Department of Chemistry, University of Southern Mississippi

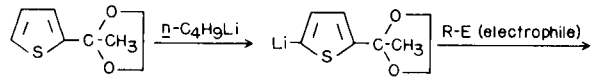
Organosilicon Compounds I.

A Novel Synthesis of Organosilicon Substituted Furfurals

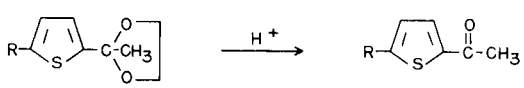
Shelby F. Thames and Homer C. Odom, Jr.

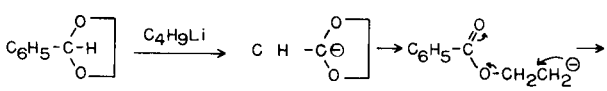
The use of the diethylacetal moiety of 2-furfuraldiethylacetal as a carbonyl blocking agent during *n*-butyllithium metalations is described. The synthesis of 5-silicon substituted furfurals is accomplished for the first time with NMR data being employed as a means of structure proof. Furthermore, the isolation of the uniquely stable organolithium salt, 5-lithio-2-furfuraldiethylacetal, is reported.

Our continuing interest in the area of organosilicon substituted heterocyclic derivatives has prompted us to extend our initial investigation of thiophene chemistry to that of its oxygen analogue, furan. The fact that we were unable to find any reports of the synthesis of silicon substituted furfurals and that these, when prepared, would function as intermediates for other research interests prompted us to investigate methods for their preparation. In an earlier communication we described the use of the 1,3-dioxolane moiety as a blocking group for 2-acetyl thiophene (1). Metalation was shown to occur exclusively at the α-position of thiophene, and as a result produced a harder base than is usually found in the nucleophilic organometallic systems which attacks dioxolanes with ring opening (equation 1.) (2). However, a report by Berlin, *et al.*, (3) suggested to us that other blocking groups might be more efficacious for the present work. These workers showed that 2-phenyl-1,3-dioxolane undergoes initial abstraction of the benzylic proton leading



I



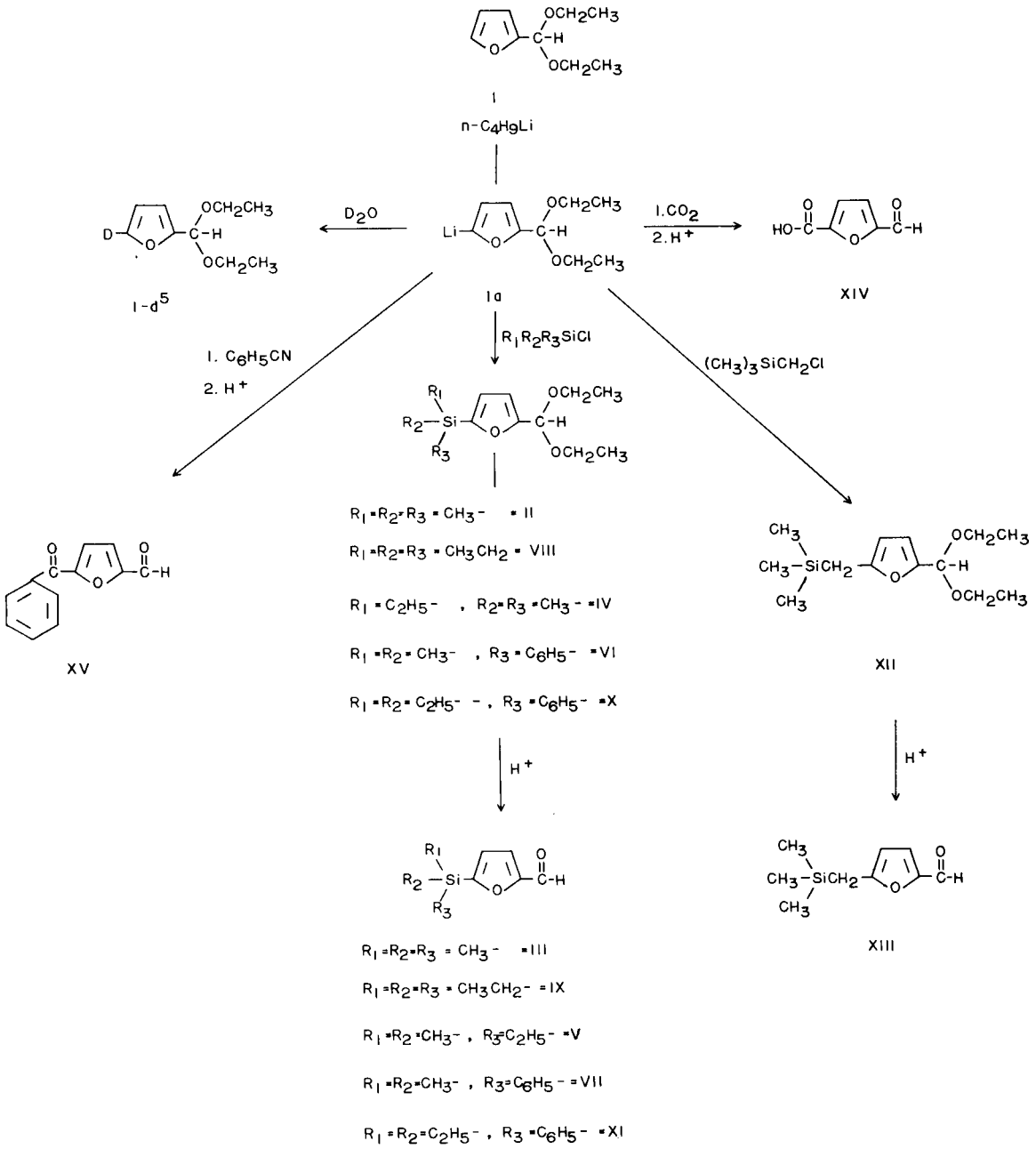


2

to the formation of ethylene and an intermediate resonance stabilized carboxylate anion (equation 2.). In the event the furfurylidene proton of 2(2-furfuryl)-1,3-dioxolane was sufficiently labile, an analogous decomposition would give rise to undesired products. It was, therefore, decided that the acetyl moiety would be employed as the carbonyl blocking agent since a mechanistic route similar to equation 2., would lead to the production of a high energy carbanion, and consequently the intended abstraction of the 5-proton of the furan substrate would be energetically favored (4).

In order to test this thesis an experiment was designed to determine the position(s) metalated on furfural diethylacetal, I, and, if possible, the relative amounts of the metalated product. An ethereal solution of I was treated with slightly less than an equivalent amount of *n*-butyllithium followed by reaction with deuterium oxide. The usual workup procedure resulted in the isolation of the deuterated product, I-d[5], Fig. 1, whose NMR spectral data was compared to that of pure I, Fig. 2. The NMR spectrum of I included: A triplet centered at 8.85 τ and integrating for the six protons of the methyl groups; a quartet centered at 6.44 τ and integrating for the four protons of the methylene groups; a singlet at 4.5 τ integrating for the proton of the furfurylidene carbon; a multiplet centered at 3.66 τ and integrating for the protons at the three and four positions of the furan nucleus; and finally, a perturbed doublet centered at 2.63 τ integrating for the one proton at the 5 position. The spectrum of I-d[5] showed identical absorption bands at 8.85-, 6.44-, and 4.5- τ, respectively. However, the multiplet centered at 3.66 τ has been resolved into a quartet centered at 3.68 τ and integrating for the three and four proton while the perturbed doublet at 2.63 τ, characteristic of the 5-proton is, for all practical purposes, absent. When consideration is taken of the peak integration and the stoichiometric ratio of reactants employed, it is reasonable to assume exclusive metalation at the 5 position. The infra-red spectra, elemental analyses and yields of desired products subsequently

SCHEME A



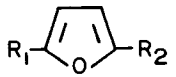
proved these data to be valid.

During this work an interesting observation was noted with respect to the stability of 5-lithio-2-furfuraldiethylacetal, Ia. This salt is extremely stable and may be readily isolated by suction filtration. The salt remains unchanged for periods exceeding 24 hours on exposure to ambient conditions. The identity of the crystalline salt was confirmed when it was filtered from solution, washed with ether, dried, and placed into an ethereal solution of triethylchlorosilane. The usual workup gave a 65% yield of product whose identity with that of an authentic sample of VIII was confirmed by comparisons of their infra-red spectra, boiling points, and refractive indices. Although Eastham and Screttas (5) have recently reported the isolation of organolithium salts as amine complexes (R_2Li_2-B) there appears to be no reports of noncomplexed organolithium salts whose stability parallels that of Ia.

This unusual stability necessitated the replacement of ether as a solvent by THF when Ia was allowed to react with reagents with less electrophilicity than the silylchlorides. When chloromethyltrimethylsilane was condensed with Ia, using ether as the solvent, none of the desired product (XII) could be isolated. However, the replacement of ether by THF resulted in a 33% yield of pure XII. In the event THF was employed as the condensation solvent, Ia was prepared in ether, filtered, washed

TABLE I

2,5- Disubstituted Furan Derivatives



Compound	R_1	R_2	Yield %	B. P. °C	Formula	Calcd. % C	Calcd. % H	Calcd. % Si	Found % C	Found % H	Found % Si
I-d[5]	D	(a)	93	82/23 mm	$C_9H_{13}O_3D$						
II	$(CH_3)_3Si$-	(a)	80	65/.5 mm	$C_{12}H_{22}O_3Si$	59.46	9.14	11.58	59.63	9.17	11.44
III	$(CH_3)_3Si$-	(b)	90	117/.23 mm	$C_8H_{12}O_2Si$	57.10	7.19	16.69	56.92	7.20	16.61
IV	$(CH_3)_2C_2H_5Si$-	(a)	78	74/.6 mm	$C_{13}H_{24}O_3Si$	60.89	9.43	10.95	60.93	9.50	11.03
V	$(CH_3)_2C_2H_5Si$-	(b)	96	61/.9 mm	$C_9H_{14}O_2Si$	59.30	7.74	15.41	59.14	7.80	15.20
VI	$(CH_3)_2C_6H_5Si$-	(a)	80	110/.15 mm	$C_{17}H_{24}O_3Si$	67.06	7.94	9.23	66.91	7.68	9.19
VII	$(CH_3)_2C_6H_5Si$-	(b)	90	94/.15 mm	$C_{13}H_{14}O_2Si$	67.79	6.12	12.19	67.83	5.94	12.69
VIII	$(C_2H_5)_3Si$-	(a)	69	120/1.8 mm	$C_{15}H_{28}O_3Si$	63.33	9.92	9.87	63.51	10.00	9.80
IX	$(C_2H_5)_3Si$-	(b)	85	100/1.0 mm	$C_{11}H_{18}O_2Si$	62.81	8.63	13.35	62.59	8.57	13.43
X	$(C_2H_5)_2C_6H_5Si$-	(a)	80	126/.15 mm	$C_{19}H_{28}O_3Si$	68.63	8.49	8.45	68.68	8.24	8.30
XI	$(C_2H_5)_2C_6H_5Si$-	(b)	92	119/.2 mm	$C_{15}H_{18}O_2Si$	69.73	7.02	10.87	69.52	7.16	10.68
XII	$(CH_3)_3SiCH_2$-	(a)	33	81/.9 mm	$C_{13}H_{24}O_3Si$	60.89	9.43	10.95	61.19	8.63	10.82
XIII	$(CH_3)_3SiCH_2$-	(b)	95	65/.9 mm	$C_9H_{14}O_2Si$	59.30	7.74	15.41	59.16	7.73	15.28
XIV	HO_2C-	(b)	80	(c)	$C_6H_4O_4$	51.44	2.87	---	51.65	2.94	---
XV	C_6H_5CO-	(b)	48	(d)	$C_{12}H_8O_3$	72.00	4.03	---	71.82	4.00	---

(a) $-CH(OC_2H_5)_2$. (b) -CHO. (c) We observed a melting point of 204°; literature melting point, 207-208° (O. Moldenhauer, G. Trautmann, W. Irion, R. Pfluger, H. Doser, D. Mastaglio, H. Marwitz and R. Schulte, *Ann. Chem.*, 580, 169 (1953). (d) 95° m.p.

with ether, and subsequently placed in anhydrous THF to which was then added the appropriate electrophile. This is necessary in that the metalation of I in THF is uncontrollable even at -15°, thereby producing extensive decomposition, while in ether the metalation proceeds smoothly at -10°. We are presently investigating the factors governing the stability of Ia as well as its potential applications.

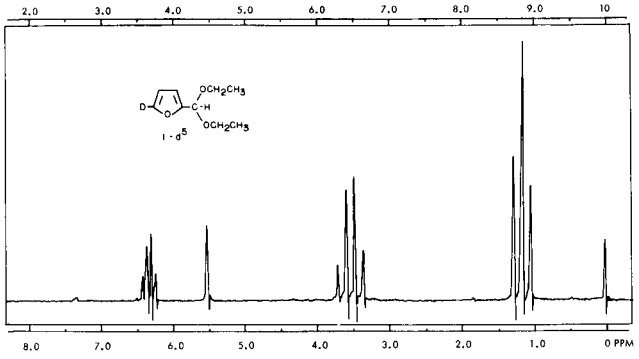


FIGURE I

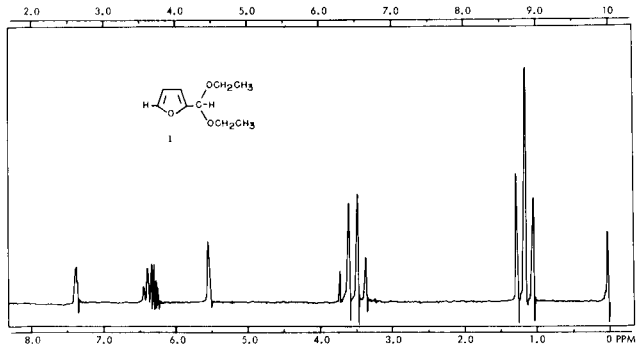


FIGURE II

In a typical experiment (Scheme A), an ethereal (anhydrous) solution of I was cooled to -15° and treated dropwise with an equivalent amount of butyllithium in hexane. Butyllithium was added at such a rate so as to maintain a temperature of -10°. After addition is complete, the appropriate electrophile was added slowly with stirring. The reaction mixture was then refluxed for 4 hours, cooled, and the lithium chloride separated by filtration. The filtrate was concentrated and fractionally distilled *in vacuo* to produce the desired 5-silicon substituted furfural diethylacetal derivative (Table I). The acetal derivatives were obtained in high yields only when care was taken to exclude all moisture and acidic materials. If either were present, a mixture of acetal and aldehyde was obtained. Hydrolysis of the acetal moiety was accomplished in high yield by dissolving the diethylacetal derivative in ether and refluxing with an aqueous solution of *p*-toluenesulfonic acid for 1 hour. The mixture was cooled, the layers separated, and the aqueous phase extracted with ether. The combined ethereal extracts were washed with 5% sodium carbonate solution until the washings remain basic, at which time the ethereal layer was dried over sodium sulfate, concentrated, and the residue distilled *in vacuo* to obtain the desired organosilicon substituted furfurals (Table I).

Compounds XIV and XV were synthesized to show the versatility of the reaction sequence.

EXPERIMENTAL

The melting points reported were determined on a Mel-Temp apparatus and are uncorrected. The infra-red spectra were determined with a Beckman IR-5 spectrophotometer. The NMR spectra were determined on a Varian A-60 spectrophotometer, with tetramethylsilane as a standard reference material. Microanalyses were performed by Galbraith Laboratories Inc., Knoxville, Tennessee. All reactions were conducted under an atmosphere of nitrogen and in anhydrous conditions. All chlorosilanes were distilled prior to use. Distillations were carried out using a 10" Vigreux Column.

Furfuraldiethylacetal (I).

A mixture of 113.7 g. (132 ml., 1.19 moles) of 2-furfural and 216 g. (240 ml., 1.46 moles) of ethyl orthoformate was placed in a 500 ml. 3-necked flask equipped with a condenser and mechanical stirrer. A warm solution of ammonium nitrate (4.5 g.) in absolute ethanol (75 ml.) was added and the mixture refluxed for 6 hours. The residual solids were removed by filtration, sodium carbonate was added (4.5 g.), and the mixture fractionally distilled to give 180 g. (90%) of I, boiling at 81-83°/23 mm, lit. b.p., 67°/13 mm (6).

5-Lithio-2-furfuraldiethylacetal (Ia).

Into a dry 250 ml. 3-necked flask equipped with condenser, nitrogen inlet, dropping funnel, thermometer, and mechanical stirrer, was placed 8.5 g. (0.05 mole) of I in 150 ml. of dry ether. The flask was placed in an ice-salt bath and cooled to -15°. To the cold stirring mixture was added 0.048 mole of butyllithium (in hexane) at such a rate so as not to exceed a reaction temperature of -10°. After addition, stirring was continued for 4 hours at ambient temperature at which time a near quantitative yield of crystalline Ia could be obtained by suction filtration.

2-Furfuraldiethylacetal-d^5 (I-d^5).

An ethereal slurry of Ia (0.015 mole) was treated with 2 g. (0.1 mole) of deuterium oxide over a 10 minute period. The organic layer was separated, dried over sodium sulfate, concentrated *in vacuo*, and the residue distilled to give 2 g. (93%) of I-d^5 boiling at 82°/23 mm.

The preparation of 5-trimethylsilyl-2-furfuraldiethylacetal (II) will serve as a general procedure for the preparation of 5-silyl substituted-2-furfuraldiethylacetals.

A suspension of Ia (0.05 mole) in 150 ml. of anhydrous ether was allowed to reflux with 5.4 g. (0.05 mole) of trimethylchlorosilane for 4 hours. The mixture was cooled, the precipitated lithium chloride was removed by filtration, and the filtrate concentrated by distillation. The residue was fractionally distilled *in vacuo* to give 9.7 g. (80%) of II boiling at 65.6°/0.5 mm.

The following substituted furfuraldiethylacetals were prepared according to the above procedure.

5-Dimethylethylsilyl-2-furfuraldiethylacetal (IV).

This compound was produced in 78% yield when Ia (0.05 mole) in anhydrous ether was allowed to react with dimethylethylchlorosilane, b.p. = 74°/0.6 mm.

5-Dimethylphenylsilyl-2-furfuraldiethylacetal (VI).

This compound was produced in 80% yield when Ia (0.05 mole) in anhydrous ether was allowed to reflux with 8.5 g. (0.05 mole) of dimethylphenylchlorosilane overnight, b.p. = 110°/0.15 mm.

5-Triethylsilyl-2-furfuraldiethylacetal (VIII).

This compound was prepared in 69% yield by allowing Ia (0.05 mole) in dry ether to react with 6.8 g. (0.046 mole) of triethylchlorosilane for 6 hours, b.p. = 120.5°/1.8 mm.

5-Diethylphenylsilyl-2-furfuraldiethylacetal (X).

This compound was prepared in 80% yield by allowing an ethereal suspension of Ia (0.05 mole) to react with 9.9 g. (0.05 mole) of diethylphenylchlorosilane for 8 hours, b.p. = 126°/0.15 mm.

The preparation of 5-trimethylsilyl-2-furfural (III) will serve as an example procedure for the preparation of 5-silylsubstituted-2-furfurals.

An ethereal solution (20 ml.) of II (8 g., 0.03 mole) was allowed to reflux with 0.1 g. of *p*-toluenesulfonic acid and 20 ml. of water for 1 hour. The layers were separated and the aqueous phase extracted with ether. The ether layer was combined with the ethereal extracts and washed with 5% sodium carbonate solution until the washings remained basic. The extracts were dried over sodium sulfate, concentrated *in vacuo*, and fractionated to give 5 g. (90%) of III boiling at 117°/0.23 mm.

The following 5-silicon substituted furfurals were prepared according to the above procedure.

5-Dimethylethylsilyl-2-furfural (V).

This compound was prepared from IV (8 g., 0.031 mole) in 96% yield, b.p. = 61°/0.9 mm.

5-Dimethylphenylsilyl-2-furfural (VII).

This compound was prepared from VI (10 g., 0.033 mole) in 90% yield, b.p. = 94°/0.15 mm.

5-Triethylsilyl-2-furfural (IX).

This compound was prepared from VIII (9.0 g., 0.032 mole) in 85% yield, b.p. = 100°/1.0 mm.

The 2,4-dinitrophenylhydrazone derivative was prepared in the usual manner. Purification was accomplished by crystallization from ethanol and sublimation to give the pure compound melting at 155°.

Anal. Calcd. for $C_{17}H_{21}N_4O_5Si$: C, 52.42; H, 5.43. Found: C, 51.97; H, 5.52.

5-Diethylphenylsilyl-2-furfural (XI).

This compound was prepared from X (11.6 g., 0.035 mole) in 92% yield, b.p. = 119°/0.2 mm.

5-Trimethylsilylmethylene-2-furfuraldiethylacetal (XII).

The lithio salt, Ia, (0.05 mole) was initially prepared in ether, filtered, washed with dry ether and dried. Tetrahydrofuran, 150 ml. distilled from lithium aluminum hydride, was then added to Ia and the resulting solution was treated with chloromethyltrimethylsilane (0.05 mole) and refluxed for 20 hours. The resulting solution was concentrated to 30 ml., anhydrous ether was added (100 ml.) and the precipitated salt was removed by filtration followed by solvent evaporation and distillation *in vacuo* to give 4.2 g. (33%) of XII boiling at 81°/0.9 mm.

5-Trimethylsilylmethylene-2-furfural (XIII).

This compound was prepared from XII in the usual manner. A yield of 95% was obtained with the liquid product boiling at 65°/0.9 mm.

2-Aldehydo-5-furoic acid (XIV).

A suspension of Ia (0.05 mole) in 150 ml. of anhydrous ether was treated for 2.5 hours with anhydrous gaseous carbon dioxide. At that time 9.5 g. of *p*-toluenesulfonic acid in 100 ml. of water was added dropwise at -10° and the resulting mixture was refluxed for 1 hour. The layers were separated and the ether evaporated to yield XIV (5.6 g., 80%) which, after several sublimations, melted at 204°.

5-Benzoyl-2-furfural (XV).

A suspension of Ia (0.05 mole) in 150 ml. of dry ether was refluxed overnight with 5.15 g. (0.05 mole) of benzonitrile, at which time the mixture was cooled to -10° and 9.5 g. of *p*-toluenesulfonic acid in 100 ml. of water was added. The resulting mixture was refluxed for 2 hours, cooled, and the layers separated. The ether was evaporated and the light tan solid which formed was sublimed to yield XV (4.8 g., 48%) melting at 95°.

Acknowledgment.

We owe our appreciation to the Faculty Research Fund of The University of Southern Mississippi, administered by Dr's. J. H. Allen and R. W. Peters, and to the Department of the Army and U. S. Army Medical Research and Development Command through contract No. DA-49-193-MD-2910 for financial aid. We are also grateful to Dr. W. H. Daudt of Dow-Corning for a generous supply of several chlorosilanes and to Mrs. Sylvia Horton Miles of the Southern Regional Research Laboratory, New Orleans, La., for running the NMR spectra.

REFERENCES

(1) S. F. Thames and J. E. McCleskey, *J. Heterocyclic Chem.*, 3, 104 (1966).

(2) R. G. Pearson, *J. Am. Chem. Soc.*, 85, 3533 (1963).

(3) K. D. Berlin, B. S. Rathore, and M. Peterson, *J. Org. Chem.*, 30, 226 (1965).

(4) Rogovik and Gol'dfarb have conducted similar experiments in the thiophene series; V. I. Rogovik and Ya. L. Gol'dfarb, *Khim. Geterotsikl. Soedin., Akad. Nauk Latv. SSR*, 657 (1965); *Chem. Abstr.*, 64, 14156h (1966).

(5) J. F. Eastham and C. G. Screttas, *J. Am. Chem. Soc.*, 87, 3276 (1965).

(6) N. Minne and H. Adkins, *ibid.*, 55, 299 (1933).

Received September 7, 1966 Hattiesburg, Mississippi 39401