Registry No.—Aluminum chloride, 7446-70-0; di-*n*-butyl-*sec*-butylacetonitrile, 41718-30-3; 3-methylvaleronitrile, 21101-88-2; di-*n*-butyl-*sec*-butylacetamide, 41718-32-5; di-*n*-butyl-*sec*-butylcarbinamine, 41718-33-6; di-*n*-butyl-*sec*-butylcarbinamine acetamide derivative, 41718-34-7; *n*-butyldimethylcarbinamine, 2626-64-4; *n*-butyldimethylcarbinol, 625-23-0; di-*n*-butylmethylcarbinol, 33933-78-7; *n*-butyl bromide, 109-65-9; ethyl acetate, 141-78-6; di-*n*-butylmethylcarbinamine, 41718-37-0; di-*n*-butylmethylcarbinamine acetamide derivative, 41718-38-1; di-*n*-butylcarbinamine, 2198-45-0; di-*n*-butylbenzylcarbinol, 41718-40-5; ethyl phenylacetate, 101-97-3; di-*n*-butylbenzylcarbinamine, 41718-41-6; di-*n*-butylbenzylcarbinamine acetamide derivative, 41718-42-7; di-*n*-butylphenylacetamide, 41718-43-8; di-*n*-butylphenylcarbinamine, 41718-44-9; di-*n*-butylphenylcarbinamine benzamide derivative, 41718-45-0; *N*-ethyltri-*n*-butylcarbinamine, 41718-46-1; 2-chlorovaleraldehyde, 41718-47-2; valeraldehyde, 110-62-3; methylene chloride, 75-09-2; 2,2-dichlorovaleric acid, 18240-68-1; 1,1,2,2-tetrachloropentylphosphoimidic trichloride, 18240-56-7; 2,2-dichlorovaleryl chloride, 41718-49-4; 2,2-dichlorovaleraldehyde, 41718-50-7; 2,2-dichloro-1-pentanol, 41718-51-8; 4-phenyl-5-nonanone, 41718-52-9; 1-phenyl-2-hexanone, 25870-62-6; *n*-propyl bromide, 106-94-5; 5-phenyl-4-nonanone, 41718-53-0; 1-phenyl-2-pentanone, 6683-92-7.

Nucleophilic Reactions of *N*-Hydroxyimide-*O*-triflates

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Reactions of *N*-hydroxysuccinimide-*O*-triflate (**1**), *N*-hydroxyphthalimide-*O*-triflate (**5**), and *N*-hydroxytetramethylsuccinimide-*O*-triflate (**6**) with various nucleophiles were investigated. Compound **1** reacts with thallous acetate to give *N*-hydroxysuccinimide-*O*-acetate. Sodium thioacetate gives the same product, indicating that the reaction proceeds by initial attack at sulfonate sulfur. Compounds **1** and **5** react with phenoxide and thiophenoxide through attack at imide carbonyl, ring opening, and Lossen rearrangement giving β-alanine and anthranilic acid derivatives, respectively. Compound **6** reacts with phenoxide and thiophenoxide at sulfonate sulfur. In no case was direct nucleophilic displacement at nitrogen or the formation of nitrenium ions indicated.

Nucleophilic substitution reactions at nitrogen are quite rare and the mechanisms are usually in doubt. Although there are several reactions reported in the literature which can be schematically considered nucleophilic displacements at nitrogen, they can be explained by different mechanisms, *e.g.*, nitrene formation, nitrenium ion formation, or addition–elimination.[1-5]

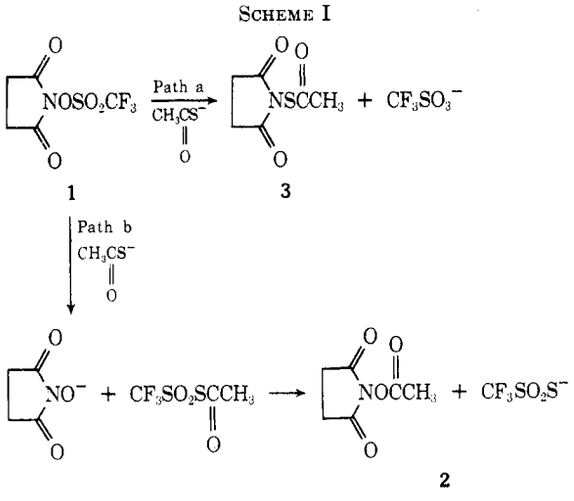
It appeared to us that a compound such as *N*-hydroxysuccinimide-*O*-trifluoromethanesulfonate (triflate)[6] might undergo direct nucleophilic displacement at nitrogen based on the following accounts. First, the group displaced would be triflate anion, considered until recently the most effective leaving group.[7,8] Second, although Gassman and Hartman[9] have shown that the N–O bond in tosyl derivatives of dialkylhydroxylamines is extremely labile, presumably forming nitrenium ion intermediates, related work by Biehler and Fleury[10] showed the proximity of electron-withdrawing groups to stabilize such derivatives.

In an effort to demonstrate the possibility of nucleophilic displacement at nitrogen, the reactivity of compound **1** and two congeners toward nucleophilic reagents was studied.

Results and Discussion

N-Hydroxysuccinimide-*O*-triflate reacted with thallous acetate in dimethylformamide giving a 53% yield of *N*-hydroxysuccinimide-*O*-acetate (**2**). If the reaction occurred by a direct displacement mechanism, it was reasoned that an approach toward the racemization-free formation of peptide active esters might be developed. Compound **2** could have formed from acetate and **1** by two mechanisms, substitution at nitrogen or a double displacement in which carboxylate attacks at sulfonate sulfur giving rise to an activated anhydride which could then acetylate the *N*-hydroxysuccinimidyl anion displaced in the first step. Insight was gained by studying the reaction of sodium thioacetate with **1** under a variety of conditions and solvent media, including dimethylformamide, dimethyl sulfoxide, dimethoxyethane, and methylene chloride. As shown in Scheme I, direct displacement (path a) would give thioacetate **3** whereas double displacement (path

SCHEME I



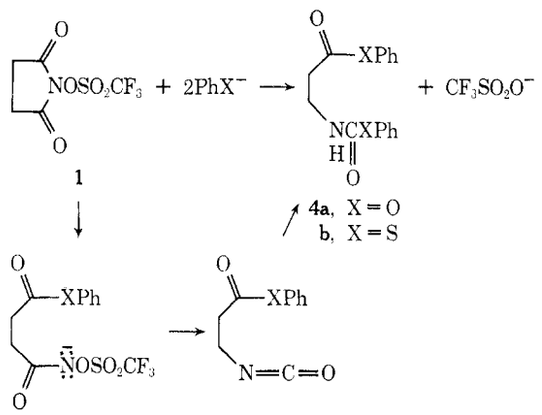
(1) J. W. Cahn and R. E. Powell, *J. Amer. Chem. Soc.*, **76**, 2565 (1954).
(2) L. A. Audrieth and L. H. Diamond, *J. Amer. Chem. Soc.*, **76**, 4869 (1954).
(3) R. Brown and W. E. Jones, *J. Chem. Soc.*, 781 (1948).
(4) (a) A. Nickon and A. Sinz, *J. Amer. Chem. Soc.*, **82**, 753 (1960); (b) A. Nickon and A. Hill, *ibid.*, **86**, 1152 (1964).
(5) D. S. Kemp and R. B. Woodward, *Tetrahedron*, **21**, 3019 (1965).
(6) T. M. Chapman and E. A. Freedman, *Synthesis*, 591 (1971).
(7) (a) R. L. Hansen, *J. Org. Chem.*, **30**, 4322 (1965); (b) A. Streitweiser, Jr., C. L. Wilkins, and E. Kiehlmann, *J. Amer. Chem. Soc.*, **90**, 1598 (1968); (c) T. M. Su, W. F. Sliwinski, and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, **91**, 5386 (1969).
(8) The "nonaflate" anion has been reported to be an even better leaving group than triflate: L. R. Subramanian and M. Hanack, *Chem. Ber.*, **105**, 1465 (1972).
(9) (a) R. G. Gassman and G. D. Hartman, *Chem. Commun.*, 853 (1972); (b) P. G. Gassman and G. D. Hartman, *J. Amer. Chem. Soc.*, **95**, 449 (1973).
(10) J. M. Biehler and J. P. Fleury, *Tetrahedron*, **27**, 3171 (1971).

b) would give acetate **2**. In each case the major product was acetate **2** showing initial attack by nucleophilic acetate at sulfur and not at nitrogen. The resulting mixed anhydride formed at the carboxyl terminus at a peptide would readily racemize the terminal amino acid residue by oxazalone formation or acylium ion formation.[11,12]

Since carboxylate is a weak nucleophile and also forms highly unstable intermediates, it was advisable to study stronger nucleophiles; sodium phenoxide and sodium thiophenoxide were selected.

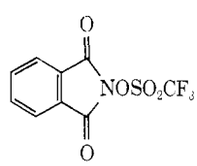
It was expected that sodium phenoxide would react with **1** to give either phenyl succinimidyl ether (attack at nitrogen) or phenyl triflate (attack at sulfur);[13] neither was detected. Instead, equimolar amounts of **1** and phenoxide gave a 54% yield of phenyl *N*-phenoxycarbonyl-β-alanate (**4a**) along with unreacted **1**. The formation of this product is shown in Scheme II.

SCHEME II

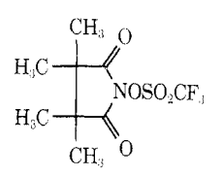


Phenoxide attacks a ring carbonyl leading to ring opening, Lossen rearrangement to an isocyanate, and reaction with a second molecule of phenoxide. Indeed, the ir spectrum of the reaction mixture showed an absorption band at 2250 cm^{-1}, characteristic of isocyanates. When thiophenoxide was used as a nucleophile, the reaction with **1** followed a similar path, forming **4b**. It was thus established that the stronger nucleophiles preferentially attack the succinimidyl carbonyl functions rather than sulfur or nitrogen. Acetate and thioacetate may also add to the carbonyl functions with the resulting tetrahedral intermediate reverting back to starting materials in a nonproductive equilibrium. A similar ring opening and rearrangement has been observed by Gross and Bilk, the reaction of dicyclohexylcarbodiimide and *N*-hydroxysuccinimide giving the succinimidyl ester of *N*-(succinimidyloxycarbonyl)-β-alanine.[14a] Also, in 1893 Lengfeld and Stieglitz[14b] observed the reaction of *N*-bromosuccinimide and sodium methoxide to give the methyl analog of **4a**. To optimize the possibility of observing reaction at nitrogen, the reaction at carbonyl had to be suppressed. Conceivably this could be done (i) by introducing conjugation with an aromatic as in *N*-hydroxyphthalimide-*O*-triflate (**5**), (ii) by introducing steric constrictions as in *N*-hydroxytetramethylsuccinimide-*O*-triflate (**6**). Triflate **5** was prepared in good yield by the reaction of the thallium(I) salt of *N*-hydroxyphthalimide with trifluoromethanesulfonic anhydride.[6] Triflate **6** was prepared in analogous fashion from *N*-hydroxytetramethylsuccinimide. The latter was prepared in the following fashion. Using a combination of procedures reported by Rathke and Lindert[15] and by Hudson and Hauser,[16] the lithium enolate of ethyl isobutyrate, prepared *in situ* by reaction of lithium *N*-isopropylcyclohexylamide, was mixed with 0.5 equiv of iodine, giving diethyl tetramethylsuccinate. The anhydride was prepared by acid hydrolysis or by saponification to the acid followed by treatment with acetic anhydride or acetyl chloride.[17] The anhydride was converted to the hydroxysuccimide analog by adapting the Orndorff and Pratt procedure.[18]

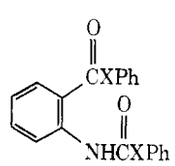
Reaction of phthalimide triflate **5** with 1 equiv of sodium phenoxide gave only ring-opened products identified as phenyl *N*-phenoxycarbonylanthranilate (**7a**), isatoic anhydride, and phenyl anthranilate, all derived from initial nucleophilic reaction at carbonyl. Reaction of **5** with 2 equiv of sodium thiophenoxide gave *S*-phenyl 2-(*S*-phenylthiocarbamyl)thiobenzoate (**7b**),



5



6



7a, X = O
b, X = S

anthranilic acid, and a small amount of a third ring-opened product which was only partially characterized. There is some literature precedence for ring-opening attack at phthalimide carbonyl groups. Harpp and Back[19] observed ring opening of *N*-(isopropylthio)-phthalimide while studying sulfenamide synthesis.

Reaction of tetramethylsuccinimide triflate (**6**) with sodium thiophenoxide did not occur in methylene chloride at −8°, but at room temperature some reaction occurred, giving diphenyl disulfide and some *N*-hydroxytetramethylsuccinimide. There was no evidence of ring-opened product and no evidence for

(11) F. Effenberger and G. Epple, *Angew. Chem., Int. Ed. Engl.*, **11**, 299 (1972).

(12) We have observed that the reaction of carbobenzyloxyglycyl-L-phenylalanine with 2,4-dinitrophenyltriflate leads to a 90% recovery of racemic dipeptide starting material.

(13) There is a great deal of precedent for attack by nucleophiles at benzene sulfonate and tosylate sulfur. See, for example, (a) J. Ferns and A. Lapworth, *J. Chem. Soc. Trans.*, **101**, 273 (1912); (b) F. G. Bordwell, B. M. Pitt, and M. Knell, *J. Amer. Chem. Soc.*, **73**, 5004 (1951); (c) J. F. Bunnett and J. Y. Bassett, Jr., *ibid.*, **81**, 2104 (1959); (d) P. G. Gassman, J. M. Hornback, and J. M. Pascone, *Tetrahedron Lett.*, 1425 (1971).

(14) (a) H. Gross and L. Bilk, *Tetrahedron*, **24**, 6935 (1968); (b) F. Lengfeld and J. Stieglitz, *Amer. Chem. J.*, **15**, 504 (1893).

(15) (a) M. W. Rathke and A. Lindert, *J. Amer. Chem. Soc.*, **93**, 2318 (1971); (b) M. W. Rathke and A. Lindert, *Tetrahedron Lett.*, 3995 (1971).

(16) B. E. Hudson, Jr., and C. R. Hauser, *J. Amer. Chem. Soc.*, **63**, 3161 (1941).

(17) P. E. Verkade and H. Hartman, *Recl. Trav. Chim. Pays-Bas*, **52**, 951 (1933).

(18) W. R. Orndorff and D. S. Pratt, *J. Amer. Chem. Soc.*, **47**, 89 (1912).

(19) D. N. Harpp and T. G. Back, *Tetrahedron Lett.*, 4953 (1971).

attack at nitrogen, particularly the formation of tetramethylsuccinimide, which could have been formed from the hypothetical sulfenamide product.[19] The products could be rationalized by nucleophilic attack at sulfonate, giving thiophenyl triflate; thiosulfonates are known to react with mercaptides to give disulfides.[20]

The reaction of **6** with sodium phenoxide gave a 78% yield of phenyl triflate. Although carbonyl attack is suppressed, the site of substitution is shifted to sulfur.

In conclusion, we have demonstrated the difficulty of nucleophilic attack at nitrogen. Of the three electrophic sites in the succinimidyl-based triflates, reaction occurred at carbonyl or sulfonate but never at nitrogen, even though triflate is such as excellent leaving group. Substitution at nitrogen could have been facile in the phthalimide case considering the analogy to phenacyl halides, which readily undergo substitution. The favorable transition state,[21] however, comes at the expense of nitrogen lone-pair delocation.

Of particular interest is the stability of the N–O bond of the triflates, particularly in light of the recent work of Gassman and Hartman.[9] The *N,N*-diacyl structure completely suppressed nitrenium ion formation. The rearrangement of the succinimide triflates to the β-alanate compounds could lead to a general synthesis of substituted dihydrouridines if compounds such as **4b** can be cyclized with ammonia. The dicyclohexylcarbodiimide–*N*-hydroxysuccinimide mixture has been shown to have utility in the coupling of peptide fragments[22] but is complicated by the rearrangement reaction discovered by Gross and Bilk;[14a] our results suggest the possible advantage of using *N*-hydroxytetramethylsuccinimide.

Experimental Section

Melting points were determined on a Kofler micro hot stage melting point apparatus and are uncorrected. Infrared spectra were recorded on a Beckman IR-8 or Perkin-Elmer 247 spectrophotometer. The nmr spectra were recorded on Varian A-D60 or T-60 spectrometers; mass spectra were obtained on an LKB Type 9000 gas chromatograph–mass spectrometer by use of either the direct probe or analytical glc columns. Elementary analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn., and by Scandinavian Microanalytical Laboratories, Herlev, Denmark. Column chromatography was carried out using Baker 3405 silica gel and the specified solvents as eluents. Preparative thick layer chromatography was performed on commercial silica gel F-254 precoated plates. All reaction solvents and chromatography eluents were carefully dried and distilled before use.

***N*-Hydroxysuccinimide-*O*-triflate (1).**—*N*-Hydroxysuccinimide-*O*-triflate (1) was prepared as previously reported.[6]

***N*-Hydroxyphthalimide-*O*-triflate (5).**—To *N*-hydroxyphthalimide (4.07 g, 0.025 mol) dissolved in a mixture of ether (200 ml) and acetone (170 ml) was added thallous ethoxide (6.22 g, 0.025 mol). After 15 min the bright orange precipitate was filtered and dried *in vacuo*, affording 8.35 g (90.5%) of the *N*-hydroxyphthalimide thallous salt which was used without further purification.

To a suspension of the salt in methylene chloride (200 ml) was added trifluoromethanesulfonic anhydride (7.7 g, 0.273 mol) in 30 ml of CH_2Cl_2. After 13 hr the reaction mixture was filtered and the filtrate was extracted twice with water. The organic layer was dried over $MgSO_4$ and evaporated *in vacuo*, affording 5.19 g (78%) of **5**: mp 90° (recrystallization from 2-propanol raised the melting point to 94–96°); ir (KBr) 1810, 1730, 1440, 1340, 1220, 790, and 690 cm^{-1}; nmr ($CDCl_3$) δ 7.9 (s, aromatic); mass spectrum *m/e* 295 (parent).

Anal. Calcd for $C_9H_4F_3NO_5S$: C, 36.6; H, 1.35; F, 19.3; N, 4.75; S, 10.85. Found: C, 36.57; H, 1.49; N, 4.64.

***N*-Hydroxytetramethylsuccinimide-*O*-triflate (6). A. Synthesis of Diethyl Tetramethylsuccinate.**—Lithium *N*-isopropylcyclohexylamide (0.63 mol, from 0.63 mol of *n*-butyllithium and 0.65 mol of isopropylhexylamine) in tetrahydrofuran (200 ml) was cooled to −78°. Ethyl isobutyrate (73.0 g, 63.0 mol) was added dropwise over 15 min followed by the addition of iodine (80 g, 0.63 g-atom) in 400 ml of tetrahydrofuran over 30 min. The reaction mixture was allowed to reach room temperature and after 50 min was quenched with acetic acid (7.6 ml). After filtration and concentration of the organic filtrate, aqueous sodium bicarbonate was added and the mixture was extracted with ethyl acetate. The organic extracts were dried over $MgSO_4$ and concentrated, and the product was distilled, giving 22 g of diethyl tetramethylsuccinate, bp 68–70° (0.3 Torr). Redistillation gave 14.3 g (23.4%) of pure product: ir ($CHCl_3$) 2990, 1720, 1470, 1260, 1130 cm^{-1}; nmr (neat) δ 1.21 (s, 12, CH_3), 1.25 (t, 6, J = 7 Hz, $OCCH_3$), 4.06 (q, 4, J = 7 Hz, OCH_2); mass spectrum *m/e* 230 (parent).

B. Tetramethylsuccinic Anhydride.—To 6.6 g of diester was added 60 ml of concentrated H_2SO_4 and the mixture was heated on a water bath for 3 hr. The reaction mixture was then poured into ice–water, and the precipitate was filtered. Recrystallization from Skelly B gave 2.99 g (57%) of anhydride: mp 140° (lit.[17] mp 152°); ir (CCl_4) 2975, 1850, 1750 cm^{-1}; nmr ($CDCl_3$) δ 1.23 (s, CH_3); mass spectrum *m/e* 84, 59 (base). From the aqueous solution, 1.73 g (35%) of diacid could be recovered.

C. *N*-Hydroxytetramethylsuccinimide.—To 25 ml of water was added hydroxylamine hydrochloride (1.55 g, 0.0223 mol), tetramethylsuccinic anhydride (2.78 g, 0.0178 mol), and sodium carbonate (1.19 g, 0.0112 mol). The reaction mixture was kept at 81–82° on a water bath for 2 hr. Cooling in an ice bath gave a solid which after crystallization from CCl_4 afforded 2.78 g (91%) of *N*-hydroxytetramethylsuccinimide: mp 130–132°; ir ($CHCl_3$) 3200, 2980, 1775, 1700 cm^{-1}; nmr ($CDCl_3$) δ 1.2 (s, 12, CH_3), 5.23 (broad, 1, OH); mass spectrum *m/e* 171 (parent).

Anal. Calcd for $C_8H_{13}NO_3$: C, 56.1; H, 7.6; N, 8.2. Found: C, 55.1; H, 7.56; N, 7.99.

D. Title Compound 6.—*N*-Hydroxytetramethylsuccinimide thallous salt (4.8 g, 0.0128 mol, prepared from *N*-hydroxytetramethylsuccinimide and thallous ethoxide in ether) was suspended in methylene chloride (65 ml) and cooled to 0°. Trifluoromethanesulfonic anhydride (5.13 g, 0.0182 mol) was added and after 1 hr at 0° the reaction mixture was allowed to come to room temperature and kept for an additional 1.5 hr. After filtration the filtrate was extracted with water, dried over Na_2SO_4, and concentrated *in vacuo*. The resulting oil solidified, giving 3.42 g (86%) of triflate **6**. Recrystallization from absolute methanol afforded 2.84 g of white needles (73.5%): mp 37°; ir (CCl_4) 2990, 1750, 1440, 1235, 1205 cm^{-1}; ir (CH_2Cl_2) an additional band at 1800 cm^{-1}; nmr ($CDCl_3$) δ 1.28 (s, CH_3); mass spectrum *m/e* 303 (parent).

Anal. Calcd for $C_9H_{12}F_3NO_5S$: C, 35.60; H, 3.97; N, 4.63; S, 10.55. Found: C, 35.79; H, 4.11, N, 4.77; S, 10.86.

Reaction of Thallium(I) Acetate with 1.—Thallous acetate (1.64 g, 0.00624 mol) and **1** (0.77 g, 0.00312 mol) were mixed in dimethylformamide (50 ml). After 20 hr the mixture was filtered and the solvent was evaporated *in vacuo*. The resulting residue was titrated with hot benzene and the product was isolated from the benzene extracts after evaporation as an oil which solidified on standing in hexane (0.259 g, 53%), single spot on tlc (silica gel H, 4% acetone in CH_2Cl_2 eluent, R_f 0.46, same as authentic **2**). See the next section for further characterization.

Reaction of Potassium Thioacetate with Triflate 1.—Potassium thioacetate (0.171 g, 0.0015 mol) and triflate **1** (0.185 g) were suspended in methylene chloride and allowed to stand for 8 days at room temperature. Filtration and evaporation left an oily residue which was chromatographed on silica gel, eluting with chloroform and chloroform–methanol (95:5). Starting material was recovered in 45% yield along with 0.0275 g (23%) of *O*-acetyl-*N*-hydroxysuccinimide (**2**): mp 133° (lit.[23] mp 129–130°); ir ($CHCl_3$) 1820, 1785, 1735, 1370, 1160 cm^{-1}; nmr ($CDCl_3$) δ 2.35 (s, 3, CH_3) 2.85 (s, 4, CH_2CH_2); mass spectrum *m/e* 157 (parent), 43 (base). The reaction was repeated in a

(20) H. Gilman, L. E. Smith, and H. H. Parker, *J. Amer. Chem. Soc.*, **47**, 851 (1925).

(21) P. D. Bartlett and E. N. Trachtenberg, *J. Amer. Chem. Soc.*, **80**, 5808 (1958).

(22) (a) E. Wünsch and F. Drees, *Chem. Ber.*, **99**, 110 (1966); (b) F. Weygand, D. Hoffmann, and E. Wünsch, *Z. Naturforsch. B*, **21**, 426 (1966).

(23) LaValle, *Gazz. Chim. Ital.*, **25**, 30 (1895).

variety of solvents (dimethoxyethane, dimethylformamide, dimethyl sulfoxide, thioacetic acid) and cations (Na^+, Tl^+) always giving **2** but not **3**.

Reaction of *N*-Hydroxysuccinimidyl Triflate (1) with Sodium Phenoxide.—Sodium phenoxide was prepared using the method of Kornblum and Lurie.[24] To sodium phenoxide (0.23 g, 0.002 mol) in dimethoxyethane (120 ml) at 0° was added **1** (0.494 g, 0.002 mol). After 26 hr at 0–4° the solvent was evaporated *in vacuo* and ethyl acetate was added. After water extraction the organic layer was dried over Na_2SO_4 and evaporated. The resulting solid was subjected to column chromatography on silica gel, which afforded 0.044 g (8.9%) of **1**, 0.020 g (11%) of phenol, and 0.155 g of a solid (mp 74–76°) which was recrystallized from benzene–hexane and identified as compound **4a**: 0.14 g (54%); mp 77°; ir (KBr) 3300, 3050, 1740, 1725, 1695 cm^{-1}; nmr ($CDCl_3$)[25] δ 2.85 (t, 2, CH_2CO), 3.61 (d t, 2, CH_2N), 5.6 (t, 1, NH), 7.0–7.55 (complex, 10, aromatic); mass spectrum *m/e* 285 (parent).

Anal. Calcd for $C_{16}H_{15}NO_4$: C, 67.4; H, 5.27; N, 4.9. Found: C, 67.25; H, 5.35; N, 4.83.

The experiment was repeated at room temperature. After 18 hr an aliquot was removed; ir showed the presence of a band at 2250 cm^{-1}. Addition of a second equivalent of sodium phenoxide eliminated this absorption.

Reaction of Sodium Thiophenoxide with 1.—To compound **1** (1.86 g, 0.0075 mol) in dimethoxyethane (200 ml) was added sodium thiophenoxide (1.09 g, 0.00825 mol) prepared by the method of Sheehan and Daves.[26] Ir spectra taken after 1 and 21 hr showed the presence of a 2270-cm^{-1} absorption. After 26 hr, thiophenol (0.8235 g, 0.0075 mol) was added and after 5 min the solvent was removed *in vacuo*. Methylene chloride (50 ml) was added and the resulting precipitate was filtered and washed. Combined filtrates were evaporated to a solid residue. Chromatography on silica gel using CH_2Cl_2, ethyl acetate, acetone, and acetone–methanol mixtures as eluents gave 0.362 g (21%) of thiophenol and 1.67 g (70%) of compound **4b**, which after recrystallization from cyclohexane had mp 104°; ir (KBr) 3275, 1700, 1680, 1650, 1220 cm^{-1}; nmr ($CDCl_3$)[24] δ 2.9 (t, 2, J = 6 Hz, CH_2CO), 3.60 (d t, 2, J = 6 Hz, CH_2N), 5.9 (broad triplet, 1, NH), 7.3–7.7 (complex, 10, aromatic); mass spectrum *m/e* 317 (parent).

Anal. Calcd for $C_{16}H_{15}NO_2S_2$: C, 60.67; H, 4.81; N, 4.32. Found: C, 60.5; H, 4.74; N, 4.41.

Small amounts of other ring-opened products were also obtained.

Reaction of Phthalimidyl Triflate (5) with Sodium Phenoxide.—To sodium phenoxide (0.435 g, 0.00374 mol) in CH_2Cl_2 (140 ml) was added **5** (1.00 g, 0.0034 mol) dissolved in CH_2Cl_2 (15 ml). After 24 hr at room temperature, the mixture was filtered, the solid was washed with CH_2Cl_2, and the combined filtrates were evaporated *in vacuo*. Column separation of the residue afforded **7a**, 0.568 g (40% based on triflate), 0.064 g (8.9%) of anthranilic acid phenyl ester, and 0.284 g (51%) of isatoic anhydride.

Compound **7a** had mp 94–95°; ir (KBr) 3275, 3050, 1740, 1700, 1120–1240 cm^{-1}; nmr (CCl_4) δ 7.0–7.7 (complex, 12, aromatic), 8.24 (dd, 1, J_1 = 1.5 Hz, J_2 = 8 Hz, aromatic), 8.55 (dd, 1, J_3 = 1.0, J_4 = 7.5 Hz, aromatic); mass spectrum *m/e* 333 (parent).

Anal. Calcd for $C_{20}H_{15}NO_4$: C, 72.0; H, 4.50; N, 4.20. Found: C, 71.45; H, 4.52; N, 4.17.

Anthranilic acid phenyl ester had mass spectrum *m/e* 213 (parent), 120 (base).

Isatoic anhydride had mp 243–245° (lit.[27] mp 243° dec); ir (KBr) 1723, 1760 cm^{-1};[28] nmr (acetone-d_6) δ 7.13–7.43 (complex, 2), 7.7 (dd, 1, J_1 = 2, J_2 = 2 Hz), 8.0 (dd, 1, J_3 = 10 Hz, J_4 = 2 Hz); mass spectrum *m/e* 163 (parent), 119 (base).

Reaction of 5 with Sodium Thiophenoxide.—To sodium thiophenoxide (0.792 g, 0.006 mol) in CH_2Cl_2 (100 ml) was added **5** (0.885 g, 0.003 mol) in CH_2Cl_2 (40 ml) over 15 min. More CH_2Cl_2 (20 ml) was added and the mixture was stirred for 8.5 hr. Thiophenol (0.33 ml, 0.003 mol) was added and stirring was continued overnight. Filtration and evaporation of the filtrate left a residue which was placed on a silica gel column for purification. Elution with benzene, methylene chloride, and acetone, respectively, afforded 0.65 g of crude **7b**, which after recrystallization from hexane was 0.56 g (51%): mp 135–136°, ir (KBr) 3050, 1700, 1630, 1575, 1190, and 900 cm^{-1}; nmr (acetone-d_6) δ 7.13–7.73 (m, 12, aromatic), 8.21 (dd, 1, J_1 = 10, J_2 = 2 Hz), 8.43 (dd, 1, J_3 = 10, J_4 = 2 Hz), 10.6 (broad s, 1, NH); mass spectrum *m/e* 365 (parent).

Anal. Calcd for $C_{20}H_{15}NO_2S_2$: C, 65.75; H, 4.12; N, 3.84; S, 17.5. Found: C, 65.82; H, 4.18; N, 4.0; S, 17.25.

Small amounts of other ring-opened products were obtained.

Reaction of *N*-Hydroxysuccinimide-*O*-triflate (6) with Sodium Thiophenoxide.—Compound **6** (0.303 g, 0.001 mol) was dissolved in CH_2Cl_2 (25 ml). After cooling to 0°, sodium thiophenoxide (0.132 g, 0.001 mol) was added. The reaction mixture was kept at −8° for 20 hr, but ir showed the presence of starting material. After 24 hr at room temperature the reaction mixture was filtered, the solid (53 mg) was washed with CH_2Cl_2, and the organic extracts were concentrated *in vacuo*. The residue was subjected to preparative thick layer chromatography, CH_2Cl_2 eluent, and showed two fractions, 0.102 g (94%) of diphenyl disulfide and 0.116 g (38.5%) of recovered starting material. Diphenyl disulfide had mp 60° (lit.[29] mp 60–61°); nmr ($CDCl_3$) δ 7.37 (complex); mass spectrum *m/e* 218 (parent), 109 (base).

The solid obtained after filtration was dissolved in water, acidified with concentrated HCl, and extracted with ethyl acetate, and the organic layer was dried over Na_2SO_4. Evaporation of the solvent afforded 0.044 g (26%) of *N*-hydroxytetramethylsuccinimide.

Reaction of 6 with Sodium Phenoxide.—To triflate **6** (0.606 g, 0.002 mol) in CH_2Cl_2 (10 ml) was added sodium phenoxide (0.464 g, 0.004 mol). After 21 hr the reaction mixture was filtered and washed with CH_2Cl_2, giving 0.659 g of solid. The combined organic filtrates were extracted with water and dried over $CaCl_2$. Evaporation gave 0.375 g of an oil which was subjected to preparative thick layer chromatography, CH_2Cl_2 eluent. Recovered was 0.340 g (78%) of phenyl triflate: bp 89–90° (30 mm) [lit.[30] bp 99–100° (60 mm)]; ir ($CHCl_3$) 3070, 1600, 1590, 1490, 1420, 1220, 1120, 880 cm^{-1}; nmr ($CDCl_3$) δ 7.3 (s, aromatic); mass spectrum *m/e* 226 (parent, base).

The solid from filtration of the reaction mixture was dissolved in water (5 ml), acidified with concentrated HCl, and extracted with CH_2Cl_2. Evaporation left an oil which after preparative thick layer chromatography afforded 0.266 g (79.5%) of *N*-hydroxytetramethylsuccinimide.

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Registry No.—**1**, 34684-40-7; **4a**, 41580-56-7; **4b**, 41580-57-8; **5**, 41580-58-9; **6**, 41580-59-0; **7a**, 33067-24-2; **7b**, 41580-61-4; *N*-hydroxypthalimide, 524-38-9; trifluoromethanesulfonic anhydride, 358-23-6; diethyl tetramethylsuccinate, 33367-54-3; lithium *N*-isopropylcyclohexylamide, 32400-20-7; ethyl isobutyrate, 97-62-1; tetramethylsuccinic anhydride, 35046-68-5; *N*-hydroxytetramethylsuccinimide, 41580-64-7; thallium acetate, 563-68-8; potassium thioacetate, 10387-40-3; sodium phenoxide, 139-02-6; sodium thiophenoxide, 930-69-8.

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