liquid samples, KBr pellet for solids). Pmr spectra were recorded with a JEOL 60 spectrometer. Mass spectra were recorded with a low-resolution Perkin-Elmer 270 instrument equipped with gas chromatographic eluate direct inlet into the ion source, with target temperatures ranging from 100 to 220°, electron energy 75 eV, and acceleration potential 2 kV. Ten highest peaks are reported (*m/e* values, relative intensity, and eventual ion interpretation are given in brackets).[10]

Aziridine was purchased from Fluka (Switzerland). *N*-Benzylaniline was prepared in 60% yield according to a method described in the literature:[11] ir 3310 m, 3010 m, 2830 w, 1603 s, 1500 s, 1455 s, 1430 m, 1360 m, 1320 s, 1265 s broad, 1180 m, 1155 m, 1095 m, 1075 m, 1060 m, 1030 m, 985 m, 865 w, 745 s broad, and 690 cm^{-1} s; mass spectrum (glc inlet, target 220°) 91 (100, C_7H_7), 183 (52, parent peak), 182 (19, immonium ion), 106 (18, loss of C_6H_5, methylene immonium ion), 77 (17, C_6H_5), 65 (17), 92 (9), 104 (9), 184 (8), and 51 (8).

***N*-Benzylaziridine.**—Aziridine (386 mmol) was added dropwise under stirring below 0° to a hexane solution of *n*-butyllithium (0.96 *N*, 386 mmol) in an atmosphere of dry argon. To this mixture in the same conditions benzyl chloride (386 mmol) was added dropwise. The resulting mixture was stirred during 12 hr at room temperature, then chilled to −10°, and treated with cold brine, and the organic layer separated. The organic layer was extracted with 15% hydrochloric acid at −15°, the separated aqueous extract was dropped carefully into 40% aqueous KOH kept at −10°, and the mixture extracted with ether, dried over sodium sulfate, and vacuum distilled. **3** was obtained as a colorless liquid: bp 87–89° (12 Torr);[12] yield 46.8%; glc homogeneous; ir 3080 m, 3000 m, 2850 w, 2680 w, 1500 w, 1460 m, 1275 m, 1160 w, 1032 w, 1010 m, 821 w, 778 s, 695 cm^{-1} s; pmr (CCl_4, τ values in ppm from TMS) 2.74 (m, 5 Ar H), 6.77 (s, 2 H), 8.38 (def t, 2 cis-H), and 9.02 (def t, 2 trans H); mass spectrum (glc inlet, target 100°) 42 (100, C_2H_4N), 91 (60, C_7H_7), 65 (15, C_5H_5), 132 (14, loss of H, immonium ion), 51 (12), 105 (10, C_7H_7N), 77 (8, C_6H_5), 39 (8, C_3H_3), 133 (7, parent peak), and 103 (5, C_7H_5N).

Benzyne Addition to *N*-Benzylaziridine.—*n*-Butyllithium (1.13 *M* in hexane, 76 mmol) was added dropwise at −13° to a well-stirred solution of fluorobenzene (23 mmol) in the amine (38 mmol) under argon. The reaction appeared slightly exothermic and the mixture promptly acquired a lively red color which eventually faded to pale yellow. The mixture was kept at −13° during 15 hr and then quenched with cold water. Hydrochloric acid (15%, 2 equiv) chilled at −15° was used to extract the amines from the organic solution chilled at −10°; the aqueous solution with the amine salts was immediately carefully added to a solution of 40% potassium hydroxide (4 equiv) in water at −15° and the resulting mixture was extracted with ether. The hexane solution containing the neutral compounds revealed only little *n*-butylbenzene at the glc analysis. It was quickly identified by mass spectrometry.[13] Glc analysis of the amine solution showed unreacted **3** (28% recovery) and *N*-benzylaniline (**4**) (14%). At higher glc temperature an amine of apparent mol wt 266 (highest *m/e* peak in its mass spectrum)[14] in *ca.* 2% yield was detected. The identifications of **3** and **4** were made on the basis of glc enhancing technique, the mass spectra, and ir and pmr spectra on samples of sufficient purity obtained by distillation.

Attempts to prepare the assumed intermediate **6**, *N*-benzyl-*N*-vinylaniline, a hitherto unknown compound, met with failure.[15]

Registry No.—**2**, 462-80-6; **3**, 1074-42-6; **4**, 103-32-2.

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(10) We are indebted to Mrs. Armida B. Giumanini of the Center for Mass Spectrometry of this University for recording the spectra.

(11) F. G. Wilson and T. S. Wheeler, "Organic Syntheses," Collect. Vol. I, Wiley, New York, N. Y., 1948, p 102.

(12) A. T. Bottini and J. D. Roberts, *J. Amer. Chem. Soc.*, **80**, 5203 (1958), reported bp 86–88° (12 Torr).

(13) H. M. Grubb and S. Meyerson, "Mass Spectrometry of Organic Ions," F. W. McLafferty, Ed., Academic Press, New York, N. Y., 1963, p 455 ff.

(14) The mass spectrum of this compound is inducive of a structure dimeric of **3** with peaks at the following *m/e* values: 91 (100), 120 (100), 175 (100), 266 (45), 134 (54), 92 (41), 146 (41), 65 (39), 132 (39), 119 (31), 42 (28), and 104 (27).

(15) Complete details will be reported at a later time.

Disproportionation of 2-Iodothiophene in Dimethyl Sulfoxide

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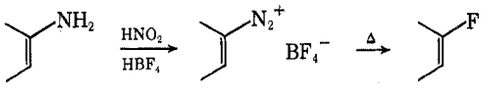
Fluorination of aromatic and heteroaromatic compounds is vested with both a theoretical and a practical interest. The method of choice for the introduction of fluorine into such structures is the two-step sequence of the preparation of a diazonium fluoroborate followed by its decomposition (Schiemann).



This method suffers from two serious drawbacks: the starting amine may not be readily available and not always do diazotation and decomposition follow the desired course.[2] A different access to fluorinated heteroaromatics in particular would therefore be desirable and with this goal we attempted to prepare 2-fluorothiophene[3] (**1**).

We attempted to make use of a nucleophilic displacement of the iodide ion by the fluoride ion in DMSO at near reflux temperature, treating 2-iodothiophene (**2**) with ammonium fluoride. To our surprise, no evidence of even trace amounts of **1** was found by gas chromatography–mass spectrometry, but a few new higher boiling compounds were formed together with some thiophene (**3**) and dimethyl sulfide. The two major higher boiling components were identified on the basis of their mass spectra as 2,5-diiodothiophene (**4**, 25%) and 5-iodo-2-thiophenaldehyde (**5**, 1.5%). Vpc–mass spectrometric inspection of other minor components of the reaction mixture ruled out the presence of isomeric diiodothiophenes and of other polyiodothiophenes. Since the spectra of the four isomeric diiodothiophenes show very similar fragmentation patterns with only tiny intensity differences, the 2,4 and 3,4 isomers were ruled out on the basis of vpc retention time ratios (Table I) and enhancing technique. Final identification of **4** was achieved by ir and pmr on an analytical sample. Vpc properties and mass spectral fragmentation of **5** were identical with those of a sample prepared by an independent route. Two well-separated minor vpc peaks eluted at much higher temperature had an identical mass spectrum fitting the elemental composition and the expected fragmentation pattern for *x,x'*-diiododithienylmethanes (**6**).

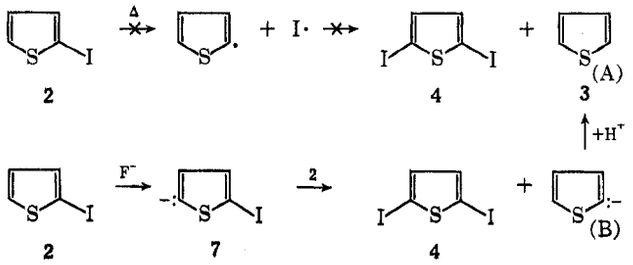
The formation of **4** may be rationalized either according to a radical mechanism (Scheme I, route A) or an

(1) (a) Work supported in part by CNR Contract 7000143-03. (b) Chemistry student.

(2) A. Roe, *Org. React.*, **5**, 194 (1949).

(3) All fluorinated thiophenes are known, but their syntheses are very costly and difficult. Compound **1** was prepared in 10–15% yield by chlorine–fluorine exchange with SbF_3 [R. T. Van Vleck, *J. Amer. Chem. Soc.*, **71**, 3256 (1949)] or by reaction of the dangerous $FClO_3$ with 2-thienyllithium at −72° in 52% yield [R. D. Shuetz, D. D. Taft, J. P. O'Brien, J. L. Shea, and H. M. Mork, *J. Org. Chem.*, **28**, 1420 (1963)]. The latter method, also used to prepare the 3 isomer, gives an inseparable mixture of the desired compound with thiophene and is therefore impractical.

SCHEME I



ionic pathway (Scheme I, route B) with catalysis by ammonium fluoride, which may be considered a strong base in cation solvating dipolar aprotic solvents. The intermediate iodinated anion **7** would then undergo iodine exchange with **2**. This type of exchange was recently observed and studied in detail by M. Reinecke,[4a] who interpreted and extended previous findings by Vaitiekunas.[4b]

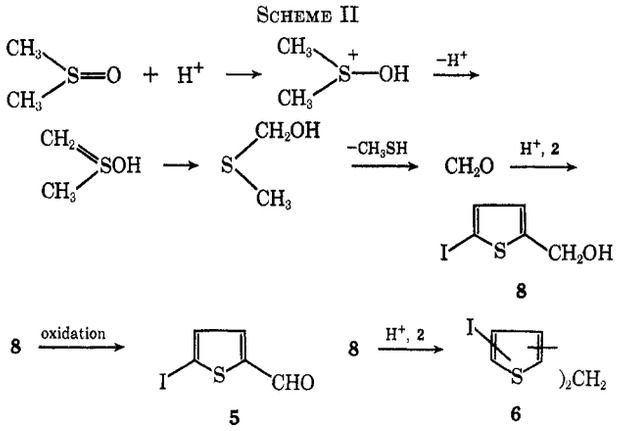
In order to establish the actual route to **4**, we first checked whether the reaction was purely thermal. Prolonged heating of pure **2** at reflux temperature did not yield any **4**. Uv irradiation was ineffective as well. This is in agreement with the fact that our reaction ran with equal yield in the dark. When **2** was heated with *N*,*N*-dimethylaniline, the expected products of a radical attack by the iodine atom or the thienyl radical on this substrate failed to materialize. Moreover, the absence of substantial amounts of free iodine and of the radical coupling product, 2,2′-dithienyl, run counter to the radical mechanism.

At this stage it was interesting to determine the role of DMSO and therefore we carried out the reaction of **2** in DMSO without fluoride. The diiodo derivative **4** was again formed in comparable yields. Parallel experiments with and without fluoride at exactly the same conditions of temperature and concentration showed that the fluoride reaction was much faster. From these results we believe that the reaction is ionic, since it is favored by presence of a base (F^-). DMSO itself may act as a proton acceptor[5] in a much less efficient way; indeed more drastic conditions and longer reaction times were required to achieve comparable yields.

The formation of the diiodothiophene **4** may be explained by a third alternative route, shown to be the mechanistic pathway through which some 2-bromothiophenes undergo selective disproportionation to thiophenes and 2,5-dibromothiophenes and discovered by Wynberg[6] recently. Though at present it is not possible to clearly rule out this possibility on a rigorous experimental basis, it must be noted that the medium for Wynberg's reaction is strongly acidic, a condition which is not realized for either DMSO alone or the DMSO–ammonium fluoride system.

The production of the iodoaldehyde **5** must involve the material participation of DMSO, which contributes the new carbon and oxygen atom. Its appearance is therefore to be related to a reaction of **2** with a decomposition product of DMSO. We propose the mechanism outlined in Scheme II. It moves its steps from

SCHEME II



the acid-catalyzed rearrangement–decomposition of DMSO in acidic solution.[7] Formaldehyde thus formed reacts under acidic catalysis (better than neutral, more likely than basic) with **2** to yield the iodo alcohol **8**, which displays reductive properties towards some of the species present in solution in going to the observed product **5** or alkylating properties to yield **6**. The latter reaction is a well known side reaction in the analogous preparation of 2-thenyl chloride from thiophene and formaldehyde in hydrochloric acid.[8] The fact that **5** and **6** are also present when the reaction was run without fluoride may be interpreted by the assumption of a high-temperature self-ionization of DMSO or assuming that a trace of an acidic product (HI) may trigger the usual decomposition of DMSO.

Experimental Section

Materials and Apparatus.—2-Iodothiophene (**2**) (Eastman) was washed with aqueous sodium thiosulphate, dried, and distilled before use; glc analysis ruled out the presence of isomeric and polyhalogenated material. Anhydrous ammonium fluoride (kept in a desiccator with P_2O_5), DMSO, and *N*,*N*-dimethylaniline were purchased from Erba (Italy). *N*-(2-Thenyl)-*N*-methylaniline was available from previous work.[9] Pure samples of 2,4- and 3,4-diiodothiophene were kindly supplied by Professor M. Tiecco of this university. Gas–liquid chromatography analyses were performed with a Perkin-Elmer 900, using a flame ionization detector on a variety of columns. Optimal results were obtained on an SF 96 4% Chromosorb P (60–80 mesh) 2-m column, to which data in Table I refer. Product

TABLE I

GLC RETENTION TIME RATIOS AT 140° OF COMPOUNDS RELATED TO THE 2-IODOTHIOPHENE REACTION IN DMSO

5-Iodo-2-thiophenaldehyde (**5**)	0.80
2,5-Diiodothiophene (**4**)	1.00
2,4-Diiodothiophene	1.10
3,4-Diiodothiophene	1.32

yields were determined with 3,4-diiodothiophene as internal standard. Mass spectra were recorded with a Perkin-Elmer 270 equipped with glc and solid inlet operating at 75 eV and 100 mA, acceleration voltage 2000 V, target temperature 150–220°. Infrared spectra were recorded with a Beckman IR-5 on the neat compounds (liquids) or with the KBr pellet technique. Proton

(4) (a) M. Reinecke, *J. Amer. Chem. Soc.*, **90**, 511 (1968), and private communication; (b) A. Vaitiekunas and F. F. Nord, *ibid.*, **75**, 1764 (1953).

(5) DMSO exhibits excellent complexing properties toward cations and superior hydrogen bonding properties even with organic compounds; see, *e.g.*, the hydrogen bonding with acetylenes. The solvating power for the anion is much lesser, thus leading to enhancement of the nucleophilicity of the relatively free anions.

(6) R. M. Kellogg, A. P. Shaap, E. T. Harper, and H. Wynberg, *J. Org. Chem.*, **33**, 2902 (1963).

(7) V. J. Traynelis and W. C. Hergenrother, *ibid.*, **29**, 221 (1964); *J. Amer. Chem. Soc.*, **86**, 298 (1964).

(8) Y. Inaba, G. Kimura, and M. Kinoene, Japanese Patent 9586 (1962).

(9) A. G. Giumanini and G. Lercker, unpublished results.

magnetic resonance spectra were recorded with a JEOL 60 in $CDCl_3$. Melting points were determined with a Kofler apparatus and are not corrected.

2-Iodothiophene (2) and NH_4F in DMSO.—2-Iodothiophene (**2**, 6.49 g, 30.9 mmol), ammonium fluoride (0.31 g, 8.5 mmol), and DMSO (6 ml) were stirred in a round-bottom flask with reflux condenser and calcium chloride valve at 170–175° (oil bath) during 6 hr. The reaction course was followed by glc and a continuous buildup of 2,5-diiodothiophene was observed during this time. The dark reaction mixture was taken up with boiling ether, filtered with Celite, washed with water, dried with sodium sulfate, and analyzed. Glc analysis of the mixture revealed unreacted **2** without contamination by the 3 isomer and a new major peak preceeded by a small peak and followed by other smaller impurities at much higher retention times. The first new peak had a retention time ratio of 0.80 (see Table I) and was identified on this basis, by enhancing technique, and by its mass spectrum as belonging to 5-iodothiophenealdehyde (**5**). The glc-determined yield of **5** was 1.5%. The largest new peak was analogously identified as 2,5-diiodothiophene (**4**, 25%, retention time ratio 1.00). While no detectable peaks had molecular ions which fitted the polyiodothiophene molecular composition, two small but still appreciable peaks had identical mass spectra with prominent ions at m/e values of 432 (M^+), 305 (−I, base peak), 178 (−2I, base peak in the less retained isomer), 134 (−CI_2S), 96 (C_5H_4S), and 82 (C_4H_2S). Distillation of the mixture allowed recovery of pure 2-iodothiophene, uncontaminated by the 3 isomer as shown by its ir.[10] The residue from this distillation was chromatographed on a 1.8 × 21 cm silica gel column using *n*-hexane as eluent; a white solid was obtained, which was recrystallized from ethanol, mp 36–37°, mmp with 2,5-diiodothiophene (**4**) 38.5–39.5°. This compound, which corresponds to the product with retention time ratio 1.00, had an ir spectrum identical with that of authentic **4**. The pmr spectrum showed a single peak as expected at τ 3.12 ppm. The reaction mixture showed no peak for either isomeric diiodothiophenes or fluorothiophenes, but small amounts of thiophene and dimethyl sulfide were detected by glc and confirmed by mass spectrometry. No attempts to optimize the yield of **4** were made, but lower and higher temperatures were found to give too slow a reaction and extensive tarring, respectively.

2-Iodothiophene in DMSO.—**2** (7.45 g, 35.4 mmol) and DMSO (5.50 g, 70.5 mmol) were heated in the dark at 190–195° during 18 hr to yield 18% (glc) of 2,5-diiodothiophene (**4**), whose identification was carried out as described in the fluoride experiment. Thiophene and dimethyl sulfide were present in the reaction mixture as well as the two isomers **6** and the aldehyde **5** in tiny amounts. Isomeric diiodothiophenes were absent.

Irradiation of 2-Iodothiophene (2).—**2** was irradiated during 18 hr without solvent at room temperature with a 254-nm mercury lamp. No **4** was formed.

"Parallel" Reactivity Tests of 2-Iodothiophene.—**2** (30 mmol) was heated in DMSO (75 mmol) with and without ammonium fluoride (11 mmol) at 165–170° during 6 hr to yield, respectively, 5 and 0.5% **4**. In either case only traces of free iodine were present.

Thermal Stability of 2-Iodothiophene (2).—**2** was heated without solvent during 15 hr at 190° (gentle reflux). No new compound could be detected by glc analysis.

2-Iodothiophene (2) and *N*,*N*-Dimethylaniline.—**2** (4.08 g, 19.4 mmol) and *N*,*N*-dimethylaniline (3.47 g, 28.8 mmol) were heated from 100 to 180° during 1.5 hr without any color change. Glc analysis showed no changes in the composition of the mixture. After 20 min at 180° the mixture turned dark blue, but glc analysis ruled out the formation of **4** and of *N*-(2-thenyl)-*N*-methylaniline (**9**). Heating the above mixture at 160° during 1 hr caused complete solidification; ether extraction did not yield any **4**; and digestion with aqueous sodium bicarbonate at 100° and extraction with ether gave a mixture which did not contain either **4** or **9**.

2,5-Diiodothiophene (4).—This compound was prepared in 17% yield from thiophene (0.121 mol), iodine (0.243 mol), and mercuric oxide (0.184 mol) in benzene according to a procedure described in the literature for 2-iodothiophene.[11] The product was recrystallized from ethanol: mp 39–40° (lit.[12] 40°); pmr ($CDCl_3$) singlet at τ 3.12 ppm; ir (KBr) 2825 (w), 2300 (w), 1380 (w), 1198 (w), 947 (m), 918 (w), 783 (s), and 727 cm^{-1} (w). The mass spectrum was essentially identical with that reported in the literature.[13] Distillation of the reaction mixture gave 24% of pure 2-iodothiophene (**2**).

5-Iodo-2-thiophenaldehyde (5).—This compound was prepared (18%) by treatment of **2** with *n*-butyllithium at −70°, followed by reaction with dry dimethylformamide in ether–hexane according to a described procedure:[14] mp 52° (lit.[15] 51–52°); ir (KBr) 1528 (s), 1503 (w), 1404 (s), 1370 (m), 1288 (m), 1223 (s), 1190 (w), 1043 (s), 950 (m), 807 (s), 743 (s), 675 (w), and 664 cm^{-1} (s); pmr ($CDCl_3$) singlets at δ 7.40 and 9.76 ppm; mass spectrum (75 eV, solid inlet 50°, chamber 150°) m/e 238 (M^+, base peak), 237 (2-I-thenoyl), 210 (C_4H_4SI), 209 (C_4H_3SI), 128 (HI), 127 (I), 111 (−I), 110 (−HI), 82 (−I, −CHO), 57, 45, 39.

Registry No.—DMSO, 67-68-5; **2**, 3437-95-4; **4**, 625-88-7; **5**, 5370-19-4.

(10) The ir spectra of the isomeric monoiodothiophenes are very different with most bands not overlapping: S. Gronowitz and R. Håkansson, *Ark. Kemi*, **16**, 309 (1960).

(11) V. Meyer and H. Kreis, *Ber.*, **17**, 1558 (1884); W. Minnis, "Organic Syntheses," Collect. Vol. II, Wiley, New York, N. Y., 1943, p 357.

(12) J. Volhard, *Justus Liebigs Ann. Chem.*, **267**, 172 (1892).

(13) S. Gronowitz and B. Åkesson, *Ark. Kemi*, **28**, 155 (1967).

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(15) R. E. Atkinson, R. F. Curts, and J. A. Taylor, *J. Chem. Soc. C*, 578 (1967).

N-Phenyl-1-thio-1,2-azetidinedicarboximide, the Phenylthiohydantoin of Azetidine-2-carboxylic Acid[1]

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L-Azetidine-2-carboxylic acid (**1**), a naturally occurring antimetabolite of proline[2] that has been isolated from the Liliaceae,[3] is unstable in mineral acids and the four-membered azetidine ring undergoes degradative ring-opening reactions.[4] Derivatives of **1** prepared in acidic media are thus suspect unless the integrity of the azetidine moiety can be shown to be intact. In our studies on the behavior of ring homologs of α-imino acids related to proline and their 2,4-dinitrophenyl-, 6-dimethylaminonaphthalene-1-sulfonyl-, and 3-phenyl-2-thiohydantoin (PTH) derivatives in various chromatographic systems,[5] it was necessary to prepare such derivatives of **1** including the PTH derivative **7a**, since **1** is the first member of this homologous series.

The procedure of Edman[6] as modified by Sjöquist[7] for the preparation of PTH amino acids, which involves the cyclization of the phenylthiocarbamoyl amino acid in aqueous acetic acid–hydrogen chloride, when applied to **1** did not yield **7a**. Heating **1** in toluene with excess phenyl isothiocyanate[8] likewise gave intractable mixtures when examined by tlc. The feasibility of cycliz-

(1) Supported in part by Grant CA-06432, United States Public Health Service.

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(3) (a) L. Fowden, *Nature (London)*, **176**, 347 (1955); (b) A. I. Virtanen, *ibid.*, **176**, 984 (1955).

(4) L. Fowden, *Biochem. J.*, **64**, 323 (1956).

(5) H. T. Nagasawa, P. S. Fraser, and J. A. Elberling, *J. Chromatogr.*, **44**, 300 (1969).

(6) P. Edman, *Acta Chem. Scand.*, **4**, 277 (1950).

(7) J. Sjöquist, *Ark. Kemi*, **11**, 129 (1957).

(8) H. T. Nagasawa, J. A. Elberling, P. S. Fraser, and N. S. Mizuno, *J. Med. Chem.*, **14**, 501 (1971).