochemistry as depicted [major isomer, δ 3.14 (t, *J* = 9 Hz, 1 H) coupled to 2.99 (t, *J* = 9 Hz, 1 H); minor isomer, δ 3.03 (t, *J* = 8.4 Hz, 1 H) coupled to 2.82 (t, *J* = 8.4 Hz, 1 H)]. Use of cyclopentenone as a trap gives **5b**[5] in 75% isolated yield (eq 2).

For subsequent reactions, dimethyl benzylidenemalonate (**10**) is employed as a standard trap in which the ratio of the TMM precursor to **10** is approximately 1:1 (concentration 0.5–1 M) with 4–8 mol % of **6** as catalyst. Cycloadding **7** to **10** in dioxane at 100 °C gives an 89% yield of methylenecyclopentane **14a**[5] (eq 3). Cyano as in **11** is chosen as an example of a reactive functional group. Gratifyingly, using 4–6 mol % of preformed $(Ph_3P)_4Pd$ as catalyst, a single regio- and stereoisomerically pure adduct **14b**[5] forms in 54% yield [δ 4.10 (d, *J* = 12.5 Hz, 1 H), 4.24 (d, *J* = 12.5 Hz, 1 H, 3.46 (d, *J* = 20 Hz, 1 H), 2.86 (d, *J* = 20 Hz, 1 H)].

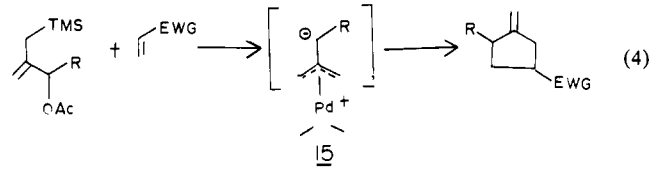


(3)

Becoming bolder, we felt that a carbonyl group would provide a most stringent test since enolization and carbonyl addition have already been established as possible reactions.[1,4b] Once again, we find smooth cycloaddition to form **14c**,[5] mp 68–69 °C, as a single regio- and stereoisomer in 59% yield [δ 4.44 (d, *J* = 10 Hz, 1 H), 4.09 (dq, *J* = 10, 2 Hz, 1 H), 3.81 (dd, *J* = 18, 1.5 Hz, 1 H), 2.87 (dq, *J* = 18, 2 Hz, 1 H)].

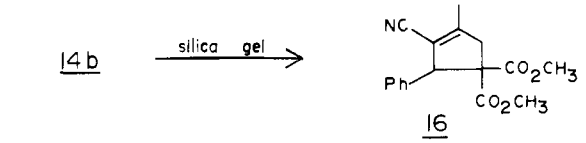
In all cases, the regioselectivity is rationalized as arising from **15**. Since R is a conjugating substituent in **2**, **7**, **11**, and **12**, **15** probably reflects the thermodynamically most stable TMM–Pd species in all these cases.[10] For synthetic reasons, an oxygen substituent would be particularly useful. However, electron–electron repulsion between the lone pairs on oxygen and the carbanion center of **15** would be expected to destabilize **15**, R = OAc. Thus, a different regioselectivity should be anticipated with **13**, if it reacts at all. Furthermore, the product, itself being an allyl acetate, may not survive the reaction conditions. In spite of all these fears, a 1:1 stereoisomer mixture of cycloadducts, both of which possess the same regiochemistry, forms in 86% yield [one isomer, δ 5.85 (dq, *J* = 7.9, 2.2 Hz, 1 H), 4.44 (d, *J* = 7.9 Hz, 1 H); second isomer, δ 6.03 (d m, *J* = 8.9 Hz, 1 H), 4.14 d, *J* = 8.9 Hz, 1 H)]. The above NMR data clearly established the regiochemistry depicted in **14d**.[5] *Thus, even an oxygen substituent does not change the regioselectivity*!

These results firmly establish this Pd-mediated [3 + 2] cycloaddition as a truly general reaction as outlined in eq 4 regardless



(4)

of the substituent. The chemoselectivity is extraordinary; thus, both reaction partners may bear substantial substitution. The mildness of the reaction conditions is further demonstrated by the fact that **14b** and **14c** easily suffer isomerization of the exocyclic double bond into the conjugated endocyclic position, but none of this isomer is detected immediately after reaction. Chromatography of **14b** quantitatively isomerizes the kinetic product to **16**.[5]



Combining the high chemo- and regioselectivity of the substituted TMM precursors with their ease of preparation greatly expands the utility of such cycloaddition methodology for five-membered rings. The divergence between this approach for cycloadditions and that employing cooligomerization with methylenecyclopropanes becomes more evident by the striking differences in regioselectivity observed where comparisons are possible. Thus,

(8) For practical convenience, use of the in situ method to generate the Pd(0) catalyst employs palladium acetate, which requires no special precautions in handling. We generally prefer to use *n*-butyllithium (2 equiv relative to palladium acetate) to have an active catalyst more reproducibly.

(9) Cf.: Trost, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1980**, *102*, 4730.

(10) The thermodynamically most stable complex does not necessarily mean it is the most reactive. Nevertheless, at present, the regioselectivity does appear to correlate with the relative stability. Also see: Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1981**, *103*, 5972. Gordon, D. J.; Fenske, R. F.; Nanninga, T. N.; Trost, B. M. *J. Am. Chem. Soc.* **1981**, *103*, 5974.

the phenyl[11] and vinyl[11,12] substituted methylenecyclopropanes give products bearing the substituents preferably to exclusively on the exocyclic methylene carbon—in contrast to the results reported herein.

Acknowledgment. We thank the National Science Foundation and the National Institutes of Health, General Medical Sciences, for their generous support of our programs.

Registry No. 1, 56407-82-0; **2**, 82823-83-4; **3a** (isomer 1), 94110-97-1; **3a** (isomer 2), 94160-61-9; **3b** (isomer 1), 94110-98-2; **3b** (isomer 2), 94160-62-0; **4**, 94110-99-3; **5a**, 94111-00-9; **5b**, 94111-01-0; **7**, 94111-02-1; **10**, 6626-84-2; **11**, 94111-03-2; **12**, 94111-04-3; **13**, 94111-05-4; **14a**, 94111-06-5; **14b**, 94111-07-6; **14c**, 94111-08-7; *cis*-**14d**, 94111-09-8; *trans*-**14d**, 94111-10-1; **16**, 94111-11-2; $(Ph_3P)_4Pd$, 14221-01-3; TMSCN, 7677-24-9; $C_2H_5CH(SCH_3)_2$, 57093-94-4; coumarin, 91-64-5; 2-cyclopenten-1-one, 930-30-3; triisopropyl phosphite, 116-17-6; palladium acetate, 3375-31-3.

(11) Bentz, P. Ph.D. Thesis, Universität Kaiserslautern, *J. Am. Chem. Soc.* **1982**. Gerner, A. Ph.D. Thesis, Ruhr-Universität Bochum, West Germany, **1978**.
(12) Binger, P.; Germer, A. *Chem. Ber.* **1981**, *114*, 3325.

Dewar Thiophene: Its Generation and Trapping with Furan

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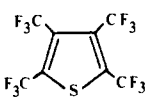
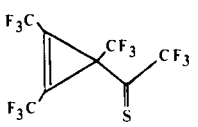
Received June 20, 1984

The Dewar structure has received considerable attention since its proposal as an alternative to the Kekulê formulation of benzene;[1] however, it was not until comparatively recently that van Tamelen and Pappas isolated the first substituted Dewar benzene[2a] and shortly after the parent compound.[2b] In heteroaromatic systems, extensive efforts have been made to obtain Dewar isomers. Substituted Dewar pyrroles[3] and pyridines[4] have been obtained by photolysis, and the first substituted Dewar furan was recently synthesized.[5] Except for Dewar pyridine[6] no parent Dewar isomers of the heteroaromatics have been reported.

The first isolation of a thiophene valence bond isomer was reported by Heicklen et al.[7a] who investigated the photolysis of 2,3,4,5-tetrakis(trifluoromethyl)thiophene (**1**). The product was



1



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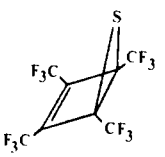


3

initially thought to be the cyclopropenylthioketone **2**;[7] however, the Dewar structure, **3** was later assigned[8] on the basis of the ^{19}F NMR spectrum.

(1) Dewar, J. *Proc. R. Soc. Edinburgh* **1866**, 82-86.
(2) (a) van Tamelen, E. E.; Pappas, S. P. *J. Am. Chem. Soc.* **1962**, *84*, 3789-3791. (b) van Tamelen, E. E.; Pappas, S. P. *Ibid.* **1963**, *85*, 3297-3298.
(3) (a) Hiraoka, H. *J. Chem. Soc., Chem. Commun.* **1971**, 1610-1611. Barltrop, J. A.; Day, A. C.; Moxon, P. D.; Ward, R. R. *Ibid.* **1975**, 786-787. (b) Barltrop, J. A.; Day, A. C.; Ward, R. R. *Ibid.* **1978**, 131-133.
(4) Barlow, M. G.; Dingwall, J. G.; Haszeldine, R. N. *J. Chem. Soc., Chem. Commun.* **1970**, 1580. Barlow, M. G.; Dingwall, J. G.; Haszeldine, R. N. *J. Chem. Soc., Perkin Trans. 1* **1973**, 1542-1545.
(5) Wirth, D.; Lemal, D. M. *J. Am. Chem. Soc.* **1982**, *104*, 847-848.
(6) Wilzbach, K. E.; Rausch, D. J. *J. Am. Chem. Soc.* **1970**, *92*, 2178-2179.
(7) (a) Braslavsky, S.; Weibe, H. A.; Heicklen, J. Publication 164-170; Center for Air Environment Studies: Pennsylvania State University, University Park, 1970. (b) Wu, E. C.; Heicklen, J. *J. Am. Chem. Soc.* **1971**, *93*, 3432-3437.
(8) Weibe, H. A.; Braslavsky, S.; Heicklen, J. *Can. J. Chem.* **1972**, *50*, 2721-2724.

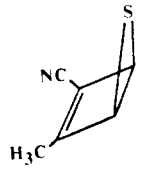
Table I. 400-MHz ^1H and 100-MHz ^{13}C NMR Data for Thiophene/Furan Diels-Alder Adducts

adduct	chem shifts, ppm[a] δ_H	δ_C	assignment[b]
5	6.31	134.9	a,a′
	4.93	79.4	b,b′
	3.37	36.9	d,d′
	2.32	51.0	c,c′
6	6.60	134.8	a,a′
	4.97	78.8	b,b′
	3.06	38.6	d,d′
	2.93	50.0	c,c′

[a] Chemical shifts in $CDCl_3$ relative to Me_4Si. [b] The prime notation is introduced to account for the magnetic nonequivalence within each set of chemically equivalent atoms.

Kobayashi et al.[9] generated **3** by direct photolysis of **1** in the gas phase and confirmed its structure by ^{19}F and ^{13}C NMR spectroscopy. **3** reverts thermally to **1** with a half-life of 5.1 h in benzene at 160 °C[9,10] and undergoes Diels-Alder cycloaddition with a variety of dienes.[9-11] More recently their studies of Dewar thiophenes have been extended to include bis- and tris(trifluoromethyl)thiophenes.[12]

Day et al.[13] have reported the formation of a Dewar thiophene while investigating the photorearrangement of cyanothiophenes. It was trapped in the form of its Diels-Alder adducts with furan. Direct proof of the adducts' structures was not provided but their NMR spectra were said to be similar to those for comparable adducts of a substituted Dewar pyrrole already isolated in the same laboratory.[3b] With either 3-cyano-2-methyl- or 3-cyano-4-methylthiophene the same Dewar isomer, **4**, was directly isolated



4

and identified by ^1H NMR. **4** undergoes formation of Diels-Alder adducts with furan and 2,5-diphenyl-3,4-benzofuran.[14] Despite extensive studies of the photolysis of thiophenes[15] the formation and isolation of their Dewar isomers is limited to the cases just described.

We now wish to present the first report on the generation and trapping of the parent Dewar thiophene. This was accomplished by irradiating (229 nm) a solution of thiophene in furan (mole ratio ~1/10) at ca. 25 °C. Capillary GC/MS analysis (OV-101, 0.3 mm × 50 m, T_1 = 115 °C, rate 2 °C/min) indicated the presence of two 1:1 thiophene and furan adducts, **5** and **6**, in a 5/3 ratio. Compounds **5** and **6** were separated by preparative GC (15% SE-30, ~6 mm × 2 m, 130 °C) and each assigned the structure of a furan Diels-Alder adduct with Dewar thiophene based on MS and ^1H and ^{13}C NMR spectroscopy.

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