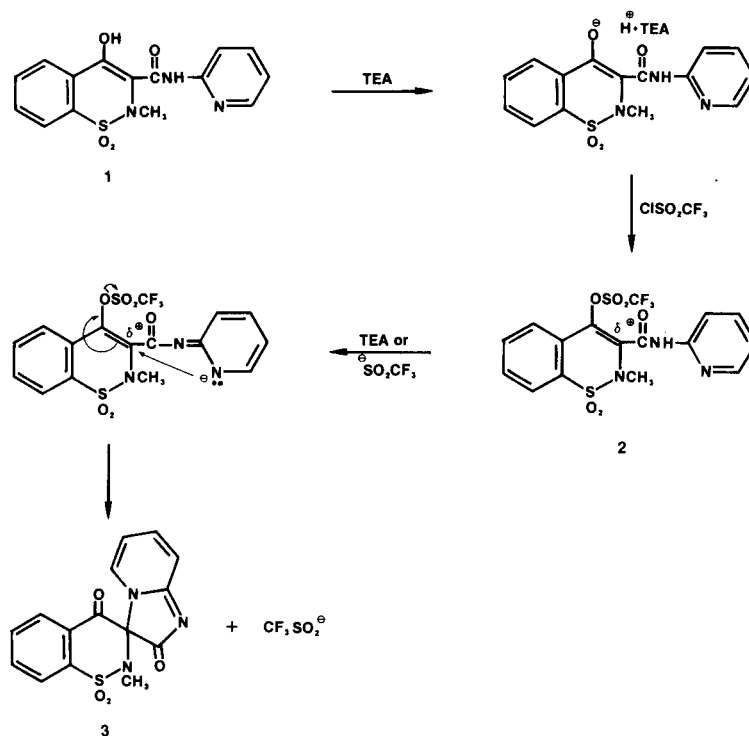


Figure 1



Scheme 3

sults in rapid O-acylation to produce **2** in a manner analogous to other sulfonyl chlorides reported earlier [3]. Unlike methanesulfonyl, however, the trifluoromethylsulfonyl moiety is extremely electronegative, creating a partial positive charge on C-3. This in turn makes the amide proton more acidic. With triethylamine present in slight ex-

cess, the amide proton is removed and the resulting negative charge is delocalized into the pyridyl ring. The electron-rich pyridyl nitrogen can then initiate a nucleophilic attack at C-3 through a 5-membered cyclic intermediate forming the new imidazo[1,2-*a*]pyridine spiro ring and simultaneously displacing trifluoromethane sulfinic acid.

Table 1

Single Crystal X-ray Crystallographic Analysis

A. Crystal Parameters	
formula	C ₁₅ H ₁₁ O ₄ N ₃ S(329.34)
crystallization medium	acetone
crystal size, mm	0.41 × 0.49 × 0.59
cell dimensions	a = 9.677(2) Å
	b = 15.996(5) Å
	c = 10.010(3) Å
	α = 90.0°
	β = 111.51(2)°
	γ = 90.0°
	V = 1441.6(7) Å ³
space group	P2 ₁ /c
molecules/unit cell	2
density obsd, g/cm ³	1.50
density calcd, g/cm ³	1.517
linear absorption coefficient, cm ⁻¹	2.51

B. Refinement Parameters

number of reflections	1551
nonzero reflections(I > 1.0σ)	1454
R-index = $\sum F_o - F_c / \sum F_o $	0.055
GOF = $[\sum w(F_o^2 - F_c^2)^2 / (m-s)]^{1/2}$	3.95
scale factor	0.860(5)
secondary extinction coefficient	1.1(3) × 10 ⁻⁶

Table 2

Atomic Coordinates for Atoms in Crystalline **3** [a]

Atom	X	Y	Z
S(1)	0.4194(2)	0.7953(0)	0.6729(1)
O(1A)	0.3074(3)	0.7317(3)	0.6168(2)
O(1B)	0.5725(2)	0.7736(3)	0.7328(1)
N(2)	0.3794(7)	0.8480(7)	0.7930(4)
C(2A)	0.4957(7)	0.8743(6)	0.9284(4)
C(3)	0.2339(6)	0.8846(5)	0.7462(3)
C(4)	0.1572(9)	0.9007(8)	0.5820(4)
C(4A)	0.2518(7)	0.9126(7)	0.4978(4)
O(4B)	0.0222(5)	0.9080(5)	0.5316(3)
C(5)	0.2114(7)	0.9644(7)	0.3781(4)
C(6)	0.3001(8)	0.9704(7)	0.2987(4)
C(7)	0.4339(7)	0.9300(7)	0.3386(4)
C(8)	0.4785(8)	0.8755(7)	0.4561(4)
C(8A)	0.3860(9)	0.8697(8)	0.5342(4)
C(9)	0.2334(8)	0.9760(8)	0.8154(5)
O(10)	0.3066(7)	1.0333(7)	0.7966(4)
N(11)	0.1415(8)	0.9738(6)	0.8907(4)
C(12)	0.0827(8)	0.8973(7)	0.8768(4)
N(13)	0.1293(8)	0.8422(7)	0.7986(4)
C(14)	0.0750(10)	0.7635(7)	0.7649(4)
C(15)	-0.0349(9)	0.7364(8)	0.8102(5)
C(16)	-0.0827(8)	0.7906(7)	0.8951(5)
C(17)			

[a] Atoms are labeled in agreement with Figure 1. The numbers in parentheses are the estimated standard deviations in the last significant digit.

Table 3

Selected Bond Distances (Å) with Estimated Standard Deviations

S(1)-O(1A)	1.443(4)	C(5)-C(6)	1.371(9)
S(1)-O(1B)	1.423(3)	C(6)-C(7)	1.369(11)
S(1)-N(2)	1.627(7)	C(7)-C(8)	1.398(11)
S(1)-C(8A)	1.765(9)	C(8)-C(8A)	1.390(11)
N(2)-C(2A)	1.470(7)	C(9)-O(10)	1.214(15)
N(2)-C(3)	1.436(10)	C(9)-N(11)	1.360(10)
C(3)-C(4)	1.566(5)	N(11)-C(12)	1.336(15)
C(3)-C(9)	1.618(14)	C(12)-N(13)	1.360(13)
C(3)-N(13)	1.466(11)	C(12)-C(17)	1.413(8)
C(4)-C(4A)	1.467(10)	N(13)-C(14)	1.358(16)
C(4)-O(4B)	1.221(9)	C(14)-C(15)	1.371(13)
C(4A)-C(5)	1.389(10)	C(15)-C(16)	1.405(13)
C(4A)-C(8a)	1.394(13)	C(16)-C(17)	1.386(11)

Table 4

Selected Bond Angles (Degrees) with Estimated Standard Deviation

O(1B)-S(1)-O(1A)	120.6(2)	C(6)-C(5)-C(4A)	120.3(8)
N(2)-S(1)-O(1A)	107.8(3)	C(7)-C(6)-C(5)	121.6(6)
C(8A)-S(1)-O(1A)	105.9(3)	C(8)-C(7)-C(6)	120.4(6)
N(2)-S(1)-O(1B)	107.9(2)	C(8A)-C(8)-C(7)	116.8(8)
C(8A)-S(1)-O(1B)	111.0(3)	C(4A)-C(8A)-S(1)	114.9(6)
C(8A)-S(1)-N(2)	102.0(4)	C(8)-C(8A)-S(1)	121.2(8)
C(2A)-N(2)-S(1)	121.3(5)	C(8)-C(8A)-C(4A)	123.4(7)
C(3)-N(2)-S(1)	116.1(3)	O(10)-C(9)-C(3)	121.4(7)
C(3)-N(2)-C(2A)	120.8(7)	N(11)-C(9)-C(3)	108.6(9)
C(4)-C(3)-N(2)	116.3(5)	N(11)-C(9)-O(10)	129.9(11)
C(9)-C(3)-N(2)	112.7(6)	C(12)-N(11)-C(9)	107.8(8)
N(13)-C(3)-N(2)	114.7(7)	N(13)-C(12)-N(11)	115.7(8)
C(9)-C(3)-C(4)	103.2(7)	C(17)-C(12)-N(11)	125.8(8)
N(13)-C(3)-C(4)	109.3(5)	C(17)-C(12)-N(13)	118.4(9)
N(13)-C(3)-C(9)	98.6(6)	C(12)-N(13)-C(3)	109.0(9)
C(4A)-C(4)-C(3)	118.2(6)	C(14)-N(13)-C(3)	126.4(7)
O(4B)-C(4)-C(3)	118.4(6)	C(14)-N(13)-C(12)	124.3(8)
O(4B)-C(4)-C(4A)	123.2(5)	C(15)-C(14)-C(13)	119.1(9)
C(5)-C(4A)-C(4)	122.4(8)	C(16)-C(15)-C(14)	118.2(10)
C(8A)-C(4A)-C(4)	120.2(7)	C(17)-C(16)-C(15)	122.6(7)
C(8A)-C(4A)-C(5)	117.4(6)	C(16)-C(17)-C(12)	117.3(5)

EXPERIMENTAL

Melting points were determined in a Thomas-Hoover capillary melting point apparatus and are uncorrected. The ir spectrum was obtained in potassium bromide pellets. The mass spectral data was determined on an AEI-MS-30 mass spectrometer. The proton-nmr spectra was recorded on a Bruker WM-250 spectrometer and chemical shift values are recorded in parts per million relative to an internal standard(tetramethylsilane). Analyses were carried out by the Physical Measurements Laboratory of Pfizer Inc.

Reaction of **1** with Trifluoromethanesulfonyl Chloride.

To 5.0 g (0.015 mole) or piroxicam (**1**) in 200 ml of dichloromethane was added 2.6 ml of triethylamine (0.019 mole). To the resulting yellow solution was added dropwise a solution of 2.0 ml (0.019 mole) of trifluoromethanesulfonyl chloride (Aldrich Chemical Co.) in 50 ml of dichloromethane. The yellow solution was stirred under nitrogen at room temperature. Tlc (9:1 dichloromethane/ethyl acetate) indicated reaction was virtually complete to form one new material (R_f 0.05) after one hour. The reaction was stirred overnight and then washed twice with saturated sodium bicarbonate solution, once with brine and then dried over anhydrous

sodium sulfate. Removal of all solvent produced a residue which was recrystallized from chloroform to give 2.70 g (54%) of **3**, mp 210° dec; ir: (μ) 5.80 (C=O), 5.89 (C=O), 7.40 (SO₂N), 8.41 (SO₂N); ¹H-nmr (deuteriochloroform): 2.99 (s, CH₃, 3H), 6.89 (t, H on C₍₁₅₎, 1H, J = 0.8 MHz), 7.19 (d, H on C₍₁₇₎, 1H, J = 0.8 MHz), 7.8 (m, H on C₍₁₆₎ and remaining aryl H, 5H), 8.23 (d, H on C₍₁₄₎, 1H, J = 0.8 MHz); ms: Calcd. M+ = 329.0400, M⁺ observed = 329.0475, m/e (relative intensity): 329 (M+, 10), 265 (C₁₅H₁₁N₃O₂+, 40), 223 (C₁₃H₅N₂O₂+, 22), 117 (C₈H₅O+, 100), 104 (C₇H₄O+, 80), 76 (C₆H₄+, 55).

Anal. Calcd. for C₁₅H₁₁O₄N₃S: C, 54.70; H, 3.37; N, 12.76. Found: C, 54.40; H, 3.48; N, 12.76.

Single-Crystal X-ray Analysis.

A representative crystal was surveyed and a 1-Å data set (maximum $\sin \theta/\lambda = 0.5$) was collected on a Syntex P1 diffractometer. The diffractometer was equipped with a graphite monochromator and molybdenum radiation ($\lambda = 0.71069$ Å). Atomic scattering factors were taken from the "International Tables for X-ray Crystallography", [4], except hydrogen which was taken from Stewart, Davidson and Simpson [5]. All crystallographic calculations were facilitated by the CRYM system [6]. All diffractometer data were collected at room temperature. Pertinent crystal, data collection, and refinement parameters are summarized in Table 1.

A trial structure was obtained by direct methods using the MULTAN program [7]. This trial structure refined routinely. Hydrogen positions were calculated wherever possible. The methyl hydrogens were located by difference map Fourier techniques. The hydrogen parameters were added to the structure factor calculations but were not refined. The final

cycles of full matrix least-squares refinement contained the scale factor, secondary extinction coefficient, coordinates, and anisotropic temperature factors in a single matrix. The shifts calculated in the final cycle were all zero. The final R-index was 0.055. A final difference Fourier revealed no missing or misplaced electron density. The refined structure was plotted using the ORTEP computer program of Johnson [8] (Figure 1). Coordinates, bond distances and bond angles are given in Tables 2-4.

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