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Fluorination with Substituted (Difluoroiodo)arenes

Ana Gregorčič and Marko Zupan*

"J. Stefan" Institute and Department of Chemistry, University of Ljubljana, 61000 Ljubljana, Yugoslavia

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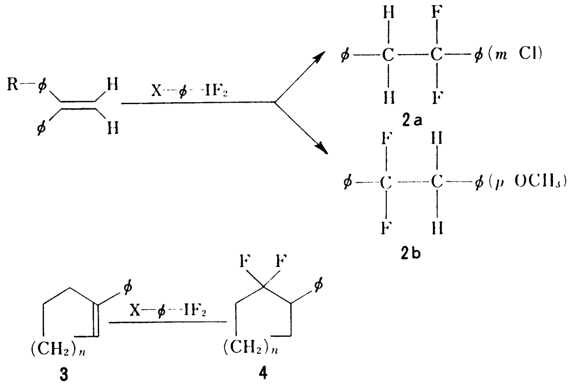
The reaction of substituted (difluoroiodo)arenes with 1-phenyl-1-(*m*-chlorophenyl)ethylene results in 1,1-difluoro-1-(*m*-chlorophenyl)2-phenylethane, with 1-phenyl-1-(*p*-methoxyphenyl)ethylene in 1,1-difluoro-1-phenyl-2-(*p*-methoxyphenyl)ethane, and with 1-phenylcyclopentene and 1-phenylcyclohexene in rearranged *gem*-difluoro compounds. The reaction with norbornene results in three products: fluoronortricyclane (9—12%), 2-*exo*-7-*syn*-difluoronorbornane (75—86%), and 2-*exo*-7-*anti*-difluoronorbornane (5—15%) depending upon the substituent on the phenyl ring in (difluoroiodo)arenes.

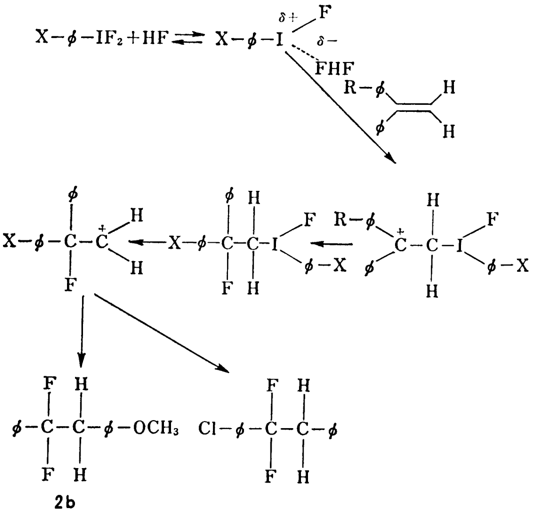
The addition of chlorine to olefinic double bonds using (dichloroiodo)benzene as a halogenating agent has received (difluoroiodo)arenes attention from several workers.[2–5] The corresponding received much more limited attention as fluorinating agents, possibly because of the difficulties involved in their preparation and storage. Three methods are of particular interest for the preparation of (difluoroiodo)arenes. The first is the method of Dimroth and Bockemüller[6] or the modified one of Garvey *et al.*[7] in which the appropriate iodosoarene is treated with 46% hydrogen fluoride in acetic acid. The method of Carpenter[8] involves one-step reaction of mercuric oxide and aqueous hydrofluoric acid with (dichloroiodo)benzene in dichloromethane. The dichloromethane solution is then used directly for fluorination. The third procedure[9] involves the electrolysis of an acetonitrile solution of silver(I) fluoride. We developed a method for the synthesis of various (difluoroiodo)arenes, using xenon difluoride as fluorinating agent in dichloromethane solution, in the presence of anhydrous hydrogen fluoride at room temperature.[10] We have recently found that (difluoroiodo)methane reacts with phenylalkenes in the presence of hydrogen fluoride as a catalyst to form the corresponding 1-fluoro-2-iodo-1-phenylalkanes,[11] and not the rearranged *gem*-difluoro compounds observed in similar fluorination reactions with (difluoroiodo)arenes.[8,12] We now report the study of fluorination of various phenylalkenes and norbornene with substituted (difluoroiodo)arenes.

Results and Discussion

(Difluoroiodo)arenes have already been used for fluorination of 1,1-diphenylene[12] and styrene[8], giving *gem*-difluoro compunds. Carpenter[8] showed that hydrogen fluoride or some other strong acid such as trifluoroacetic acid is necessary as a catalyst in the fluorination reaction, and proposed an ionic mechanism with the phenonium ion as the intermediate. We obtained evidence which supports the phenonium ion intermediate by the fluorination of 1-phenyl-1-(*m*-chlorophenyl)ethylene (**1a**), 1-phenyl-1-(*p*-methoxyphenyl)ethylene (**1b**) with substituted (difluoroiodo)arenes (Scheme 1). The reactions resulted in 1,1-difluoro-1-(*m*-chlorophenyl)-2-phenylethane (**2a**) and 1,1-difluoro-1-phenyl-2-(*p*-methoxyphenyl) ethane (**2b**), respectively. The structures of the products were estabished on the basis of their NMR data (δF-100 ppm (t, $J_{\mathrm{FH}}=15$ Hz)) for **2a** and (δF-105.2 ppm (t, $J_{\mathrm{FH}}=16.5$ Hz)) for **2b**, which correspond to those of *gem*-difluoro compounds. In the mass spectrum the fragments for the product **2a** were the tropylium ion *m/e* 91 and the difluorochlorobenzylium ion *m/e* 161, indicating phenyl group migration. On the other hand, product **2b** showed as fragments the methoxytropylium ion *m/e* 121 and the difluorobenzylium ion *m/e* 127, which indicates *p*-methoxyphenyl group migration. The fluorination of the phenyl-substituted cycloolefins, 1-phenylcyclopentene (**3a**) and 1-phenylcyclohexene (**3b**), with (difluoroiodo)arenes also resulted in the formation of *gem*-difluoro compounds (**4**) (Scheme 1), which could be identified by their NMR and mass spectral data. We were unable to detect any trace of



Scheme 1.



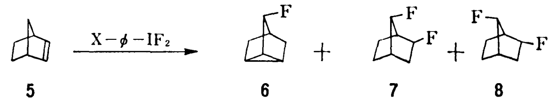
Scheme 2.

iodofluoro compounds. In the light of these experiments we suggest a mechanism similar to that proposed by Carpenter[8] (Scheme 2). It might be expected that in the presence of hydrogen fluoride, substituted (difluoroiodo)arenes behave as electrophiles (reactions were completely quenched when no hydrogen fluoride was added), adding to an olefin, thus forming a carbonium ion, which is then attacked by the fluoride ion. In the next step, dissociation of the carbon iodine bonds results in the formation of carbonium ion, accompanied by phenyl group or *p*-methoxyphenyl group migration.

The reaction of a bicyclic olefin, norbornene, has been utilized for elucidating the mechanism and stereochemistry of various reactions.[13–18] It is possible (from the identification of the products) to discriminate the three possible mechanistic pathways leading to the products; (i) a concerted *cis*-molecular addition, (ii) a free radical reaction, (iii) a reaction path proceeding *via* cationic intermediates.

We have studied the fluorination reaction of various substituted (difluoroiodo)arenes with norbornene. Reactions resulted in the formation of three products, which could be separated by preparative GLC. The first product shows in its ^{19}F NMR (rel to CCl_3F) spectrum a doublet of triplet at −218.2 ppm, and in H NMR spectrum at $\delta = 5.05$ ppm a doublet of triplet signal which corresponds to the proton bonded on the same carbon atom as the fluorine atom, with the characteristic geminal F–H coupling constant of 69 Hz. The product **6** was synthesised independently by addition of hydrogen fluoride to norbornadiene,[19] which made it possible to determine the structure of the first product as fluoronortricyclane (**6**). Both of the remaining products showed a similar mass spectrum with the molecular peak m/e 132, which suggests the structure of the difluoro compounds. The basic peak for both of the products m/e 81 corresponds to the splitting off of the fragment $-CHF_2$. In the mass spectra of both compounds, the fragments were m/e 99, 86, 85, 72, which correspond to the splitting off of $-CH_2F$, $-C_2H_3F$, $-C_2H_4F$, and C_3H_5F fragments, respectively. From the extraordinary similarity of the mass spectra we concluded that the two compounds are remarkably alike. The product obtained in the lower yield (5—13%), shows in its ^{19}F NMR spectra two signals; one at −176.2 ppm as doublet of multiplet, corresponding to an *exo*-bonded fluorine atom, and the other at −232.3 ppm as doublet of triplet, which corresponds to fluorine bonded at C7. In the proton spectrum we have observed two signals for hydrogen atoms at lower field, the first at $\delta = 4.28$ ppm as doublet of multiplet, corresponding to an *endo*-bonded hydrogen atom, and the second signal at $\delta = 5.48$ ppm as doublet, which corresponds to a hydrogen atom at C7 (see Experimental).

The main product formed in the fluorination of norbornene with substituted (difluoroiodo)arenes shows an NMR spectrum very similar to that of the previously described one.[18] In the ^{19}F spectrum we observed a signal at −179.5 ppm as doublet of multiplet and the second at −223.5 ppm as doublet of multiplet. In the proton NMR we observed two protons at a lower field, one at 5.1 ppm as a doublet of doublet and the other at 5.21 ppm as a doublet. From the data we were unable to decide the stereochemistry at position C7. However, from a detailed comparison of the NMR spectra with the literature ones[18] the stereochemistry on C7 could be confirmed. If we compare the chemical shifts for protons bonded at C7 in various substituted norbornane derivatives[18] we see that the one in the 2-*exo*-7-*anti* isomer is at a lower field than the one in the 2-*exo*-7-*syn* isomer. The chemical shift for the proton at C2 is at a higher field in the 2-*exo*-7-*anti* isomer (but not in all cases) than in the 2-*exo*-7-*syn* isomer. Tanner and Van Bostelen[18] established the stereochemistry at the Carbon 7 also by chemical transformations, *i.e.*, dehydrofluorination and reduction. From the data mentioned above, we can conclude that the main product, formed in 75—86% yield, is 2-*exo*-7-*syn*-difluoronorbornane (**7**), and the third product, obtained in 5—13% yield, is 2-*exo*-7-*anti*-difluoronorbornane (**8**) (Scheme 3).



Relative yields[a)]

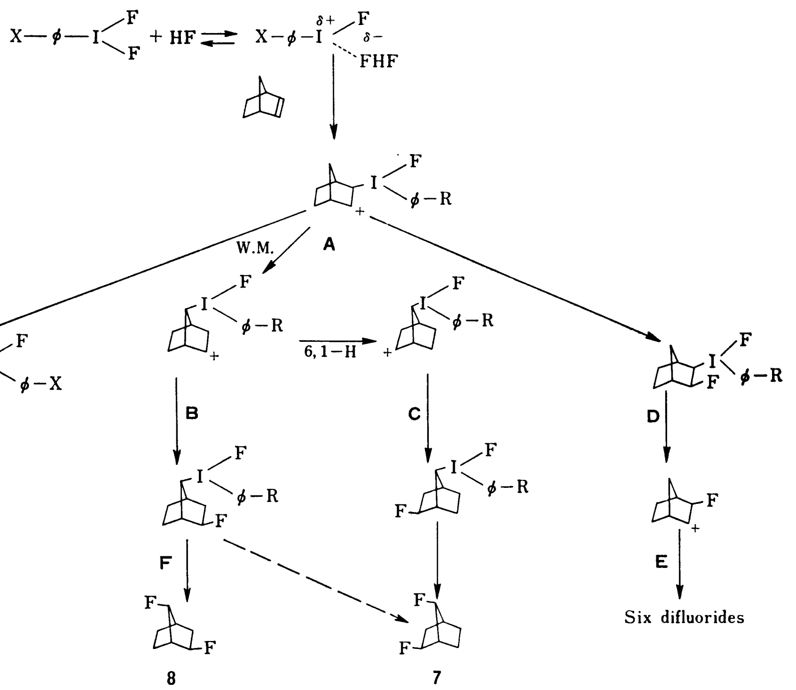
X	6	7	8
p-OCH$_3$	12	75	13
m-OCH$_3$	18	74	8
H	9	84	7
m-Cl	6	88	6
m-NO$_2$	9	86	5

a) Determined by GLC.

Scheme 3.

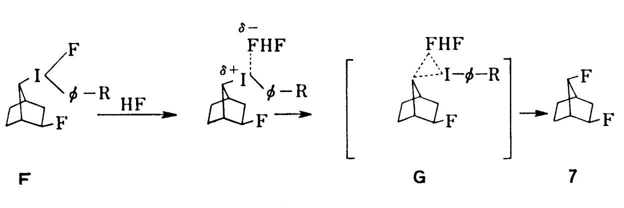
We have studied the effect of groups bonded to benzene ring on the distribution of the products formed in the reaction of norbornene with substituted (difluoroiodo)arenes. The ratios of the products were established by VPC. Each reaction was repeated several times the average data being presented in Scheme 3. We observed no isomerisation of the products under the reaction and isolation conditions or during the course of isomerisation. The data (Scheme 3) show a very high yield (86%) of 2-*exo*-7-*syn*-difluoronorbornane (**7**) formed in the reaction with the *m*-nitro derivative. On the other hand, with electron donating substituents bonded to the benzene ring of (difluoroiodo)arenes, we observed a lower amount of product **7** and a higher amount of compound **8**.

The formation of three products could be explained by the reaction of norbornene with the polarized molecule of (difluoroiodo)arenes with hydrogen fluoride, thus primarily forming the carbonium ion A (Scheme 4) which undergoes the Wagner-Meerwein rearrangement, in turn forming ions B, which could be attacked by the nucleophile, leading to the product F. The S_N2 substitution of the aryliodo function by fluoride anion can produce 2-*exo*-7-*anti*-difluoronorbornane (**8**). Carbonium ion B can undergo the hydride 6—1 shift, thus forming carbonium ion C, followed by nucleophilic attack of fluoride anion and



Scheme 4.

S_N2 substitution of aryliodo function, resulting in the formation of 2-*exo*-7-*syn*-difluoronorbornane (**7**). The next possibility for an explanation of the formation of difluoro compounds could be the attack of fluoride anion on the primarily formed carbonium ion A, thus forming the adduct D, and dissociation of carbon–iodine bond leading to formation of fluorocarbonium ion E, which would rearrange by Wagner-Meerwein and hydride shift, resulting in six difluoro compounds. The β-fluorocarbonium ion E formed in the reaction of xenon difluoride with norbornene undergoes rearrangement, thus forming six difluoro compounds[20] after fluoride anion attack. From the results we could eliminate this reaction pathway. However, we suggest another possible explanation for the formation of product **7** in a high yield (Scheme 5). The intermediately formed compound F can be polarized by hydrogen fluoride and *via* the transition state G results in difluoro compounds.



Scheme 5.

Experimental

IR spectra were recorded with a Perkin-Elmer 257 spectrometer, ^1H and ^{19}F NMR spectra with a Jeol JNM-PS-100 from CCl_4 solution with TMS or CCl_3F as an internal reference. Mass spectra and high resolution measurements were taken on a CEC-21-110 spectrometer. Gas-Liquid partition chromatography was carried out on a Varian Aerograph Model 1800 and TLC on Merck PSC-fertigplatten SILICA GEL F-254.

Materials. Pure samples of olefins were prepared by known methods: 1-phenyl-1-(*m*-chlorophenyl)ethylene,[21] 1-phenyl-1-(*p*-methoxyphenyl)ethylene,[21] 1-phenylcyclopentene,[22] 1-phenylcyclohexene.[22] Other commercial olefins were distilled or purified by VPC to conform with published physical and spectral data. Substituted iodobenzenes were prepared by known methods from corresponding amino derivatives and distilled before use. Dichloromethane was purified[23] and stored over molecular sieves. Hydrogen fluoride of Fluka Purum quality was used, and xenon difluoride was prepared by the photosynthetic method[24] with a purity better than 99.5%.

Substituted (Difluoroiodo)benzenes. Substituted iodobenzene (1.1 mmol) was dissolved in dichloromethane (5 ml) at room temperature. Anhydrous HF (1—3 mmol) was introduced into the reaction mixture and pure XeF_2 (1.1 mmol) was added under stirring. After a few second the colourless solution turned dark green, xenon gas being evolved. Gas evolution ceased after 45 min (for *p*-OCH_3, or 3 h for the *m*-NO_2 derivative) and the reaction appeared to be complete. The solution was used for fluorination of olefins.

General Procedure for Fluorination with Substituted (Difluoroiodo)arenes: To a solution of the previously prepared substituted (difluoroiodo)arenes was added 1 mmol of olefin under stirring at room temperature. After 2 h the reaction mixture was diluted with dichloromethane (15 ml), washed with 10 ml of 5% $NaHCO_3$, dried over anhydrous Na_2SO_4, the solvent being evaporated *in vacuo*. The crude products were separated by preparative TLC or GLC.

1,1-Difluoro-1-(m-chlorophenyl)-2-phenylethane (**2**)*:* The product was separated by preparative TLC (silica gel, methanol : chloroform = 1 : 9) yield 50% of oily product. NMR δF-100 ppm (t), $\delta H=3.25$ (t), ppm, $\delta\phi=7.2$ (m) ppm, $J_{FH}=15$ Hz. Mass spectrum: calcd for $C_{14}H_{11}ClF_2$ *m/e* 252.0517, found *m/e* 252.0510, *m/e*: 254 (M^++2,4%), 252 (M^+, 12%), 215 (40), 179 (40), 178 (46), 163 (10), 161 (30), 91 (100), 89 (18), 77 (20), 76 (20), 75 (16), 51 (25).

1,1-Difluoro-1-phenyl-2-(p-methoxyphenyl)ethane (**2b**)*:* The product was separated by preparative TLC (silica gel, methanol : chloroform = 1 : 9), yield 55% of yellow oily product. NMR δF-105.0 (t) ppm, δH = 3.3 (t) ppm, δOCH_3 = 3.7 (s) ppm, $\delta\phi$ = 7.2 (m) ppm, J_{FH} = 16.5 Hz. Mass spectrum: calcd for $C_{15}H_{14}F_2O$ *m/e* 248.1008, found *m/e* 248.1008, *m/e*: 248 (100%, M^+), 209 (46), 197 (40), 165 (46), 139 (40), 127 (46), 121 (60), 77 (40).

*1-Phenyl-2,2-difluorocyclopentane (**4a**)*: The product was separated by preparative TLC (silica gel, cyclohexane: chloroform = 4 : 1), yield 60% of yellow oily product. NMR δF-101.3 (m) ppm, $\delta\phi$ = 7.3 (m) ppm, δH = 2 (m) ppm. Mass spectrum: calcd for $C_{11}H_{12}F_2$ *m/e* 182.0902, found *m/e* 182.0911, *m/e*: 182 (M^+, 3%), 155 (14), 154 (100, 153 33 (33), 152 (21), 117 (47), 115 (50), 77 (10), 76 (17).

*1-Phenyl-2,2-difluorocyclohexane (**4b**)*: The product was separated by preparative TLC (silica gel, methanol: chloroform = 1 : 9), yield 63% of yellow oily product. NMR δF-103.5 (m) ppm, $\delta\phi$ = 7.5 (m) ppm, δH = 1.7 (m) ppm. Mass spectrum: calcd for $C_{12}H_{14}F_2$ *m/e* 196.0125, found *m/e* 196.0160, *m/e*: 196 (M^+, 35%), 176 (9), 173 (9), 158 (14), 154 (55), 153 (21), 152 (13), 130 (22), 129 (17), 128 (30), 127 (100), 117 (37), 104 (30), 91 (33), 77 (38), 69 (48), 68 (55), 58 (34).

Products Formed in the Fluorination of Norbornene: Separated by preparative GLC (Chromosorb Regular 100-DDP 10%, ϕ 3/8′×2 m, stainless steel column).

Fluoronortricyclane (6): Yield 8% of volatile, white waxy solid product, mp (sealed capillary) 44—45 °C, lit,[19] 48—50 °C. NMR (CCl_4): δF-218.2 (dt) ppm, δH = 5.05 (dt) ppm, J_{FH} = 69 Hz. Mass spectrum: calcd for C_7H_9F *m/e* 112.0688, found *m/e* 112.0697.

*2-*exo*-7-*syn*-Difluoronorbornane (7)*: Yield 68% of volatile, white waxy solid product, mp (sealed capillary) 116—119 °C, lit,[18] 95—97 °C. NMR (CCl_4): δF2-179.5 (dm) ppm, δF7-223.5 (dm) ppm, δH_2 = 5.1 (dd) ppm, δH7 = 5.2 (d) ppm, J_{F2H2} = 60 Hz, J_{F2H} = 40 Hz, J_{F7H7} = 63 Hz, J_{F7H} = 12.6 Hz. Mass spectrum: calcd for $C_7H_{10}F_2$ *m/e* 132.0752. Anal. calcd for $C_7H_{10}F_2$: C, 63.60; H, 7.63; found C, 63.32; 7.40.

*2-*exo*-7-*anti*-Difluoronorbornane (8)*: Yield 6% of volatile, waxy solid product, mp (sealed capillary) 101—102 °C, lit,[18] 107—110 °C. NMR (CCl_4): δF2-176.2 (dm) ppm, δF7-232.3 (dt) ppm, δH2 = 4.28 (dm) ppm, δH7 = 5.48 (d) ppm, J_{F2H2} = 60 Hz, J_{F2H} = 30 Hz, 7.5 Hz, J_{F7H7} = 65 Hz, J_{F7H} = 3 Hz. Mass spectrum calcd for $C_7H_{10}F_2$ *m/e* 132.0750, found *m/e* 132.0753. Anal. calcd for $C_7H_{10}F_2$: C, 63.60; H, 7.63, found C, 63.44; H, 7.70.

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References

1) Presented in part at 5 th European Symposium on Fluorine Chemistry, Aviemore, September 1974.

2) D. F. Banks, *Chem. Rev.*, **66**, 243 (1966).

3) D. H. R. Barton and E. Miller, *J. Am. Chem. Soc.*, **72**, 370 (1950).

4) S. J. Cristol, F. R. Stermitz, and P. S. Ramey, *J. Am. Chem. Soc.*, **78**, 4939 (1956).

5) D. D. Tanner and G. C. Gidley, *J. Org. Chem.*, **33**, 38 (1968).

6) O. Dimroth and W. Bockemüller, *Ber.*, **64**, 516, 522, (1931).

7) B. S. Garvey, Jr., L. F. Halley, and C. F, Allen, *J. Am. Chem. Soc.*, **59**, 1827 (1937).

8) W. Carpenter, *J. Org. Chem.*, **31**, 2688 (1966).

9) H. Schmidt and H. Meinert, *Angew. Chem.*, **72**, 109 (1960).

10) M. Zupan and A. Pollak, *J. Fluorine Chem.*, in press.

11) M. Zupan and A. Pollak, *Tetrahedron Lett.*, **1975**, 3576.

12) J. Bornstein, M. R. Borden, F. Nunes, and H. I. Tarlin, *J. Am. Chem. Soc.*, **85**, 1909 (1963).

13) R. C. Fahey, *Top. Stereochem.*, **3**, 237 (1968).

14) J. A. Berson, "Carbonium Ion Rearrangement in Bridged Bicyclic Systems," in Molecular Rearrangements, Vol. 1, Part 2, ed by P. de Mayo, Interscience, New York (1963), p. 111.

15) T. G. Traylor, *Acc. Chem. Res.*, **2**, 152 (1969).

16) D. R. Marshall, P. Reynolds-Warnhoff, E. W. Warnhoff, and J. R. Robinson, *Can. J. Chem.*, **49**, 885, (1971).

17) H. C. Brown and Kwang-Tin Liu, *J. Am. Chem. Soc.*, **97**, 2469 (1975).

18) D. D. Tanner and P. Van Bostelen, *J. Am. Chem. Soc.*, **94**, 3187 (1972).

19) M. Hanack and W. Kaiser, *Justus Liebigs Ann. Chem.*, **1962**, 657, 12.

20) M. Zupan, A. Pollak, and A. Gregorčič, presented in part at Sastanak Kemičara Hrvatske 1975, Zagreb, Yugoslavia. We isolated: 2-*exo*-3-*exo*-, 2-*exo*-3-*endo*-, 2-*exo*-5-*exo*-, 2-*exo*-5-*endo*-, 2-*exo*-7-*syn*- and 2-*exo*-7-*anti*-difluoronorbornane.

21) J. E. Dubois, A. F. Hegarty, and E. D. Bergmann, *J. Org. Chem.*, **37**, 2218 (1972).

22) E. W. Garbisch, *J. Org. Chem.*, **26**, 4165 (1961).

23) J. H. Mathews, *J. Am. Chem. Soc.*, **48**, 562 (1926).

24) S. M. Williamson, *Inorg. Syn.*, **11**, 147 (1968).