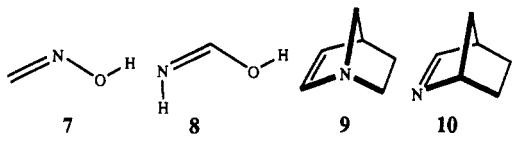

7 8 9 10

3-21G	33.2	0.0	16.7	0.0
6-31G*	39.0	0.0	22.1	0.0
MP2/6-31G*	34.7	0.0	21.3	0.0

kcal/mol at the highest level. The bridge constrains the C-N-C angle to be 104° (the value in a typical amine is around 110°) and prevents enamine conjugation. These two factors contribute to make the Diels-Alder adduct 6 more unstable than 5 and are manifested as well in the higher energy of the TS 4.

In summary, the long-standing problem of the different reactivity of oxazole and isoxazole in Diels-Alder cycloadditions has been addressed by ab initio calculations, and the higher activation barrier and endothermicity of the isoxazole reaction can be seen as the reason for that difference. This conclusion is generally applicable to hetero-Diels-Alder reactions. There are many five-membered heterocycles with two heteroatoms. No Diels-Alder reactions are known where two heteroatoms are directly bonded so that one heteroatom appears at a bridgehead in the cycloadduct.[12] The reason is the same as that identified here for isoxazoles.

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(11) The total energies (au) are the following: 1-azanorbornene (9) -285.242 59 (RHF/3-21G), -286.830 01 (RHF/6-31G*//3-21G), -287.768 58 (RMP2/6-31G*//3-21G); 2-azanorbornene (10) -285.269 26 (RHF/3-21G), 286.865 22 (RHF/6-31G*//3-21G), -287.802 50 (RMP2/6-31G*//3-21G).

(12) An exception to this assertion is the Diels-Alder reaction of benzisoxazoles with *N*-phenylmaleimide; see: Taylor, E. C.; Eckroth, D. R.; Bartulin, J. *J. Org. Chem.* **1966**, *32*, 1899. In this case, aromatization of the cycloadduct appears to be the driving force of the reaction.

Electrolytic Partial Fluorination of Organic Compounds. 4.[1] Regioselective Anodic Monofluorination of 4-Thiazolidinones and Its Application to the Synthesis of Monofluoro β-Lactams

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Summary: Anodic partial fluorination of sulfur-containing heterocycles has been performed for the first time: 2-aryl-4-thiazolidinones 1 were monofluorinated highly regioselectively. In addition, thermolysis of the sulfones derived from fluorinated 1 provided monofluoro β-lactams in excellent yields.

Fluoro organic compounds have special chemical and physical properties. Particularly, partially fluorinated compounds are useful in the fields of material science and medicinal chemistry.[2] Therefore, selective direct fluorination is becoming increasingly important. Among selective oxidative fluorination,[3] anodic partial fluorination is attractive because fluorine atoms can be introduced into organic molecules in one step under safe conditions. However, in contrast to well-established anodic perfluorination, anodic partial fluorination has been unexplored owing to low selectivity for the fluorination and low nucleophilicity of fluoride ions.[4-6] Therefore, the development of methods for efficient selective anodic partial fluorination is an important goal of modern organofluorine research.

Recently, we achieved regioselective anodic monofluorination of sulfides bearing various electron-withdrawing groups using $Et_3N{\cdot}3HF$ as a supporting electrolyte.[7] Furthermore, we reported the first example of the successful anodic monofluorination of simple alkyl phenyl sulfides.[8]

Partially fluorinated heterocycles are the focus of much biological interest.[2,9] However, very few examples of successful anodic partial fluorination of heterocycles have been reported up to date.[10] They are limited to only nitrogen- and oxygen-containing heterocycles, and the yields are generally quite low. To the best of our knowledge, no successful electrochemical fluorination of sulfur-containing heterocycles has been reported so far.

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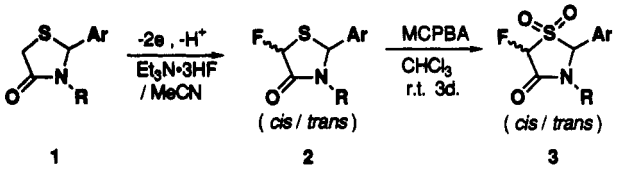
Table I. Anodic Monofluorination of 4-Thiazolidinones 1 and Oxidation of 2

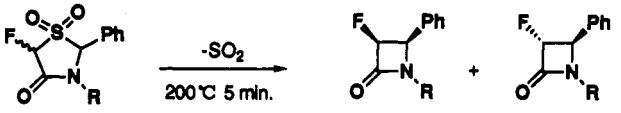


1 2 3

run	substrate	Ar	R	electricity (F/mol)	product yield (%)	product cis:trans[a]
1	1a	1-naphthyl	Me	3.8	(2a) 79	29:71
2	1b	Ph	H	7.0	(2b) 14	35:65
3	1c	Ph	Me	4.5	(3c) 42	35:65
4	1d	Ph	*i*-Pr	3.9	(3d) 59	45:55
5	1e	Ph	Ph	6.1	(2e) 84	43:57
6	1f	Ph	CH_2Ph	4.5	(3f) 65	46:54

[a] Determined by ^{19}F NMR spectra.

Table II. Formation of Monofluoro β-Lactams 4 by Pyrolysis of 3



3 4 (*cis*) + 4 (*trans*)

substrate	(cis:trans)	R	yield (%)	cis:trans[a]
3c	(35:65)	Me	(4c) 86	0:100
3d	(45:55)	*i*-Pr	(4d) 80	39:61
3f	(46:54)	CH_2Ph	(4f) 84	19:81

[a] Determined by ^{19}F NMR spectra.

In this paper, we report the first successful regioselective anodic monofluorination of sulfur-containing heterocycles such as 4-thiazolidinones and novel transformation of the fluorinated 4-thiazolidinones into biologically interesting monofluorinated β-lactams.

The anodic monofluorination of 4-thiazolidinones 1, which are easily prepared from thioglycolic acid and imines,[11] was carried out at constant current in an undivided cell.[12] In order to avoid deposition of polymerized products on the anode, the polarity of electrodes was alternated every 10 s. When the fluorinated products 2 were unstable, they were converted into the corresponding sulfone derivatives 3 by oxidation with *m*-chloroperbenzoic acid (MCPBA) to establish their molecular structures (runs 3, 4, and 6 in Table I). In this case, it was found that the stereochemistry of the products was not changed after the oxidation.

As shown in Table I, the anodic fluorination smoothly proceeded to provide the corresponding monofluorinated products in good yields except for one case owing to instability of fluorinated product (run 2).[13] Such high yields are unusual in the anodic partial fluorination of heterocycles. In our reactions, fluorine was exclusively introduced at the position α to both the sulfur atom and the carbonyl group. Although benzylic anodic substitution is known to easily take place, benzylic fluorination did not occur at all. In addition, no aromatic fluorination was observed either. Therefore, this fluorination is highly regioselective. It was also found that the stereochemistry was affected by both substituents Ar and R.

Hitherto known methods for the preparation of α-fluoro sulfides required expensive, unstable, or troublesome reagents, such as xenon difluoride[14] and (dimethylamino)sulfur trifluoride (DAST).[15] Recently, *N*-fluoro-2,4,6-trimethylpyridinium triflate has also been shown to be a useful fluorinating reagent.[16] However, fluorination of 1, for example, with the latter reagent resulted in no formation of 2. Fluorination by DAST was also attempted using the sulfoxide derived from 1c as a model compound; however, no desired fluorinated product 2c was formed. Therefore, this electrochemical fluorination is much superior to the conventional chemical methods.

Finally, we attempted transformation of fluorinated sulfones 3 into biologically interesting monofluoro β-lactams 4. Thermolysis of 3 at 200 °C for just 5 min gave the desired products 4 in almost pure state without purification in excellent yields. The products 4 are richer in the trans form than are the starting 3. Thermodynamic stability probably accounts for the predominant or preferential formation of trans derivatives during thermolysis. Monofluoro β-lactams may be used not only as synthetic intermediates for the preparation of fluorinated β-lactam antibiotics but also as building blocks for carbohydrates and amino acids. However, only limited reports have been made of the synthesis of such compounds.[17] Very recently,

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(12) The electrolysis was performed at a platinum anode and cathode (3 × 4 cm) in 0.37 M Et_3N·3HF/MeCN (50 mL) containing 5 mmol of 1 at ambient temperature. After the starting 1 was completely consumed (TLC monitoring), the electrolysis solution was neutralized with 5 mL of 29% aqueous ammonia. The acetonitrile was removed by evaporation and 100 mL of water was added and then extracted with CH_2Cl_2 (40 mL × 3). The extracts were dried ($MgSO_4$) and the residue was passed through short column chromatography (silica gel, CH_2Cl_2) to provide crude product 2. The cis/trans ratios (de) of 2 were determined by the measurement of ^{19}F NMR of the crude 2. The trans isomer was established on the basis of a large long-range coupling between the fluorine and the hydrogen at the 2-position: Jackson, L. M.; Sternhell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, 2nd ed.; Pergamon Press: Oxford, 1968; p 334. Stereoisomers, 2a (cis), 2a (trans), 2c (cis), 2c (trans), and 2e (trans) were separated by silica gel TLC (hexane:AcOEt = 7:3–1:1). The products 2c, 2d, and 2f were treated with 3.5 equiv of *m*-CPBA in $CHCl_3$ at rt for 3 days, and the resulting sulfone derivatives 3c, 3d, and 3f were isolated as stereoisomeric mixtures by silica gel TLC (hexane:AcOEt = 7:3–1:1). However, 2b was so unstable, its oxidative conversion into sulfone failed. In this case, only ^{19}F NMR and MS and HRMS spectra could be obtained.

(13) Purrington, S. T.; Pittman, J. H. *Tetrahedron Lett.* **1987**, *28*, 3901.

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Welch et al. have reported stereoselective formation of 3-fluoro-β-lactams via ketene–imine condensation.[17] However, their stereochemistry is completely reversed to ours since they observed that the cis form was solely or predominantly formed.[18]

In conclusion, we have succeeded in anodic monofluorination of sulfur-containing heterocycles for the first time and developed a convenient preparation of monofluoro β-lactams.

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Supplementary Material Available: ^1H NMR, IR, MS, and high-resolution MS data for all new compounds (4 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(18) For example, the reaction of monofluoroacetic acid chloride with ethylidene aniline in the presence of triethylamine provided cis 4c solely in 33%.

Intramolecular Mitsunobu Displacement with Carbon Nucleophiles: Preparation of α-Nitrocyclopropanes

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Summary: γ-Nitroalkanols are converted to α-nitrocyclopropanes with inversion of configuration in good to excellent yields using diethyl azodicarboxylate and Ph_3P.

Three-membered carbocycles are present in a wide range of terrestrial and marine natural products, inter alia, insecticides,[1] pheromones,[2] fatty acids,[3] terpenoids/steroids,[4] and antibiotics.[5] They are also intermediates in primary and secondary metabolism and show promise as mimetics of biolabile groups.[6] As a consequence of their inherent strain energy, functionalized members of this class have proven to be exceedingly versatile synthetic reagents.[7] Cyclopropanes are most often prepared by intra- and intermolecular addition of sulfur ylides, diazoalkanes, or carbenoids to unsaturated systems, and considerable attention has been devoted to the development of stereocontrolled modifications of these approaches.[7,8] In contrast, comparatively few chiral cyclopropanes have been made via nucleophilic displacement.[9]

We report herein that treatment of a wide variety of γ-nitroalkanols with a preformed complex of diethyl azodicarboxylate (DEAD) and triphenylphosphine affords α-nitrocyclopropanes[10] in good to excellent yields. The reaction proceeds rapidly at ambient tempertaure under essentially neutral conditions in benzene or THF. This represents a highly efficient intramolecular variant[11] of the Mitsunobu[12] displacement procedure in which a nitronate anion acts as a carbon nucleophile resulting in a new carbon–carbon bond. Competitive alkylation of the oxygens in the ambident nitronate anion is not observed.

Some representative annulations are summarized in Table I. Acyclic primary (entry 1) and secondary (entry 2) nitro alcohols react smoothly as do related carbocycles

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