Table I. Products from the Thermolysis of **1a**

entry	conditions			products[a]						
		1a (mg)	T (°C)	*t* (min)	**3a**	**4a**	**8a** + **9a** + isomers	**10a**	**11a**	**12a**	recovery[b]
1	GC	7	300[c]		5	1		89	4	1	50[d]
2	ampoule	5	200[e]	5	<1	4	<1	13	6	77	ca. 20[d]
3	ampoule	5	175[e]	5	2		>95			1	ca. 100[f]
4	ampoule	5	150[e]	5	<1		>90				*g*
5	ampoule	*h*	200	5	1	8		2	10	54	ca. 20[f]

[a] In percent of total recovery; furthermore, <1% of methylindanes was present in many runs. [b] In percent of **1a**. [c] Injector: 300 °C; oven: 200 °C; 1.5 m 15% SE-30 on Chromosorb W; 60 mL H_2/min. [d] Isolated yield (preparative GC). [e] A KOH-pretreated Pyrex ampoule of 0.5-mL contents was used. [f] Determined from ^1H NMR with C_6H_6 as internal standard. [g] Not determined; 6% of **1a** was present. [h] The product mixture (**8a**, **9a** + isomers) from entry 3 was used.

When this mixture was heated separately to 200 °C (entry 5), it lead to extensive formation of polymer (broad signals in the ^1H NMR spectrum) and a ratio of **11a**:**12a** similar to that in entry 2; this indicates that **8a** and **9a** are intermediates for **11a** and **12a**.

The most unexpected aspect of these reactions is the rather clean transformation of the "*meta*"-bridged **1a** to the *para*cyclophane **12a**; this is all but straightforward and signals deepseated rearrangements. Remarkable also is the formation of (substituted) arene cage dimers[12-14] like **8a**-**10a** in a single operation. While the parent benzene dimer corresponding to **10a**, which has C_2 symmetry, is known,[12] the D_{2h} benzene dimer corresponding to **8a** and **9a** has not been reported to our knowledge.

A rationalization of our results is given in Scheme I. The essential postulate is the thermal isomerization of **1a** to **2a**. This step is presumably slightly endothermic (MNDO:$\Delta H_f°$ (**1a**) = 74.6 kcal·mol^{-1}; $\Delta H_f°$ (**2a**) = 77.1 kcal·mol^{-1})[15] and rate determining; the high aromatization temperature required for a short-bridged Dewar benzene has precedent.[16] The ensuing transformation of **2a** to **11a** (or to **12a**, respectively) involves four remarkable [4 + 2] reactions (Scheme I). The first two are Diels-Alder reactions and proceed via **5a** to **8a** (or, for a different orientation of the two bridges, via **6a** to **9a**).[17] The ease of these unprecedented benzene dimerizations stems from the high-energy content of **2a** (e.g., MNDO: ΔH (2 × **2a** → **9a**) = −59.5 kcal·mol^{-1}). The two following steps from **8a** to **11a** (or from **9a** to **12a**), are retro versions of the first two [4 + 2] reactions. While **2a** → **8a** involves the formation of the four vertical bonds of the cage, the indicated four horizontal bonds are cleaved for **8a** → **11a**. This latter process is thermodynamically favorable because it furnishes two unstrained benzene rings.[18] Note that the initially unexpected para substitution pattern of **12a** follows naturally from the proposed mechanism.

Support for Scheme I comes from deuterium-labeling experiments: **1b** gave **11b** and **12b**; **1c** gave **11c** and **12c**, which is identical with **12b**. The position of the label in **11b,c** was unambiguously deduced from the ^1H NMR spectra.[10] Also, **1c** furnished **8c** and **9c** with the predicted changes of the assignable ^1H NMR signals (e.g., collapse of the olefinic doublets at δ = 6.09 and 6.12 ppm to (br) singlets).

The genesis of **10a** is less obvious. It may proceed as depicted by a [4 + 2] dimerization of **2a** to yield **7a**. An intramolecular Diels-Alder reaction of **7a** (corresponding to that of **5a** or **6a**) is prohibited by bridge strain; instead, a formal [2 + 2] addition may get a chance to furnish **10a**. Again, deuterium labeling[10] supports this course of events.

Acknowledgment. We thank M. Hogenbirk for experimental contributions in the initial stages of this investigation and Professor H. D. Martin for unpublished data on the parent benzene dimer[12] corresponding to **10a**.

Supplementary Material Available: Listing of spectral, GCMS, and HRMS data (4 pages). Ordering information is given on any current masthead page.

(12) Martin, H. D.; Pföhler, P. *Angew. Chem.* **1978**, *90*, 901.
(13) (a) Yang, N. C.; Horner, M. G. *Tetrahedron Lett.* **1986**, *27*, 543. (b) Yang, N. C.; Hrnjez, B. J.; Horner, M. G. *J. Am. Chem. Soc.* **1987**, *109*, 3158.
(14) Higuchi, H.; Kobayashi, E.; Sakata, Y.; Misumi, S. *Tetrahedron* **1986**, *42*, 1731.
(15) Jenneskens, L. W.; De Kanter, F. J. J.; De Wolf, W. H.; Bickelhaupt, F. *J. Comput. Chem.*, in press.
(16) Van Straten, J. W.; Turkenburg, L. A. M.; De Wolf, W. H.; Bickelhaupt, F. *Recl. Trav. Chim. Pays-Bas* **1985**, *104*, 89 and references cited.
(17) (a) The regiochemistry of the first step finds an analogy in the Diels-Alder reactions of [5]metacyclophane: Turkenburg, L. A. M.; Blok, P. M. L.; De Wolf, W. H.; Bickelhaupt, F. *Angew. Chem.* **1982**, *94*, 291. (b) For a [4 + 2] addition analogous to the second step, see: Westberg, H. M; Cain, E. N.; Masamune, S. *J. Am. Chem. Soc.* **1969**, *91*, 7512.
(18) The last one of these cycloreversions is analogous to the cleavage of *o,p'*-dibenzene into two benzene molecules: Braun, R.; Kummer, M.; Martin, H. D.; Rubin, M. B. *Angew. Chem.* **1985**, *97*, 1054.

N-Substituted Organo(silyliminomethyl)stannanes: Synthetic Equivalent to Organosilylcarbonyl Anion and Carbonyl Dianion

Yoshihiko Ito,* Takaharu Matsuura, and Masahiro Murakami

Department of Synthetic Chemistry
Faculty of Engineering
Kyoto University, Kyoto 606, Japan

Received June 22, 1987

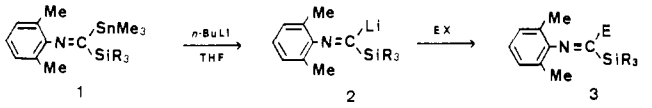
Acylmetals are often involved as important intermediates in transition-metal-catalyzed reaction with carbon monoxide. Synthetic utilities of some acylmetal compounds such as acylferrate anions[1] and related organometallic compounds[2] have been demonstrated. However, acylmetals, which are readily available and widely utilizable as synthetic reagents for nucleophilic introduction of acyl group have been so far limited. Recently, we have reported[3] a new synthesis of N-substituted organo(silyliminomethyl)stannanes by palladium(0)-catalyzed reaction of isocyanide with organosilylstannanes. Herein we wish to report that ((2,6-xylylimino)(trialkylsilyl)methyl)stannane is selectively transmetallated at −78 °C with *n*-butyllithium to generate in situ ((2,6-xylylimino)(trialkylsilyl)methyl)lithium, which serves as a versatile acylmetal equivalent reacting with various electrophiles. Of special interest is that the reaction of ((2,6-xylylimino)(trialkylsilyl)-methyl)lithium with carbonyl compounds makes it possible to introduce successively a second electrophile on the imino carbon with concurrent Brook-type migration of the trialkylsilyl group from imino carbon to oxygen.

A dark brown solution of ((2,6-xylylimino)(trialkylsilyl)-methyl)lithium **2**, which is prepared in THF at −78 °C by treatment of ((2,6-xylylimino)(trialkylsilyl)methyl)trialkylstannane **1** with *n*-butyllithium (Scheme I), reacted immediately with a variety of electrophiles (MeOH, Me_3SiCl, EtBr, *n*-BuBr) to give

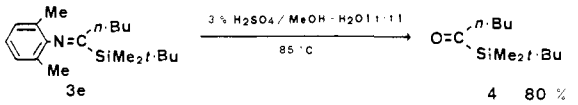
(1) For review, see: Collman, J. P. *Acc. Chem. Res.* **1975**, *8*, 342.
(2) (a) Walborsky, H. M.; Niznik, G. E. *J. Am. Chem. Soc.* **1969**, *91*, 7778. (b) Niznik, G. E.; Morrison, W. H., III; Walborsky, H. M. *J. Org. Chem.* **1974**, *39*, 600. (c) Seyferth, D.; Weinstein, R. M. *J. Am. Chem. Soc.* **1982**, *104*, 5534. (d) Ito, Y.; Imai, H.; Matsuura, T.; Saegusa, T. *Tetrahedron Lett.* **1984**, *25*, 3091. (e) Seyferth, D.; Hui, R. C. *J. Am. Chem. Soc.* **1985**, *107*, 4551.
(3) Ito, Y.; Bando, T.; Matsuura, T.; Ishikawa, M. *J. Chem. Soc., Chem. Commun.* **1986**, 980.

0002-7863/87/1509-7888$01.50/0 © 1987 American Chemical Society

Scheme I



Scheme II



Scheme III

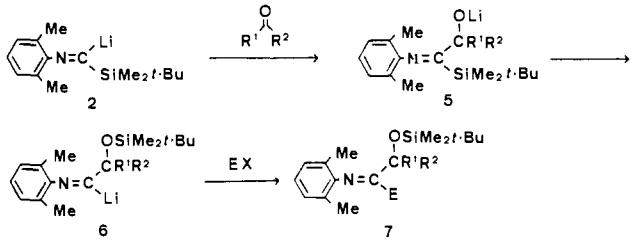


Table I. Reaction of **2** with Electrophiles

$-SiR_3$	electrophile	prod.[a]	prod. no.	yield, %
$-SiMe_2$-*t*-Bu	MeOH	Xy-N=C(-H)-$SiMe_2$t-Bu	**3a**	74
$-SiMe_3$	Me_3SiCl	Xy-N=C(-$SiMe_3$)$_2$	**3b**	84
$-SiMe_2$-*t*-Bu	Me_3SiCl	Xy-N=C(-$SiMe_3$)-$SiMe_2$t-Bu	**3c**	73
$-SiMe_2$-*t*-Bu	EtBr	Xy-N=C(-Et)-$SiMe_2$t-Bu	**3d**	75
$-SiMe_2$-*t*-Bu	*n*-BuBr	Xy-N=C(-*n*-Bu)-$SiMe_2$t-Bu	**3e**	76

[a] Xy- = 2,6-xylyl-.

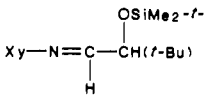
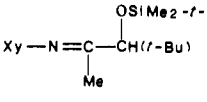
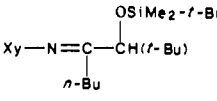
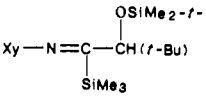
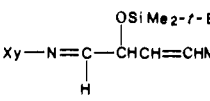
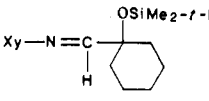
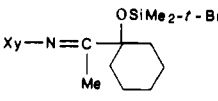
the corresponding (2,6-xylylimino)(trialkylsilyl)methyl derivatives **3**[4] in good yields[5] (Table I).

The alkylated product was successfully hydrolyzed to afford the corresponding acylsilane in good yield. For instance, **3e** was treated with 3% solution of H_2SO_4 in MeOH–H_2O (1:1) at 85 °C for 12 h to give the acylsilane 4 in 80% yield (Scheme II). The present reaction provides a general and facile method for preparation of a variety of acylsilanes.

Next, pivalaldehyde was allowed to react with ((2,6-xylylimino)(trialkylsilyl)methyl)lithium **2** to afford aldimine **7a** in 58% yield by quenching with MeOH. This finding shows that an initial adduct **5** is readily converted to ((2,6-xylylimino)alkylmethyl)-lithium **6** by the Brook-type migration of silyl group from imino carbon to oxygen in **5** (Scheme III). Indeed, treatment of the reaction mixture with alkyl halides gave the expected alkylated products, α-silyloxyketimines **7b–d** in moderate to good yields. Similarly, **2** underwent the addition to ketones, followed by the treatment with electrophiles to give the corresponding α-silyl-oxyimines[6] (Table II).

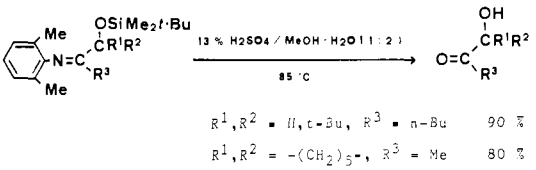
The imines produced were hydrolyzed by the treatment with dilute H_2SO_4 to give the corresponding α-hydroxy ketones in good yields (Scheme IV). The imine was also converted to α-silyl-oxycarbonyl compound by the reaction with $MeOSO_2CF_3$ (2 equiv of $MeOSO_2CF_3$, CH_2Cl_2, room temperature, 14 h), e.g., **7f** →

Table II. Synthesis of α-Silyloxyimines

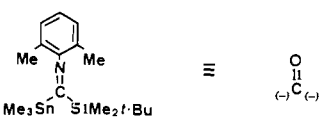
R^1R^2C=O	EX	product[a]	yield, %
t-BuCHO	MeOH	 **7a**	58
	MeI	 **7b**	78
	n-BuBr[b]	 **7c**	40
	Me_3SiCl	 **7d**	62
MeCH=CHCHO	MeOH	 **7e**	53
	MeOH	 **7f**	66
	MeI[b]	 **7g**	58

[a] Xy- = 2,6-xylyl-. [b] Two equiv of HMPA were added before the addition of alkyl halide.

Scheme IV



1-(*tert*-butyldimethylsilyloxy)-1-cyclohexanecarbaldehyde (87%). In the present reactions, ((2,6-xylylimino)(trialkylsilyl)methyl)-stannanes **1** functions as a synthetic equivalent to a carbonyl dianion[7] which can introduce two different electrophiles on the carbonyl carbon atom. Noteworthy is that two carbon–carbon bond formations on carbonyl carbon can be achieved in one pot with ((2,6-xylylimino)(trialkylsilyl)methyl)stannane by use of 1 equiv of *n*-butyllithium.



A representative experimental procedure is as follows. To a stirred solution of ((2,6-xylylimino)(*tert*-butyldimethylsilyl)-methyl)(trimethyl)stannane (0.431 g, 1.05 mmol) in THF (4 mL) was added dropwise a solution of *n*-butyllithium (1.26 mmol) in hexane at −78 °C under nitrogen. The mixture was stirred at the same temperature for 30 min, and then 0.150 mL (1.38 mmol) of pivalaldehyde was added at once. After 30 min, 0.160 mL (2.57 mmol) of methyl iodide was added, and stirring was continued for 30 min at −78 °C. Then the dry ice–EtOH bath was removed,

(4) All new compounds reported gave satisfactory IR and NMR (cyclohexane as an internal reference) spectra. Spectral data for selected products are as follows. **3c**: IR (neat) 1594, 1552 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ −0.14 (s, 9 H), 0.24 (s, 6 H), 1.02 (s, 9 H), 1.99 (s, 6 H), 6.74–7.10 (br m, 3 H). **3d**: IR (neat) 1590 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.25 (s, 6 H), 0.82 (t, J = 8.0 Hz, 3 H), 1.05 (s, 9 H), 2.00 (s, 6 H), 2.13 (q, J = 8.0 Hz, 2 H), 6.77–7.10 (br m, 3 H).

(5) ((2-Tolylimino)(trialkylsilyl)methyl)lithium, which may be similarly generated at −78 °C in THF from the corresponding ((2,6-xylylimino)(trialkylsilyl)methyl)stannane, was not sufficiently stable for synthetic elaboration.

(6) **7a**: IR (neat) 1666, 1594 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.09 (s, 3 H), 0.12 (s, 3 H), 0.93 (s, 9 H), 1.04 (s, 6 H), 2.17 (s, 6 H), 4.00 (d, J = 6.0 Hz, 1 H), 6.85–7.17 (br m, 3 H), 7.65 (d, J = 6.0 Hz, 1 H). **7b**: IR (neat) 1654, 1594 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.07 (s, 3 H), 0.13 (s, 3 H), 0.95 (s, 9 H), 1.06 (s, 3 H), 1.66 (s, 3 H), 2.04–2.11 (br, 6 H), 4.12 (s, 1 H), 6.80–7.17 (br m, 3 H). **7d**: IR (neat) 1586 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.17 (s, 9 H), 0.27 (s, 3 H), 0.35 (s, 3 H), 0.77 (s, 9 H), 1.06 (s, 9 H), 2.04 (s, 3 H), 2.15 (s, 3 H), 4.04 (s, 1 H), 6.73–7.15 (br m, 3 H).

(7) Baldwin, J. E.; Adlington, R. M.; Bottaro, J. C.; Kolhe, J. N.; Perry, M. W. D.; Jain, A. U. *Tetrahedron* **1986**, *42*, 4223.

and the mixture was warmed to room temperature. Extractive workup of the reaction mixture with ether followed by Kugelrohr distillation gave imine (**7b**, 0.284 g, 78%, bath temperature 155 °C/0.18 mmHg).

Further extensions of the present methodology are now in progress in our laboratory.

Supplementary Material Available: Spectral data (IR, ^{1}H NMR) for **3**, **4**, and **7** (5 pages). Ordering information is given on any current masthead page.

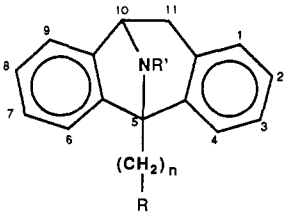
Fluoride-Induced Formation and Ring Opening of Cyclic Sulfamates from Hydroxy Triflamides. Synthetic and Mechanistic Studies†

Terry A. Lyle,* Catherine A. Magill, and Steven M. Pitzenberger

Merck Sharp and Dohme Research Laboratories West Point, Pennsylvania 19486

Received July 29, 1987

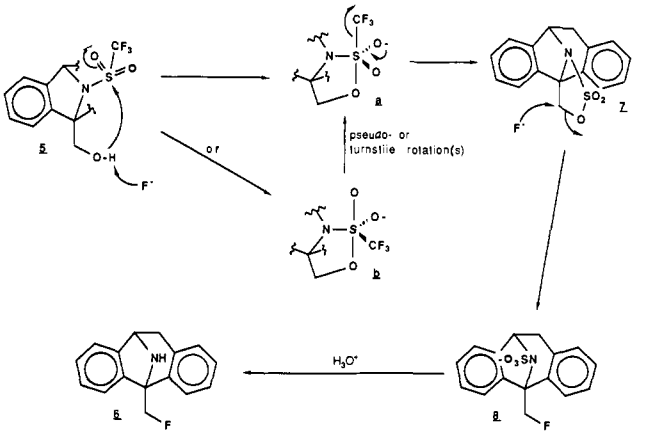
Introduction of fluorine into organic molecules has become an increasingly important field, particularly in the realm of biologically active compounds. Due to its modest steric requirements and unique electronic properties, fluorine has been extensively utilized in medicinal chemistry to influence the metabolism, bioactivity, and physical properties of pharmaceuticals.[1] Another rapidly expanding area of interest is the use of ^{18}F-labeled compounds as biological tools for imaging with use of Positron Emission Tomography (PET).[2] Due to its 110-min half-life, it is desirable to incorporate ^{18}F in the final or penultimate step of a reaction sequence as rapidly as possible. In the course of our efforts directed toward developing a method for the introduction of ^{18}F into the noncompetitive *N*-methyl-D-aspartate antagonist MK-801 (**1**),[3] we discovered an interesting series of reactions which provided a solution to the labeling problem as well as a potentially general method for the stereospecific synthesis of β- and γ-fluorinated secondary amines.



	n = 1		n = 2
1	R = R' = H (MK-801)	**10**	R = F R' = H
2	R = OH R' = H	**16**	R = OH R' = H
3	R = OSO_2CF_3 R' = H	**17**	R = OSO_2CF_3 R' = H
4	R = OSO_2CF_3 R' = SO_2CF_3	**18**	R = OSO_2CF_3 R' = SO_2CF_3
5	R = OH R' = SO_2CF_3		
6	R = F R' = H		
9	R = H R' = SO_2CF_3		

A common approach to ^{18}F labeling involves the displacement of reactive esters with fluoride in the latter stages of a reaction sequence.[4] In an attempt to use this method, the unprotected

Scheme I



alcohol **2**[5] was treated with triflic anhydride and pyridine to afford the desired sulfonate ester **3**.[6a,7a] However, the reaction mixture contained a large amount of yellow polymeric material (presumably derived from the pyridine used as a base in the reaction)[8] which made purification impractical. A modified procedure utilizing an excess of triflic anhydride and 2,6-di-*tert*-butyl-4-methylpyridine[8] was applied to the alcohol **2** with very different results. The products of the reaction were the bis-sulfonylated material **4**[6b,7a,d,e] and the trifluoromethanesulfonamide **5**[6b,9,7a,c,e] (68%) in a ratio of approximately 1:3. Presumably, the more hindered base is less effective in removing the sterically hindered hydroxyl proton, thus allowing preferential sulfonylation at nitrogen.

Quite unexpectedly, treatment of **5** with 0.21 M tetra-*n*-butylammonium fluoride in CH_3CN at 65 °C for 25 min, followed by brief exposure to aqueous acid, gave rise to the desired fluoro compound **6**[6b,9,7a-c] (71%). In order to elucidate the mechanism of this rather remarkable transformation, the following experiments were carried out. Treatment of **5** with this $(n\text{-Bu})_4N^+F^-$ solution at 22 °C produced a new product which was isolated by chromatography and shown to be the cyclic sulfamate **7**[6b,9,10] (54%) (Scheme I). The formation of this intermediate necessarily involves loss of the trifluoromethyl group from the triflamide, a process which is unprecedented to our knowledge. In order to examine further the reaction mechanism, the reaction was followed by ^{19}F NMR to determine the fate of the trifluoromethyl group. When two equivalents of the $(n\text{-Bu})_4N^+F^-$ solution were added to a solution of **5** in CD_3CN, the complete disappearance of the signal from the F_3CSO_2N group of **5** (s, −75.0 ppm, relative to $CFCl_3$) was noted within 2 min, and two new resonances had appeared in a 10:1 ratio: a doublet (78 Hz) at −78.3 ppm, corresponding to trifluoromethane[11] and a smaller triplet (12 Hz) at −79.1 ppm corresponding to CDF_3.[12] This indicates that the fluorinated product is initially a trifluoromethyl anion, and thus this reaction represents a sulfur-based version of the well-known haloform reaction of α-trihalomethyl ketones. When the triflamide **5** was treated with F^- at 65 °C and worked up with aqueous $NaHCO_3$, the fluoromethyl sulfamate **8**[7a] appeared to be the only product. It was smoothly converted to **6** upon exposure to aqueous

† Dedicated to the Memory of Professor Guido H. Daub, 1920-1984.

(1) (a) *Biomedical Aspects of Fluorine Chemistry*; Filler, R., Kobayashi, Y., Eds.; Elsevier Biomedical: *Amsterdam*, 1982. (b) Kollonitsch, J.; Patchett, A. A.; Marburg, S.; Maycock, A. L.; Perkins, L. M.; Doldouras, G. A.; Duggan, D. E.; Aster, S. D., *Nature (London)* **1978**, *274*, 906-908. (c) Welch, J. T. *Tetrahedron* **1987**, *43*, 3123-3197.

(2) Raichle, M. E. *Annu. Rev. Neurosci.* **1983**, *6*, 249-267.

(3) Wong, E. H. F.; Kemp, J. A.; Priestly, T.; Knight, A. R.; Woodruff, G. N.; Iverson, L. L. *Proc. Natl. Acad. Sci. U.S.A.* **1986**, *83*, 7104-7108.

(4) Chi, D. Y.; Kilbourn, M. R.; Katzenellenbogen, J. A.; Welch, M. J. *J. Org. Chem.* **1987**, *52*, 658-664, and references therein.

(5) Presented at the 193rd Meeting of the American Chemical Society, Denver, CO; April 1987; ORGN 218.

(6) (a) Purified by preparative RP-HPLC. (b) Purified by silica gel chromatography.

(7) The following physical data were consistent with the assigned structure: (a) 300 MHz ^{1}H NMR. (b) 75 MHz ^{13}C NMR. (c) 282 MHz ^{19}F NMR. (d) Mass spectrum. (e) IR.

(8) Stang, P. J.; Treptow, W. *Synthesis* **1980**, 283-284.

(9) A satisfactory C, H, and N microanalysis was obtained for a purified sample.

(10) Mp 242-244 °C; ^{1}H NMR ($CDCl_3$) δ 5.19 (d, 8.9 Hz, HC-C_5), 5.38-5.41 (m, HC-C_5, H_{10}); IR 1360, 1185 (SO_2); M^+ = 299.

(11) *The Chemist's Companion*; Gordon, A. J., Ford, R. A. *John Wiley and Sons*: 1972.

(12) Jensen, H.; Schaumburg, K. *Mol. Phys.* **1971**, *22*, 1041-1054.

0002-7863/87/1509-7890$01.50/0 © 1987 American Chemical Society