Electrophilic Addition of Chlorosulfonyl Isocyanate to Ketones. Reaction with Aromatic Ketones[1a]

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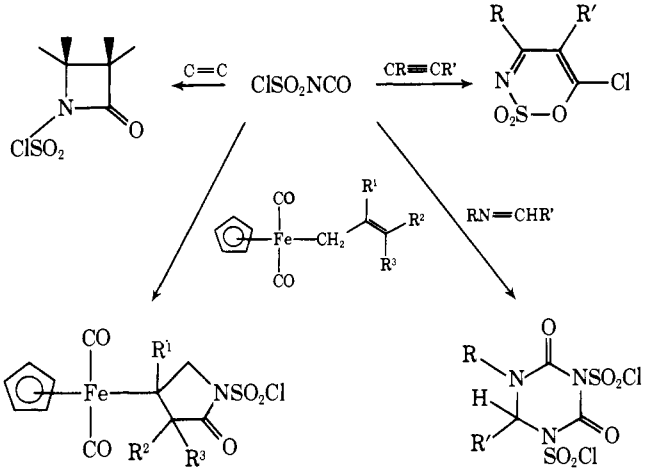
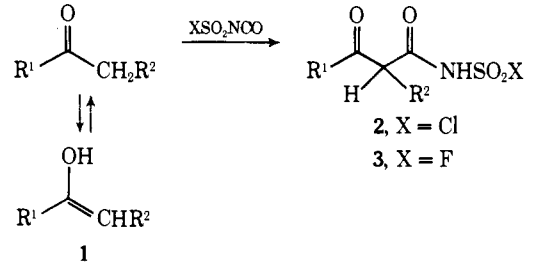
Abstract: Electrophilic addition of chlorosulfonyl isocyanate (CSI) to "aromatic" ketones **1** ($R^1COCH_2R^2$, R^1 and/or R^2 = aryl) was found to be a synthetically versatile reaction, producing 2*H*-1,3-oxazine-2,4(3*H*)-diones (**6**) when dichloromethane was the solvent and 1,2,3-oxathiazin-4(3*H*)-one 2,2-dioxides (**4**) as well (if R′ = aryl) in diethyl ether solvent. A number of additional products are observed in low yield. An examination of substituent effects and nmr studies indicates that the determining factor in the oxathiazine:oxazine ratio is the position of the keto–enol equilibrium in the intermediate *N*-chlorosulfonyl-β-ketocarboxamide, **2.** After the initial formation of **2,** the reaction takes one of the following routes. (1) A second electrophilic addition to the enol can occur to produce a malonamide derivative **23,** as evidenced by the isolation of **23a** and **23f** under appropriate conditions. In solution, **23** readily eliminates CSI to regenerate **2.** This sequence can serve as a synthetic route from ketones to malonamides and malononitriles. (2) CSI can act as a Lewis acid upon **2,** abstracting a chloride to eventually produce an *N*-sulfonylamine **15** which then cyclizes to **4.** (3) Reaction of CSI with the enol form of **2** can produce the enol carbamate **25.** Cyclization of this intermediate with loss of sulfamoyl chloride then leads to **6.** Evidence supporting the proposed overall mechanism is provided.

The remarkable electrophilicity of chlorosulfonyl isocyanate (CSI) has found numerous applications in synthetic organic chemistry.[2] Notable among these are 2 + 2 cycloadditions with a variety of olefins, leading to β-lactam derivatives. In some cases, especially with di- or polyolefinic substrates, rearrangements can occur to give heterocyclic products other than β-lactams. Reaction of CSI with acetylenes leads to 6-chloro-1,2,3-oxathiazine 2,2-dioxides.[3] Metal assisted 3 + 2 cycloadditions have been reported with CSI[4] and recently[5] reactions with imines have been described.



We are now showing that ketones, **1,** likewise are capable of interaction with CSI, leading to a variety of products.[6]

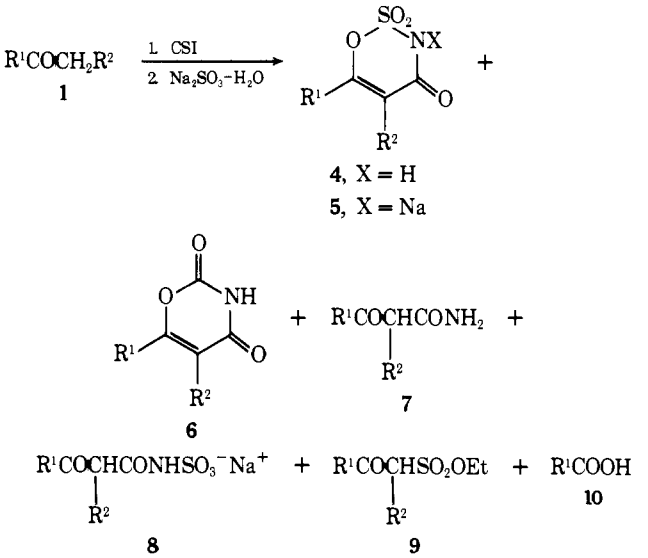


This reaction is initiated by electrophilic attack of CSI upon the enol tautomer of the ketone with subsequent formation of a β-ketocarboxamide **2.** The ability of this initial adduct to undergo further transformations is responsible for the synthetic usefulness of this reaction.[6] Analogously, fluorosulfonyl isocyanate (FSI) has been reported to yield **3.**[7] The present paper elaborates upon the initial report[6a] and describes a number of new findings which help establish mechanistically the events which occur subsequent to the initial electrophilic attack of CSI upon the enol.

Results and Discussion

Reaction of CSI with Aromatic Ketones. Treatment of "aromatic" ketones (**1,** R^1 and/or R^2 = aryl) with 2–3 equiv of CSI provided 1,2,3-oxathiazin-4-(3*H*)-one 2,2-dioxides, **4,** and 2*H*-1,3-oxazine-2,4-(3*H*)-diones, **6,** as the major products. Isolation of the products was carried out, after reductive hydrolysis with aqueous sodium sulfite,[8] by extraction of the basic solution with ether. This provided the crude oxazines **6.** Acidification of the aqueous phase and reextraction gave oxathiazines **4.** In a number of cases, additional minor products were also observed (Scheme I).

Scheme I



The basic extract often contained sulfonate esters **9,** whereas the acidic extract sometimes yielded carboxylic acids **10.** In certain instances β-ketocarboxamides **7** or their sulfonate salts **8** separated from the aqueous phase upon standing (Table I). Occasionally during the sodium sulfite work-up,

Table I. Product Distribution from Reaction of "Aromatic" Ketones, **1**, with CSI

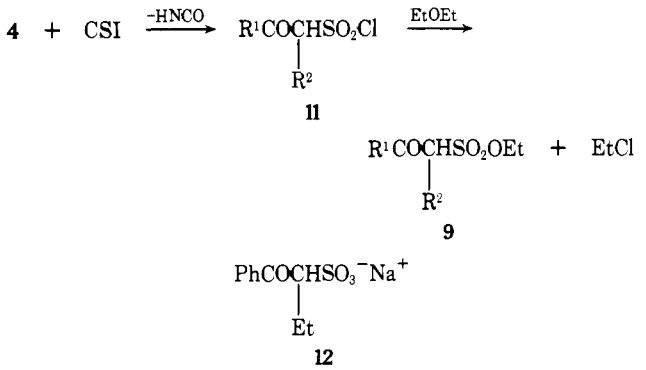
Entry	Compd	R^1	R^2	Solvent	Reaction temp, time	% **4**	% 6	% other
1	a	Ph	Me	Ether	Reflux, 7 days	41.5[a]	28.4	
2				CH_2Cl_2	Reflux, 6 days		43.0	
3	**b**	Ph	Et	Ether	Reflux, 7 days	41.2	7.7	**12** (4.2)
4				CH_2Cl_2	RT,[d] **11** days		14.8	**7b**[b] (34.5)
5				CH_2Cl_2	RT, 28 days		45.5	**7b**[b] (5.2)
6	**c**	Me	Ph	Ether	RT, 4 hr		70.6	
7	**d**	$PhCH_2$	Ph	Ether	RT, 4 days		61.0	**8d** (9.6)
8	**e**	Ph	Ph	Ether	RT, 7 days	28.4	13.6	**9e** (18.5)
							4.7	**8e** (58.2), **10a** (4.9)
9	**f**	$-o-C_6H_4(CH_2)-$		Ether	RT, 4.5 days	19.8[a]	30.3	
10	g	Ph	PhCO	Ether	RT, 9.5 hr		11.1	**8g** (11.2)
				CH_2Cl_2	RT, 3 days		9.8	**8g** (14.9)
11	h	p-$MeOC_6H_4$	Me	Ether	RT, 22.5 hr	2.6[c]		**9h** (40.5), **10h** (2.7), **22** (7.3)
12	i	p-MeC_6H_4	Me	Ether	RT, 7 days	30.4	3.0	**9i** (6–10),[c] **10i** (5.2)[c]
13	**a**	Ph	Me	Ether	RT, 8 days	40.9	8.8	**9a** (10–15),[c] **10a** (13.9)
14	**j**	p-ClC_6H_4	Me	Ether	RT, 6 days	20.7	13.2	**9j** (10–15),[c] **10j** (8.5)

[a] Reference 7. [b] Reference 20. [c] Yields estimated by nmr. [d] RT = room temperature.

sodium salts **5** of the oxathiazines separated from the mixture and were filtered prior to the extraction steps. Yields of these salts **5** are included with the yields of **4** in Table I. Sulfonate salts **8** were convertible into the corresponding amides **7** by treatment with aqueous acid or by refluxing in toluene for a short period of time.

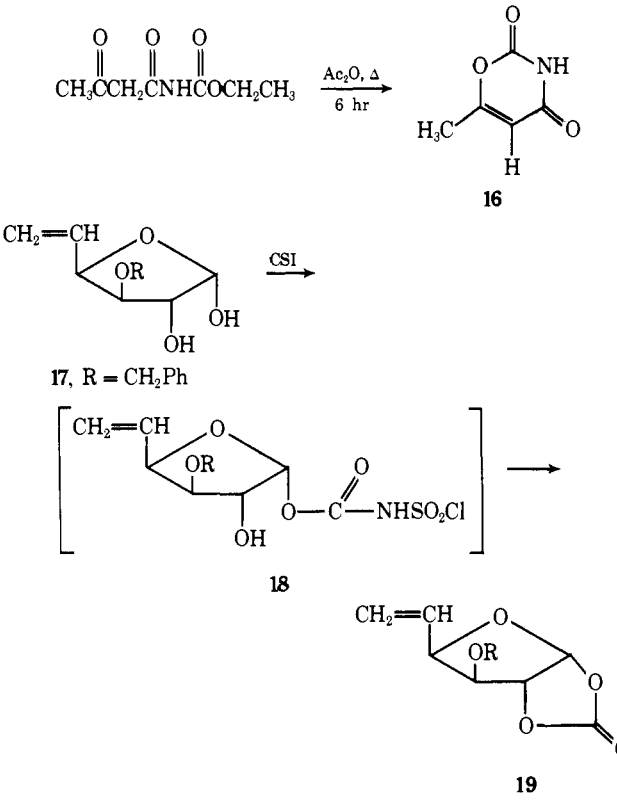
The origin of the amide products is quite clear. Complete hydrolysis of the intermediate *N*-chlorosulfonyl-β-ketocarboxamide (**2**) will produce **7**, whereas incomplete hydrolysis under basic conditions will lead to **8**; these types of reactions are already precedented in CSI chemistry.[2a] The source of sulfonate esters **9** is a little more difficult to explain. The ethoxy group must necessarily come from the solvent, diethyl ether, thus suggesting the intermediacy of the sulfonyl chloride **11** (Scheme II) which may then react

Scheme II



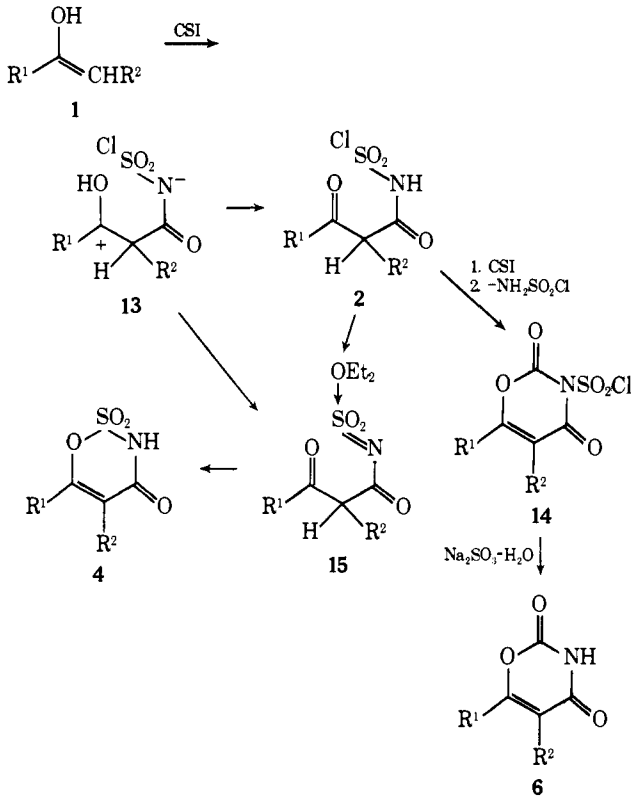
with solvent to give **9** and ethyl chloride. This cleavage may be catalyzed by traces of SO_3, known to be present in CSI, or by CSI itself.[9] The formation of species such as **11** is not entirely unprecedented, since reaction of CSI with anisole produces bis(4-methoxyphenyl) sulfone as the only product.[10] Sodium butyrophenone-α-sulfonate (**12**), obtained as the monohydrate in one reaction (Table I, entry 3), probably arose from hydrolysis of sulfonate ester **9b** or from **11** during chromatography (see Experimental Section). The precursor of carboxylic acids **10** will be discussed below.

Initial attack of CSI upon the enol form of ketones **1** is expected to produce the 1,4-dipole **13** and subsequently amide **2** *via* a proton shift (Scheme III).[6a] Additional evidence is now provided by the isolation and characterization of **2b** (see below). Amide **2** can further react with a second equivalent of CSI and cyclize with loss of sulfamoyl chloride to give **14.** An analogy for this cyclization is the preparation of oxazine **16**,[11] while, in CSI chemistry, the formation[9] of **19** from vicinal diol **17** appears to involve a similar elimination *via* intermediate **18.** Additional evidence supporting loss of sulfamoyl chloride from **21**, rather than loss of HCl and sulfimide, is presented in a succeeding paper.[12]

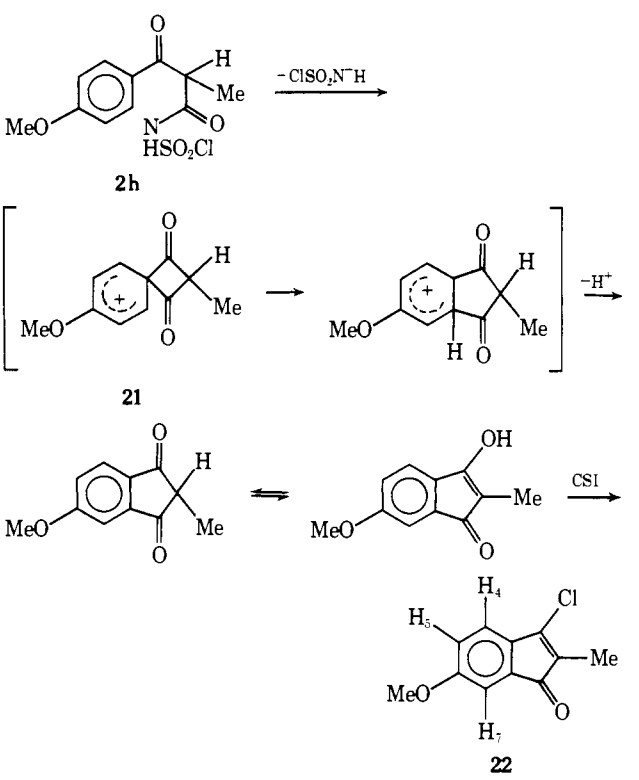


Formally, oxathiazines **4** could be formed simply by cyclization of amides **2** with loss of HCl. In fact, treatment of *N*-fluorosulfonyl-β-ketocarboxamides, **3**, with base does lead to oxathiazines.[7] However, a satisfactory explanation must take into account the results indicated in Table I, namely that compounds of type **4** arise only when ether is employed as solvent and also that oxathiazines are not produced in those cases where $R^1 \neq$ aryl (entries 6 and 7). An attractive alternative especially in view of the work of Burgess and Williams[13] on the preparation and reactions of the tetrahydrofuran complex of methyl *N*-sulfonylurethane (**20**) is that the *N*-sulfonylamine **15** is an intermediate, derived from either 1,4-dipole **13** or from **2.** Ring closure fol-

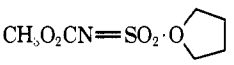
Scheme III



Scheme IV



lowed by a proton transfer would then give **4**. Thus the initial results (Table I, entries 1-9) seem to be consistent with



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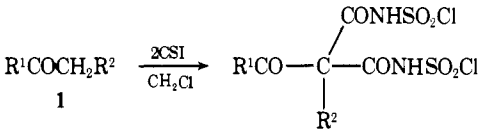
the idea that oxathiazine formation would occur only if R^1 was capable of supplying sufficient stabilization to the positive center of dipole **13** to allow its transformation into **15**. In an effort to obtain additional evidence, a study of substituent effects upon product distribution was undertaken utilizing substituted propiophenones (**1a**, **h-j**). The results are shown in Table I, entries 11-14.

Substituent Effects on Product Distribution. When *p*-methoxypropiophenone (**1h**) was allowed to react with CSI in ether, a new type of product was obtained from the basic extract. Spectral data and elemental analysis indicated that this compound was an indenone. The structure was firmly established as 3-chloro-6-methoxy-2-methylindenone (**22**) with the help of nmr chemical shifts induced by Sievers' reagent, $Eu(fod)_3$. Gradual addition of the shift reagent transformed the ABC pattern of the aromatic hydrogens into an AMX pattern, with $J_{AM} = 8$, $J_{AX} = 2$, and $J_{MX} \sim 0$ Hz. Assuming coordination of the europium reagent with the carbonyl oxygen,[14] this result is consistent only with the methoxy group at position 6, with a 2-Hz meta coupling between H_5 and H_7 and an 8-Hz ortho coupling between H_4 and H_5. A possible mechanism for the formation of **22** involves the spirocyclic intermediate[15] **21** (Scheme IV). Rearrangement, loss of a proton, and eventual chlorination of the enol form by excess CSI leads to the observed product. CSI has recently been observed to act as a chlorinating agent.[16] Preferential enolization occurs as shown due to the conjugative effect of the *p*-oMe group.

In addition to the indenone **22**, ethyl *p*-methoxypropiophenone-α-sulfonate (**9h**) was produced in about 40% yield along with low yields of oxathiazine **4h** and *p*-methoxybenzoic acid (**10h**). The reason for the high yield of sulfonate ester in this case, as compared to the other examples studied is unclear. The sulfonate esters were obtained as oils which could not be rigorously purified. However, they were readily identified by comparison of their spectral properties with those of **9e**, isolated as the pure compound.

Comparison of the relative amounts of oxazines **6** to oxathiazines **4** as a function of the substituents (Table I, entries 11-14) is quite interesting. As the substituent constant σ becomes more positive, proportionately more oxazine **6** is produced. Surprisingly, however, the results correlate much better with σ than with σ^+.

Concentration Effects. Malonamides and Malononitrile Synthesis. All room temperature reactions listed in Table I were carried out using 1 ml of solvent/mmol of ketone **1**. If, however, propiophenone (**1a**) was allowed to react with CSI in dichloromethane (0.5 ml/mmol of **1a**), a colorless precipitate unexpectedly formed as the reaction progressed. This very hygroscopic compound, obtained in 62.4% yield (average of several runs), was identified as *N,N'*-bis(chlorosulfonyl)benzoyl(methyl)malonamide (**23a**) on the basis of chemical reactions (see below) and spectral data. In a similar fashion, α-tetralone **1f** produced **23f** in 22% yield.



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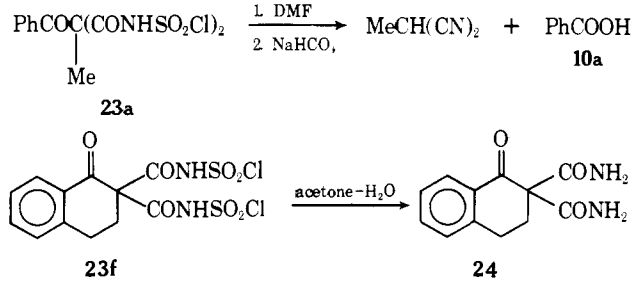
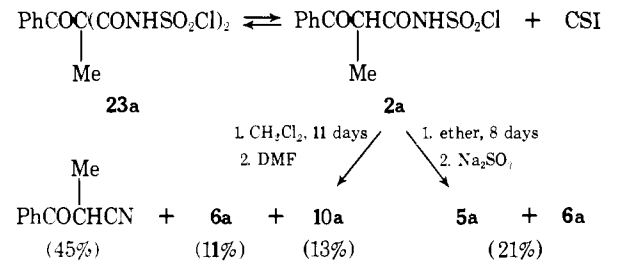
Reductive hydrolysis of **23a** with aqueous sodium sulfite produced benzoic acid **10a** in 95% yield, thus establishing the source of the acids **10** observed above. The other expected product, methyl malonamide, was undoubtedly lost due to high solubility in the aqueous phase. However, treatment of **23a** with excess dimethylformamide (DMF)[17] followed by hydrolysis with aqueous bicarbonate allowed the isolation of methyl malononitrile (47%) and **10a** (83%). Treatment of **23f** with wet acetone provided malonamide **24** in 82% yield.



The malonamide derivative **23a** possessed an additional intriguing property. When suspended in dichloromethane, it appeared to dissolve slowly. A check of the infrared and nmr spectra of the mixture indicated the reason: **23a** had eliminated 1 equiv of CSI to produce β-ketoamide **2a**, (Scheme V)![18] If, after 11 days, the mixture was treated

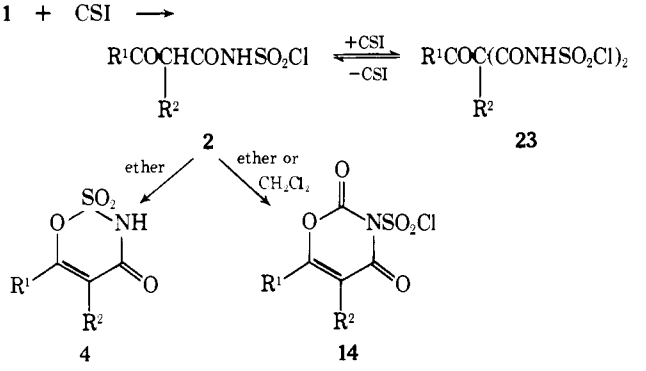
Scheme V



with DMF, the β-ketonitrile[6b] corresponding to **2a** was obtained as the major product along with smaller amounts of oxazine **6a** and benzoic acid (**10a**). A similar experiment employing ether as solvent yielded oxathiazine **4a** (21%) and a small amount of oxazine **6a.**

These results add a new dimension to the electrophilic addition of CSI to ketones. It is now apparent that following the formation of the initial adduct **2**, several alternatives for further reaction are available (Scheme VI). The

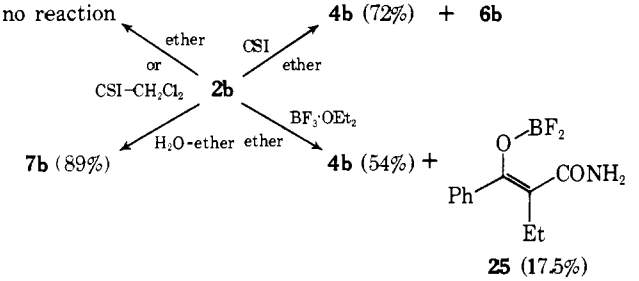
Scheme VI



malonamides **23** are obviously the kinetic products but are not isolated unless conditions are chosen such that they precipitate from the reaction medium. If **23** is not precipitated, CSI is eliminated regenerating amide **2** which is eventually removed from the equilibrium by formation of thermodynamic products **4** and **14.** The results also verify a direct route to oxathiazines **4** from amides **2**, which will be discussed below following the presentation of additional evidence.

Under conditions conducive to malonamide formation, butyrophenone **1b** does not produce any **23b.** This is due to the insolubility of the intermediate monoamide **2b.** In fact, when CSI is allowed to react with excess **1b**, followed by concentration of the reaction mixture *in vacuo*, 2-benzoyl-*N*-chlorosulfonylbutyramide (**2b**) can be isolated in 73.5% yield. Amide **2b** is relatively stable if precautions are taken to preclude contact with moisture. Dissolution of **2b** in ether induced no cyclization within a period of 13 days. In fact, treatment of **2b** with 1 equiv of CSI in CH_2Cl_2 also gave no reaction in 7 days. If, however, the addition was repeated in ether, oxathiazine **4b** was produced in 72% yield, along with a small amount of oxazine **6b** (Scheme VII). Boron trifluo-

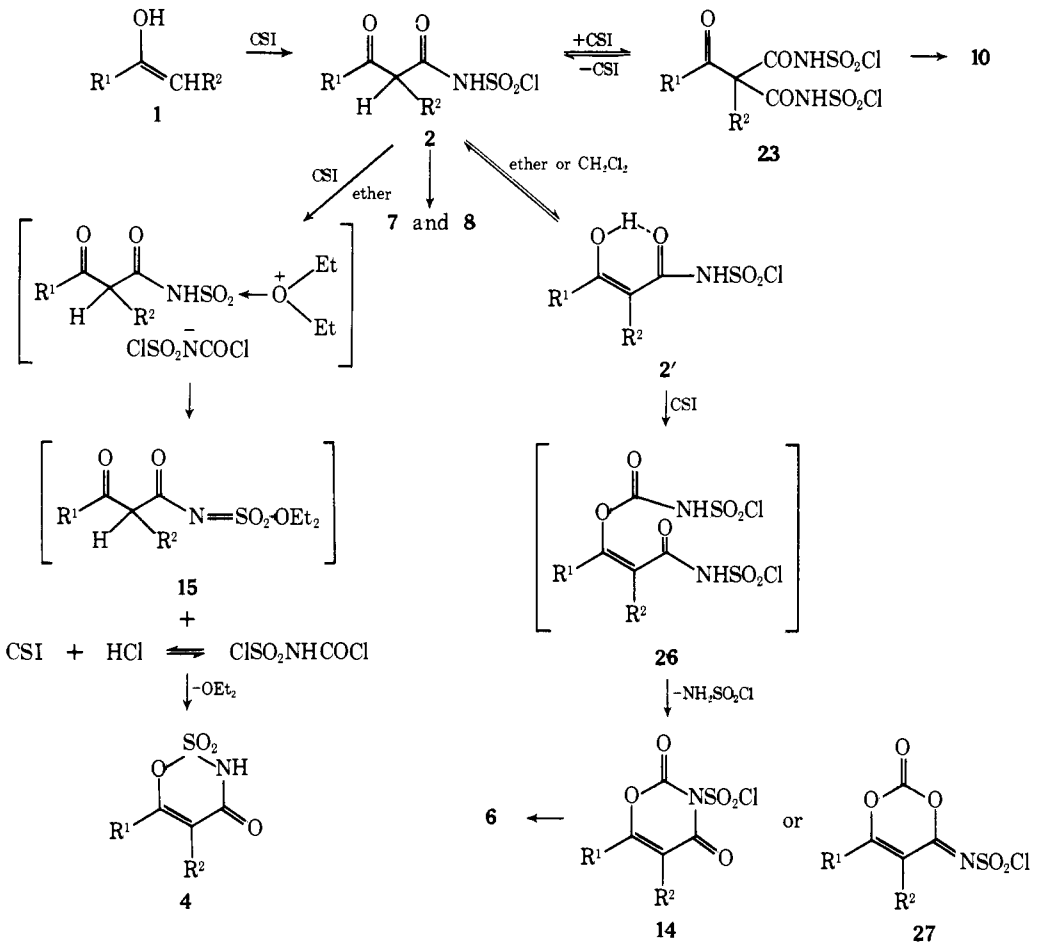
Scheme VII



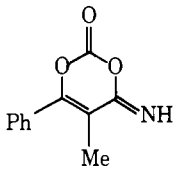
ride etherate also induced cyclization of **2b** to **4b**, thus seeming to verify the role of CSI as a Lewis acid. The boron difluoride complex **25** isolated as a by-product in this reaction was not unexpected.[19] A few drops of water in ether were sufficient to hydrolyze **2b** to 2-benzoylbutyramide[20] **7b** in 89% yield.

Mechanism of Oxazine and Oxathiazine Formation. The foregoing results now allow the formulation of an overall rationale for the reaction of CSI with "aromatic" ketones **1** (R^1 or R^2 = Ar) (Scheme VIII). The first step necessarily involves electrophilic attack upon the enol with subsequent formation of β-keto carboxamide **2.** Thereafter, a rapid equilibrium, which largely favors **2**, is set up between **2** and the malonamide **23.** When ether is the solvent, CSI, acting as a Lewis acid,[9] can abstract a chloride from **2**, thus producing *N*-sulfonylamine **15** following a proton transfer. Oxathiazine **4** then forms upon ring closure of **15.** β-Ketoamide **2** can also exist in the enol form **2′**. Assuming that the second equivalent of CSI reacts with the enolic hydroxyl group to produce intermediate **26**, the substituent effects upon product distribution can be explained. Electron-withdrawing groups on the termini of a 1,3-dicarbonyl system are known to increase the stability of the enol relative to the keto form.[21] Thus electron-withdrawing substituents on R^1 will tend to increase the concentration of enol **2′**, thereby raising the relative amount of oxazine **6** produced, in accordance with the observed results. The effect of groups R^2 on the keto-enol equilibrium is not so clear.[21] If the assumed mechanism is correct, however, it would appear that the enol is strongly favored when R^2 = Ph (ketones **1c** and **1d**). In order to test this prediction, ketones **1a, 1c,** and **1d** were treated with 0.98 equiv of CSI in carbon tetrachloride, and the reaction was monitored by nmr. In all cases, the enol form **2′** was readily distinguished from starting ketones **1** and β-ketoamide **2.** Both amides **2c** and **2d** were found to exist in >60% as the enol tautomer. In contrast to this, amide **2a** was present largely as the diketo form (17% enol). Thus the ready transformation of ketones **1c** and **1d** into oxazines can be understood to occur as a result of the favorable keto-enol equilibrium. Ring closure of intermediate **26** through nitrogen would lead directly to oxazine **14.** Due to the nonavailability of the lone pair on nitrogen, however, oxygen closure would seem more likely, producing a carbonate **27** which may then rearrange in the reaction medium or during work-up. In fact, when phenyl-2-propanone **1c** was allowed to react with CSI, a few crystals of material were obtained which appeared to be the carbonate **28.** The infrared spectrum of this material was quite different from those of the other oxazines **6**, notably in the NH and carbonyl stretching regions ($\nu_{C=O}$ = 1795, $\nu_{C=N}$ = 1680

Scheme VIII



cm^{-1}). This material rearranged to **6c** on melting.



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In conclusion, ketones **1** were found to react with CSI, the products being the oxazines **4** (that can serve as precursors to the biologically interesting uracils)[6a] and/or oxathiazines **6** (potential artificial sweeteners)[7] as well as α-cyano ketones[6b] or malononitriles, depending upon the reaction conditions and the degree of enolization. A mechanistic rationale is presented that explains the multiple pathway available in this system and involves an isolable β-ketoamide intermediate.

Experimental Section

Melting points (taken on a Fisher-Johns block) are uncorrected. Infrared spectra were obtained using a Perkin-Elmer 457 instrument. Nmr spectra were recorded on a Varian A-60A or EM-360 spectrometer with TMS as an internal standard. Mass spectra were taken on a Varian M.A.T. CH-5 instrument. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn., or by Atlantic Microlab, Inc., Atlanta, Ga.

Reaction of "Aromatic" Ketones 1a–i with CSI. General Procedure. To a stirred solution (ambient temperature) of the ketone (10 mmol) in dry ether or CH_2Cl_2 (10 ml) was added 2.3 equiv of CSI by syringe. The reaction was protected from moisture, and monitored by nmr or ir spectroscopy. Upon completion of the reaction, the mixture was added dropwise to a mixture of ether and 25% aqueous sodium sulfite solution while the pH was maintained at 7–8 by NaOH addition. The organic layer was separated and the aqueous layer extracted twice more with ether. The combined organic layers were dried (Na_2SO_4) and evaporated *in vacuo* to give the crude "basic" extract. The aqueous layer was then acidified (H_2SO_4) to pH 1–2 and extracted three times with ether. These extracts were combined, dried (Na_2SO_4), and evaporated *in vacuo* to give the crude "acidic" extract. Recrystallization of the basic extract from acetone–Skellysolve "B" gave oxazines **6.** The mother liquor from **6** often consisted largely of sulfonate esters **9.** Recrystallization of the acidic extract from acetone–Skellysolve "B" gave oxathiazines **4** and in some cases, carboxylic acids **10.**

Variations in this procedure are noted under the appropriate ketones.

Propiophenone (1a, 4.00 g, 29.9 mmol) in 10 ml of CH_2Cl_2 was added dropwise to CSI (8.95 g, 63 mmol) in 15 ml of CH_2Cl_2. The mixture was refluxed 4 days, then stirred at room temperature an additional 2 days, hydrolyzed with H_2O–ice, and extracted three times with CH_2Cl_2. The extract was dried (Na_2SO_4) and evaporated *in vacuo* to yield 3.7 g of orange oil. This oil was triturated with boiling CCl_4 and filtered to give 2.9 g of orange-brown solid. Recrystallization from acetone–CCl_4 gave 2.6 g (43%) of 5-methyl-6-phenyl-2*H*-1,3-oxazine-2,4(3*H*)-dione (**6a**) as a pale yellow solid: mp 180–182° (an analytical sample was prepared by recrystallization from methanol, mp 184.5°); ir (KBr) 3140, 3055, 1775, 1740, 1700, 1670, 1635, 1450, and 1405 cm^{-1}; nmr ($CDCl_3$) τ 7.93 (s, 3), 2.47 (br s, 5), and 1.37 (br s, 1); *m/e* (%) M^+ 203 (61.0), 160 (31.0), 132 (29.5), 105 (100), and 77 (72.0).

Anal. Calcd for $C_{11}H_9O_3N$: C, 65.02; H, 4.46; N, 6.89. Found: C, 64.92; H, 4.43; N, 6.83.

Propiophenone (1a, 2.00 g, 14.9 mmol, refluxing ether, 7 days) gave 860 mg (28%) of **6a** from the basic extract. The aqueous layer, upon standing overnight, deposited 1.395 g (36%) of 5-methyl-6-phenyl-1,2,3-oxathiazin-4(3*H*)-one 2,2-dioxide, sodium salt **5a,** as colorless needles: mp 285–287° dec; ir (KBr) 3575, 3500–3000, 1635, 1580, 1380, 1320, 1310, 1200, 1015, 810, 760, and 705 cm^{-1}; nmr (DMSO-d_6) τ 8.16 (s, 3), 2.48 (s, 5). The aci-

dic extract gave 203 mg (6%) of 5-methyl-6-phenyl-1,2,3-oxathiazin-4(3*H*)-one 2,2-dioxide (**4a**) as a colorless solid: mp 122.5° (lit.[7b] 123°); ir (KBr) 3080, 2720, 1680, 1650, 1630, 1420, 1365, 1205, 1155, 1070, 1005, 940, 840, 765, and 705 cm^{-1}; nmr ($CDCl_3$) τ 7.88 (s, 3), 2.42 (s, 5), and −0.01 (br s, 1); *m/e* (%) M^+ 239 (43.0), 160 (4.1), 158 (5.0), 147 (19.0), 146 (41.8), 132 (32.2), 105 (100), and 77 (18.2).

Anal. Calcd for $C_{10}H_9O_4NS$: C, 50.21; H, 3.79; N, 5.86. Found: C, 50.07; H, 3.86; N, 5.79.

Butyrophenone (**1b,** 4.43 g, 29.9 mmol, refluxing ether, 7 days). Recrystallization of the crude basic extract gave 500 mg (8%) of 5-ethyl-6-phenyl-2*H*-1,3-oxazine-2,4(3*H*)-dione (**6b**) as colorless needles: mp 132–133°; ir (KBr) 3150, 3050, 1765, 1665, 1630, 1440, 1405, 1220, 1180, 775, 755, and 705 cm^{-1}; nmr ($CDCl_3$) τ 8.82 (t, J = 7.5 Hz, 3), 7.49 (q, J = 7.5 Hz, 2), 2.41 (s, 5), 0.26 (br s, 1); *m/e* (%) M^+ 217 (41.0), 174 (13.2), 146 (41.2), 131 (9.5), 105 (100), and 77 (76.7).

Anal. Calcd for $C_{12}H_{11}O_3N$: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.58; H, 5.16; N, 6.58.

Chromatography of the mother liquor of **6b** on neutral alumina ($CHCl_3$) gave several fractions containing small amounts of unidentifiable oils. Elution of the column with CH_3OH yielded a colorless oil, which upon trituration with $CHCl_3$ gave 338 mg (4%) of sodium butyrophenone-α-sulfonate monohydrate (**12**) as a colorless solid: mp 258–60° dec; ir (KBr) 3430, 1680, 1450, 1350, 1220, 1060, 990, 770, 735, 702, and 690 cm^{-1}; nmr (DMSO-d_6) τ 9.22 (t, J = 7.5 Hz, 3), 8.00 (m, 2), 5.45, and 5.35 (d of d, J = 8.5 and 6.0 Hz, 1), 2.28–2.58 (m, 3), 1.80 −2.03 (m, 2).

Anal. Calcd for $C_{10}H_{11}O_4SNa{\cdot}H_2O$: C, 44.76; H, 4.88; S, 11.95; N, 0.00. Found: C, 44.98; H, 4.23; S, 11.94; N, none or trace.

The acidic extract gave 3.11 g (41%) of 5-ethyl-6-phenyl-1,2,3-oxathiazin-4(3*H*)-one 2,2-dioxide (**4b**) as a colorless solid: mp 113–113.5°; ir (KBr) 3270, 3100, 2980, 2770, 1685, 1630, 1392, 1360, 1205, 1160, 875, 840, 770, and 700 cm^{-1}; nmr ($CDCl_3$) τ 8.83 (t, J = 7.5 Hz, 3), 7.45 (q, J = 7.5 Hz, 2), 2.40 (s, 5), 0.27 (br s, 1); *m/e* (%) M^+ 253 (31.8), 238 (3.2), 188 (7.8), 173 (5.1), 172 (6.1), 161 (10.6), 160 (20.3), 146 (33.8), 105 (100), and 77 (49.3).

Anal. Calcd for $C_{11}H_{11}O_4NS$: C, 52.17; H, 4.38; N, 5.53. Found: C, 52.30; H, 4.39; N, 5.63.

Butyrophenone (**1b,** 1.48 g, 10 mmol, CH_2Cl_2, 11 days). The basic extract gave 321 mg (15%) of **6b.** The acidic extract gave 345 mg of 2-benzoylbutyramide **7b,** mp 151–152° (lit.[20] 153–153.5°). Upon standing several days the aqueous layer deposited 314 mg more of **7b,** total 659 mg (34.5%).

Butyrophenone (**1b,** 740 mg, 5 mmol, CH_2Cl_2, 28 days) gave 494 mg (45.5%) of **6b** and 50 mg (5%) of **7b.**

Phenyl-2-propanone (**1c,** 2.0 g, 14.9 mmol, ether, 4 hr) produced 2.06 g (71%) of 6-methyl-5-phenyl-2*H*-1,3-oxazine-2,4(3*H*)-dione (**6c**) as a pale yellow solid. Recrystallization gave a few colorless needles: mp 144–145°; ir (KBr) 3150, 3050, 1830, sh on 1795, 1765, 1680, 1425, 1270, 1020, 860, 760, and 705 cm^{-1}. A sample of this material, melting at 144–145°, was allowed to cool and resolidify, whereupon remelting occurred at 164–165°. The residue from the mother liquor was treated with activated carbon and recrystallized twice to give **6c** as colorless needles: mp 166.5°, ir (KBr) 3220, 1760, 1695, 1405, 1250, 1015, 790, 760, and 705 cm^{-1}; nmr ($CDCl_3$) τ 7.86 (s, 3), 2.40–2.83 (m, 5), and 0.44 (br s, 1); *m/e* (%) M^+ 203 (40.3), 160 (74.6), 118 (100), 90 (34.6), 89 (24.2), and 43 (85.5).

Anal. Calcd for $C_{11}H_9O_3N$: C, 65.02; H, 4.46; N, 6.89. Found: C, 64.94; H, 4.56; N, 6.69.

1,3-Diphenyl-2-propanone (**1d,** 2.10 g, 10 mmol, ether, 4 days) gave 1.70 g (61%) of 6-benzyl-5-phenyl-2*H*-1,3-oxazine-2,4(3*H*)-dione (**6b**) as colorless needles: mp 137–137.5°; ir (KBr) 3170, 3070, 1765, 1705, 1400, 820, 760, and 700 cm^{-1}; nmr ($CDCl_3$) τ 6.30 (s, 2), 2.37–2.98 (m, 10), 0.77 (br s, 1); *m/e* (%) M^+ 279 (30.9), 236 (32.9), 145 (100), 117 (10.0), 91 (33.5), 89 (31.7), and 65 (12.4).

Anal. Calcd, for $C_{17}H_{13}O_3N$: C, 73.11; H, 4.69; N, 5.02. Found: C, 73.30; H, 4.82; N, 4.95.

Upon standing 3 days, the aqueous layer deposited 340 mg (10%) of 2,4-diphenyl-3-oxobutyramide-*N*-sulfonic acid, sodium salt (**8d**) as a colorless solid: mp 88–90°; ir (KBr) 3500, 3220, 1705, 1685, 1455, 1240, 1045, 765, and 700 cm^{-1}; nmr (DMSO-d_6) τ 6.14 (s, 2), 4.90 (br s, 1), 2.60–3.00 (m, ~11), −0.33 (br s, 1). Upon attempted recrystallization from methanol–water, **8d** was converted into 2,4-diphenyl-3-oxobutyramide (**7d**): mp 165–167.5°; ir (KBr) 3490, 3185, 1700, 1625, 765, 755, 710, and 700 cm^{-1}; nmr (DMSO-d_6) τ 6.14 (s, 2), 5.06 (s, 1), 2.50–2.90 (m, ~11), 2.30 (br, 1); *m/e* (%) M^+ 253 (69.8), 236 (37.0), 210 (6.7), 162 (62.2), 146 (47.0), 145 (100), 135 (67.3), 118 (26.9), 117 (15.1), 91 (95.8), 90 (18.5), 89 (26.1).

Deoxybenzoin (**1e,** 1.96 g, 10 mmol, ether, 7 days). During work-up a colorless solid appeared which was filtered and washed with water and ether: 365 mg (10%) of 5,6-diphenyl-1,2,3-oxathiazin-4(3*H*)-one 2,2-dioxide, sodium salt (**4e**), mp 237–241° dec; ir (KBr) 3500, 3415, 3250, 1660, 1625, 1565, 1385, 1295, 1185, 1170, 1045, 750, and 700 cm^{-1}; nmr (acetone-d_6) τ 2.77 and 2.73 (2s). Dissolution in water, acidification, and reextraction converted **4e** into 5,6-diphenyl-1,2,3-oxathiazin-4(3*H*)-one (**5e**). Recrystallization of the crude basic extract gave, as the first crop of pale yellow crystals, 361 mg (14%) of 5,6-diphenyl-2*H*-1,3-oxazine-2,4(3*H*)-dione (**6e**): mp 220–222°; ir (KBr) 3200, 3100, 1750, 1700, 1390, 1245, 775, 710, and 695 cm^{-1}; nmr (acetone-d_6) τ 2.69 and 2.63 (2 s, 10), −0.83 (br s, 1); *m/e* (%) M^+ 265 (65.5), 222 (75.8), 165 (12.9), 105 (100), 89 (12.9), 78 (98.4), and 77 (84.6). An analytical sample was prepared by two more recrystallizations, colorless crystals, mp 222–223°.

Anal. Calcd for $C_{16}H_{11}O_3N$: C, 72.44; H, 4.18; N, 5.28. Found: C, 72.28; H, 4.08; N, 5.16.

The mother liquor from **6e,** upon standing a short while, deposited 561 mg (19%) of ethyl deoxybenzoin-α-sulfonate (**9e**) as yellow crystals. The analytical sample (colorless needles) melted at 126–126.5°: ir (KBr) 1685, 1450, 1360, 1285, 1175, 995, 930, 920, 765, 735, 705, and 695 cm^{-1}; nmr ($CDCl_3$) τ 8.75 (t, J = 7 Hz, 3), 5.76 (q, J = 7 Hz, 2), 3.70 (s, 1), 2.19–2.75 (m, 8), and 1.90–2.12 (m, 2); *m/e* (%) M^+ 304 (2.0), 195 (1.8), 167 (8.2), 166 (4.0), 165 (11.2), 152 (6.3), 118 (4.0), 106 (14.7), 105 (100), 90 (11.2), 89 (6.0), and 77 (40.7).

Anal. Calcd for $C_{16}H_{16}O_4S$: C, 63.15; H, 5.30; S, 10.52. Found: C, 63.30; H, 5.42; S, 10.39.

The acidic extract gave 571 mg (19%) of **4e** as a colorless solid: mp 225° with prior softening; ir (KBr) 3400, 3100, 3000, 2770, 1685, 1395, 1365, 1195, 765, 755, 705, and 695 cm^{-1}; nmr (acetone-d_6) τ 2.60 (br s, 10) and 2.47 (br s, 1); *m/e* (%) M^+ 301 (76.5), 222 (51.0), 165 (16.8), 105 (100), 89 (7.7), and 77 (35.6). An analytical sample melted at 233.5–234.5° after several recrystallizations.

Anal. Calcd for $C_{15}H_{11}O_4NS$: C, 59.80; H, 3.68; N, 4.65. Found: C, 59.57; H, 3.53; N, 4.52.

Deoxybenzoin (**1e,** 1.96 g, 10 mmol, CH_2Cl_2, 7 days). During work-up a tan colored solid formed and was filtered: 1.98 g (58%) of 2-benzoyl-2-phenylacetamide-*N*-sulfonic acid, sodium salt (**8e**), mp 163–165°; ir (KBr) 3590, 3480, 3180, 1685, 1675, 1475, 1260, 1220, 1050, 765, and 700 cm^{-1}; nmr (DMSO-d_6) τ 4.27 (br s, 1), 4.13 (s, 1), 2.20–2.90 (m, 8), and 1.74–2.02 (m, 2).

The basic extract gave 125 mg (5%) of **6e,** and the acidic extract gave 60 mg of tan colored solid shown by nmr and ir to be mainly benzoic acid **10a.**

α-Tetralone (**1f,** 1.46 g, 10 mmol, ether, 4.5 days). The basic extract gave 653 mg (30%) of 1,2-dihydronaphtho[3,4-*e*]-2*H*-1,3-oxazine-2,4(3*H*)-dione (**6f**) as off-white needles: mp 253–255° dec (from MeOH); ir (KBr) 3190, 3070, 1750, 1685, 1650, 1410, 1160, 775, and 750 cm^{-1}; nmr (DMSO-d_6) τ 6.89–7.60 (m, 4), 2.45–2.70 (m, 3), 2.21–2.43 (m, 1), and −1.67 (br s, 1); *m/e* (%) M^+ 215 (100), 172 (80.8), 144 (31.3), 118 (49.6), 116 (21.7), 115 (33.1), and 90 (23.9). Recrystallization twice from ethanol gave an analytical sample, colorless needles, mp 258.5–260° dec.

Anal. Calcd for $C_{12}H_9O_3N$: C, 66.97; H, 4.22; N, 6.51. Found: C, 67.10; H, 4.23; N, 6.67.

The acidic extract gave 500 mg (20%) of 1,2-dihydronaphtho[3,4-*e*]-1,2,3-oxathiazin-3*H*-one 2,2-dioxide (**4f**) as colorless crystals: mp 210–211° (lit.[7b] 216°); ir (KBr) 3070, 2965, 2730, 1665, 1630, 1395, 1335, 1205, 1140, 795, and 765 cm^{-1}; nmr (acetone-d_6) τ 6.75–7.43 (m, 4), 2.35–2.67 (m, 3), 2.13–2.33 (m, 1), and 0.50 (br s, 1); *m/e* (%) M^+ 251 (65.0), 172 (44.4), 170 (100), 144 (86.2), 118 (75.0), 116 (44.8), 115 (70.0), 90 (40.8), 89 (25.3), 78 (46.5), and 77 (16.7).

Anal. Calcd for $C_{11}H_9O_4NS$: C, 52.59; H, 3.61; N, 5.58. Found: C, 52.75; H, 3.65; N, 5.47.

Dibenzoylmethane (1g, 1.0 g, 4.47 mmol, ether, 9.5 hr). The crude basic extract gave 241 mg of orange solid. Dissolution in a small amount of benzene and standing 24 hr allowed precipitation of 185 mg (11%) of 2-benzoyl-3-phenyl-3-oxopropionamide-*N*-sulfonic acid, sodium salt (**8g**): mp 247–249° dec; ir (KBr) 3400 (broad), 1660, 1595, 1250, 1230, 1060, 750, 695 cm^{-1}; nmr (D_2O) τ 2.13–2.33 (m, 2), 2.57–3.06 (m, 8). The mother liquor of **8g** gave 49 mg (5% recovery) of **1g** identified by nmr. The acidic extract yielded 635 mg of a pale yellow foam which resisted attempts at recrystallization. Finally it was dissolved in ether and placed in the freezer overnight. Upon warming to room temperature, the solution deposited colorless crystals, mp 195–198° dec. The mass spectrum indicated M^+ 293 for the oxazine and its typical breakdown pattern but also showed *m/e* 329, M^+ of the oxathiazine, probably present as a minor contaminant. Recrystallization from benzene–Skellysolve "B" gave 145 mg (11%) of 5-benzoyl-6-phenyl-2*H*-1,3-oxazine-2,4(3*H*)-dione (**6g**), mp 200–203°. Two recrystallizations from benzene gave an analytical sample: mp 202–203°; ir (KBr) 3170, 3060, 1785, 1700, 1660, 1390, 980, 910, 770, and 690 cm^{-1}; nmr (acetone-d_6) τ 2.22–2.68 (m, 8), 1.74–1.98 (m, 2), and −0.91 (br s, 1); *m/e* (%) M^+ 293 (4.5), 250 (1.1), 249 (1.1), 222 (1.3), 105 (12.2), 79 (8.0), 78 (100), and 77 (24.9).

Anal. Calcd for $C_{17}H_{11}O_4N$: C, 69.62; H, 3.78; N, 4.78. Found: C, 69.76; H, 3.88; N, 4.75.

Dibenzoylmethane (1g, 1.0 g, 4.47 mmol, CH_2Cl_2, 3 days). The basic extract furnished 128 mg (10%) of **6g** (from benzene). The acidic extract gave 629 mg of pale yellow foam which displayed an nmr similar to that of **6g**; however, it resisted all attempts at crystallization. Concentration of the aqueous layer allowed isolation of 520 mg (14%) of sulfonate salt **8g**.

Substituent Effects on Product Distribution. *p*-Methoxypropiophenone (1h, 3.28 g, 20 mmol, ether, 22.5 hr). The crude basic extract (a red oil) was dissolved in a small amount of ether and placed in the refrigerator overnight to deposit 306 mg (7%) of 3-chloro-6-methoxy-2-methylindenone (**22**) as red-orange needles: mp 110–112°; ir (KBr) 1705, 1480, 1440, 1295, 1275, 1235, 1035, 980, and 830 cm^{-1}; nmr ($CDCl_3$) τ 8.13 (s, 3), 6.17 (s, 3), and 2.83–3.30 (m, 3); *m/e* (%) M^+ 210 (35.3) and 208 (100), 195 (2.7), 193 (7.7), 173 (91.9), 145 (69.6), 130 (8.6), 102 (28.0), 101 (14.6), 76 (10.4), and 75 (16.7); an analytical sample melted at 112.5–113° (from ether).

Anal. Calcd for $C_{11}H_9ClO_2$: C, 63.32; H, 4.36; O, 15.34. Found: C, 63.21; H, 4.50; O, 15.45.

The filtrate from **22** yielded 2.20 g of a red oil consisting almost entirely of ethyl *p*-methoxypropiophenone-α-sulfonate (9h) (crude yield 40.5%): nmr ($CDCl_3$) τ 8.67 (t, J = 7 Hz, 3) 8.27 (d, J = 7 Hz, 3), 6.09 (s, 3), 5.67 (q, J = 7 Hz, 2), 4.81 (q, J = 7 Hz, 1) 2.97 (d, J = 9 Hz, 2), and 1.95 (d, J = 9 Hz, 2). Chromatography on alumina (benzene) gave only polymeric materials. Alternatively, treatment of the crude sulfonate ester 9h with hydroxylamine also produced polymer. The acidic extract gave 560 mg of yellow solid. Recrystallization yielded 145 mg (3%) of *p*-methoxybenzoic acid **10h.** Further recrystallization of the residue failed to purify the oxathiazine **4h** present.

***p*-Methoxypiopiophenone (1h** 6.56 g, 40 mmol, ether 44 hr). The crude basic extract was placed under high vacuum in an attempt to distill sulfonate ester 9h. Even with heating up to 50°, no 9h was obtained, the crude product polymerizing in the pot. The crude acidic extract was recrystallized from chloroform. The first crop gave 146 mg of *p*-methoxybenzoic acid (**10h**). The second and third crops yielded 373 mg of a colorless solid. Recrystallization gave 328 mg of colorless crystals determined by nmr to consist of 282 mg (3%) of 6-*p*-anisyl-5-methyl-1,2,3-oxathiazin-4(3*H*)-one 2,2-dioxide (**4h**) and 46 mg of acid **10h** (total yield, 192 mg, 3%). Repeated fractional recrystallization yielded an analytical sample of **4h:** mp 167.5–168°; ir (KBr) broad absorption 3200–2300, 1640, 1590, 1360, 1265, 1195, 1180, 850, 840, and 790 cm^{-1}; nmr ($CDCl_3$) τ 7.84 (s, 3), 6.08 (s, 3), 2.92 (d, J = 9 Hz, 2), 2.38 (d, J = 9 Hz, 2), and 2.00 (br mound, 1); *m/e* (%) M^+ 269 (38.4), 190 (2.7), 177 (6.7), 176 (12.1), 162 (5.4), 146 (14.3), 136 (9.8), 135 (100), 107 (6.7), 92 (13.4), and 77 (17.0).

Anal. Calcd for $C_{11}H_{11}NO_5S$: C, 49.07; H, 4.12. Found: C, 48.99; H, 4.10.

***p*-Methylpropiophenone (1i,** 2.96 g, 20 mmol, ether, 7 days). During work-up, a colorless precipitate appeared, and was filtered and identified as 5-methyl-6-*p*-tolyl-1,2,3-oxathiazin-4(3*H*)-one 2,2-dioxide, sodium salt (**5i**): ir (KBr) 1630, 1585, 1375, 1335, 1200, 1190, and 1180 cm^{-1}. This salt was dissolved in water, acidified, and extracted with ether to give 1.30 g of 5-methyl-6-*p*-tolyl-1,2,3-oxathiazin-4(3*H*)-one 2,2-dioxide (**4i**): mp 159.5–160°; ir (KBr) 3090, 2980, 2760, 1680, 1615, 1395, 1365, 1215, 1210, 1200, 1160, 1080, 825, 775, 765, and 720 cm^{-1}; nmr (DMSO-d_6) τ 7.98 (s, 3), 7.58 (s, 3), 2.25–2.68 (m, 4), and −2.67 (s, 1), *m/e* (%) M^+ 253 (26.1), 174 (3.0), 161 (3.7), 160 (13.5), 146 (19.4), 119 (100), and 91 (42.5).

Anal. Calcd for $C_{11}H_{11}NO_4S$: C, 52.17; H, 4.38; N, 5.53. Found: C, 52.28; H, 4.40; N, 5.51.

The basic extract was recrystallized to yield 130 mg (3%) of 5-methyl-6-*p*-tolyl-2*H*-1,3-oxazine-2,4(3*H*)-dione (**6i**): mp 174–175°; ir (KBr) 3160, 3050, 1775, 1755, 1700, 1655, 1630, 1435, 1400, 1235, 1175, 1115, 835, and 770 cm^{-1}; nmr (acetone-d_6) τ 7.92 (s, 3), 7.55 (s, 3), 2.28–2.75 (m, 4, AA′BB′), and −0.23 (br s, 1); *m/e* (%) M^+ 217 (27.0), 174 (8.0), 146 (10.2), 120 (8.9), 119 (100), and 91 (42.5).

Anal. Calcd for $C_{12}H_{11}O_3N$: C, 66.35; H, 5.10. Found: C, 66.49; H, 5.15.

The filtrate from **6i** consisted of ethyl *p*-methylpropiophenone-α-sulfonate (9i, crude yield 6–10%) plus polymer. The acidic extract yielded 376 mg of a pale yellow solid, determined by nmr to consist of 236 mg of oxathiazine **4i** (total yield 1.54 g, 30%) and 141 mg (5%) of *p*-toluic acid (**10i**).

Propiophenone (1a, 2.68 g, 20 mmol, ether, 8 days). Recrystallization of the crude basic extract gave 355 mg (9%) of oxazine **6a.** The mother liquor was evaporated, redissolved in ether, passed through a short column of silica gel, and evaporated to give 436 mg of a yellow oil, consisting largely of ethyl propiophenone-α-sulfonate (**2a**): ir (neat) 1685, 1450, 1355, 1180, 1010, and 925 cm^{-1}; nmr ($CDCl_3$) τ 8.70 (t, J = 7 Hz, 3), 8.28 (d, J = 7 Hz, 3), 5.68 (q, J = 7 Hz, 2), 4.74 (q, J = 7 Hz, 1), 2.28–2.67 (m, 3), and 1.80–2.05 (m, 2); *m/e* (%) M^+ 242 (4.5), 105 (100), and 77 (31.0). The acidic extract gave 2.30 g of colorless solid, determined by nmr to be a mixture of 1.96 g (41%) of oxathiazine (**4a**) and 0.34 g (14%) of benzoic acid (**10a**).

***p*-Chloropropiopenone (1j,** 3.37 g, 20 mmol, ether, 6 days). During work-up, a colorless precipitate appeared. It was filtered and identified as 6-(4′-chlorophenyl)-5-methyl-1,2,3-oxathiazin-4(3*H*)-one 2,2-dioxide, sodium salt (**5j**): ir (KBr) 1645, 1585, 1375, 1320, 1205, 1095, 1015, and 860 cm^{-1}. This salt was dissolved in water, acidified, and extracted with ether to give 830 mg of 6-(4′-chlorophenyl)-5-methyl-1,2,3-oxathiazin-4(3*H*)-one 2,2-dioxide (**4j**): mp 174–175°; ir (KBr) 3100, 2980, 2760, 1685, 1620, 1400, 1360, 1210, 1155, 1100, 1080, 1005, and 830 cm^{-1}; nmr (DMSO-d_6) τ 7.99, (s, 3), 2.28 (s, 4), and 1.70 (br s, 1); *m/e* (%) M^+ 275 (10.2) and 273 (23.5), 196 and 194 (<1), 168 (5.2) and 166 (17.8), 141 (35.7) and 139 (100), 113 (11.5) and 111 (35.7).

Anal. Calcd for $C_{10}H_8NO_4SCl$: C, 43.89; H, 2.95. Found: C, 44.14; H, 3.09.

The crude basic extract was recrystallized to give 629 mg (13%) of 6-(4′-chlorophenyl)-5-methyl-2*H*-1,3-oxazine-2,4(3*H*)-dione (**6j**) as a colorless solid: mp 203–204°; ir (KBr) 3150, 3020, 2850, 1770, 1710, 1635, 1415, 1180, 1105, 1020, 840, 770, and 755 cm^{-1}; nmr (DMSO-d_6) τ 8.00 (s, 3), 2.39 (s, 4), and −1.38 (br s, 1); *m/e* (%) M^+ 239 (11.7) and 237 (33.8), 196 (3.8) and 194 (13.0), 168 (7.0) and 166 (20.2), 141 (32.2) and 139 (100), 113 (10.6), and 111 (31.0).

Anal. Calcd for $C_{11}H_8O_3NCl$: C, 55.59; H, 3.40. Found: C, 55.44; H, 3.45.

The filtrate from **6j** yielded 1.02 g of yellow oil, containing about 68% of ethyl *p*-chloropropiophenone-α-sulfonate (**9j,** crude yield 10–15%) by nmr, plus polymer.

The crude acidic extract was recrystallized to give 320 mg of yellow solid. Recrystallization from acetone gave 265 mg (9%) of *p*-chlorobenzoic acid (**10j**) as colorless crystals displaying an ir spectrum identical with Sadtler's. The mother liquor yielded 300 mg of oxathiazine (**4j,** total yield 1.13 g, 21%).

Conversion of Sulfonate Salts 8 into β-Ketocarboxamides 7. 2,4-Diphenyl-3-oxobutyramide-*N*-sulfonic acid, sodium salt (**8d,** 150 mg, 0.42 mmol), was refluxed in toluene (5 ml, 20 min) and filtered and the solvent was removed *in vacuo* to give 85 mg (90%) of 2,4-diphenyl-3-oxobutryamide (**7d**) as colorless needles.

2-Benzoyl-2-phenylacetamide-*N*-sulfonic acid, sodium salt (**8e,** 338 mg, 0.99 mmol), was dissolved in 15 ml of water, and 2 drops

of concentrated HCl were added. The mixture was stirred at ambient temperature for 2 hr, and solvent was removed *in vacuo*. The residue was triturated with acetone, filtered, treated with activated carbon, and refiltered and the solvent was removed to give 189 mg (80%) of 2-benzoyl-2-phenylacetamide (**7e**) as colorless needles: mp 171–173° (lit.[19] 171.5–173.5°); ir (KBr) 3400, 3165, 1685, 1650, 1210, 1010, 855, 780, 755, 720, 705, and 695 cm^{-1}; nmr (acetone-d_6) τ 5.04 (br s, 2), 4.13 (s, 1), 2.28–2.78 (m, 8), and 1.76–1.95 (m, 2); *m/e* (%) M^+ 239 (25.2), 222 (27.5), 196 (10.7), 165 (11.1), 152 (4.6), 118 (40.5), and 105 (100).

Preparation of Malonamides 23. The general procedure for the reaction of ketones **1** with CSI was used except that only 5 ml of dichloromethane was used per 10 mmol of **1**. The reaction was monitored by ir. The colorless malonamide **23** which had precipitated during the reaction was rapidly filtered and dried in a vacuum dessicator. The filtrate was worked up as usual with aqueous sodium sulfite.

Propiophenone (**1a**, 1.34 g, 10 mmol, 5 days) gave 2.61 g (62.4%, average of several runs) of *N,N'*-bis(chlorosulfonyl)benzoyl(methyl)malonamide (**23a**): mp 103–104° dec; ir (KBr) 3290, 3170, 1735, 1665, 1465, 1440, 1390, 1275, 1180, 1165, 1070, 890, 750, and 710 cm^{-1}; nmr (CD_3CN) τ 8.01 (s, 3), 2.08–2.50 (m, 5), and −0.12 (br s, 2); *m/e* (%) no M^+, 239 (5.4), 143 (2.7), 141 (6.1), 122 (10.4), 106 (100), and 105 (81.8). Work-up of the filtrate with sodium sulfite gave 281 mg (14%) of oxazine **6a** from the basic extract. The acidic extract gave 115 mg (7%) of β-ketoamide **7a**, 56 mg (5%) of benzoic acid (**10a**), and 23 mg (1%) of oxathiazine **4a** as determined by nmr integration.

α-Tetralone (**1f**, 1.46 g, 10 mmol, 8 days) gave 974 mg (23%) of 2,2-bis(*N*-chlorosulfonylcarboxamido)-1-tetralone (**23f**): mp 93–94° dec; ir (KBr) 3190, 2850 with tailing to ~2300, 1710, 1670, 1600, 1455, 1425, 1390, 1310, 1235, 1200, 1120, 880, and 780 cm^{-1}; nmr (CD_3CN) τ 6.14–7.75 (m, 4), 2.30–2.78 (m, 3), 1.83–2.13 (m, 1), and 0.00 (br s, 2); *m/e* (%) no M^+, 315 and 313 (<2), 289 and 287 (<2), 251 (15.4), 183 (10.1), 172 (16.6), 170 (16.3), 145 (34.4), 144 (37.9), 118 (41.7), 116 (17.4), 115 (34.0), 106 (77.0), 90 (21.0), and 80 (100). Work-up of the filtrate gave 225 mg (10%) of oxazine **6f**.

Reductive Hydrolysis of 23a. Malonamide **23a** (1.99 g, 4.76 mmol) was dissolved in ether and worked up with aqueous sodium sulfite in the normal manner. The acidic extract yielded 550 mg (95%) of benzoic acid **10a**, mp 120–122°, identified by comparison with an authentic sample.

Treatment of 23a with DMF. 23a (2.78 g, 6.16 mmol) was suspended in 20 ml of CH_2Cl_2, and DMF (2.14 g, 29.3 mmol) was added slowly. The mixture was stirred at ambient temperature for about 1 hr, then the solvent was removed. Sodium bicarbonate (25 ml of a 5% aqueous solution) was added, followed by solid $NaHCO_3$ until the solution remained basic. The mixture was stirred for 2 hr, then extracted four times with ether. The combined organic layers were dried (Na_2SO_4), and the solvent was removed to give 231 mg (47%) of methyl malononitrile: mp 33–35° (lit.[22] 36–37°); ir (KBr) 2275, 1455, 1390, 1265, 1130, 1070, 1025, and 810 cm^{-1}; nmr ($CDCl_3$) τ 8.26 (d, J = 7.5 Hz, 3) and 5.89 (q, J = 7.5 Hz, 1); *m/e* (%) M^+ 80 (11.2), 79 (50.0), 53 (100), 52 (34.8), 51 (17.1), and 41 (18.8). Acidification (H_2SO_4) and reextraction of the aqueous phase gave 623 mg (83%) of benzoic acid **10a**.

Hydrolysis of 23f. 23f (246 mg, 0.57 mmol) was dissolved in 5 ml of acetone, a few drops of water were added, and the mixture was allowed to stand overnight. The colorless crystals which had separated were then filtered to give 109 mg (82%) of 2,2-bis(carboxamido)-1-tetralone (**24**): mp 219–222°; ir (KBr) 3365, 3195, 1715, 1675, 1645, 1300, 1225, 1100, 910, 795, 750, and 710 cm^{-1}; nmr (DMSO-d_6) τ 7.42 (m, 2), 7.03 (m, 2), 2.30–2.96 (m, 7) and 1.93–2.20 (m, 1); *m/e* (%) M^+ 232 (3.8), 189 (34.6), 188 (100), 172 (5.4), 171 (32.7), 144 (30.8), 118 (40.4), 116 (19.2), 115 (42.3), and 90 (40.4).

Anal. Calcd for $C_{12}H_{12}O_3N_2$: C, 62.06; H, 5.21; N, 12.06. Found: C, 61.97; H, 5.23; N, 12.09.

Transformations of 23a in Solution. A. 23a (2.5 g, 5.98 mmol) was suspended in 20 ml of dry CH_2Cl_2 and stirred at ambient temperature. After 2 days a large amount of **23a** appeared to have dissolved. At this time the solution exhibited a strong isocyanate band (ν = 2160 cm^{-1}) in the ir region. After 4 days, all of **23a** had dissolved. At 5 days, nmr indicated the presence of only (>95%) monoamide **2a**. At 8 days there was still 91% of the **2a** and at 11 days nmr indicated a 87:13 mixture of **2a**:oxazine **14a**. DMF (1.93 g, 26.4 mmol) was added and the mixture was stirred for 30 min, evaporated *in vacuo*, dissolved in ether, washed three times with water, dried (Na_2SO_4), and evaporated again to yield 668 mg of a pale yellow oil, determined by nmr ($CDCl_3$) to consist of 432 mg (46%) of 2-benzoylpropionitrile,[6b] 141 mg (11%) of oxazine **6a**, and 95 mg (13%) of benzoic acid (**10a**); ir (neat) is essentially identical with that of 2-benzoylpropionitrile. **B. 23a** (2.7 g, 6.45 mmol) was dissolved in 10 ml of anhydrous ether, stirred at ambient temperature, and monitored by nmr, reaction time in days (% cyclic products): 2 (31%), 6 (40%), 8 (50%). At 9 days the mixture was worked up with Na_2SO_3 as usual. The crude basic extract gave 408 mg of a yellow oil shown by nmr to contain some oxazine **6a** along with a lot of polymer. The acidic extract gave 417 mg of a pale yellow oil containing mainly oxathiazine **4a** along with some benzoic acid (**10a**) and polymer. Recrystallization gave 324 mg (21%) of **4a**.

Preparation of 2-Benzoyl-*N*-chlorosulfonylbutyramide 2b. Butyrophenone (**1b**, 8.88 g, 60 mmol) was dissolved in 30 ml of dry CH_2Cl_2, and CSI (3.52 ml, 40 mmol) was added. The mixture was refluxed for 20 hr, then slowly concentrated *in vacuo* until it solidified. The solid was filtered and washed with CH_2Cl_2. Repetition of this process gave two more crops, total 8.63 g (74%) of **2b** as a colorless solid: mp 117.5–119°; ir (KBr) 3110, 1710, 1700, 1450, 1385, 1285, 1195, 1130, 895, 850, 780, and 700 cm^{-1}; nmr (CD_3CN) τ 8.98 (t, J = 7 Hz, 3), 8.00 (p, J = 7 Hz, 2), 5.57 (t, J = 7 Hz, 1), 2.26–2.63 (m), and 1.84–2.12 (m) total of six; *m/e* (%) M^+ 291 and 289 (<1), 261 (1.6), 253 (5.1), 175 (2.3), 160 (1.6), 146 (3.7), 130 (5.4), 106 (8.8), 105 (100), and 77 (45.8).

Reactions of 2b. A. 2b (1.45 g, 5 mmol) was dissolved in 20 ml of anhydrous ether and stirred at ambient temperature. Essentially no reaction could be detected up to 13 days by nmr. Removal of solvent gave a yellowish solid shown by nmr to consist mainly of **2b** along with some of the hydrolysis product **7b**. Repetition of the reaction in 10 ml of dry CH_2Cl_2 with addition of CSI (0.5 ml, 5.7 mmol) again showed no reaction up to 7 days.

B. 2b (1.45 g, 5 mmol) was placed in 10 ml of anhydrous ether and CSI (0.5 ml, 5.7 mmol) added. After 9 days, nmr indicated about 84% conversion to cyclic products. The reaction was stirred 2 more days, then worked up with Na_2SO_3 as usual. The basic extract yielded 300 mg of pale yellow oil shown by nmr and tlc to contain oxazine **6b** along with polymer. The acidic extract gave 910 mg (72%) of oxathiazine **4b**.

C. 2b (1.45 g, 5 mmol) was placed in 10 ml of anhydrous ether, 0.5 ml of BF_3 etherate was added, and the mixture was stirred at ambient temperature. After 15 days, nmr indicated >60% conversion to product, therefore work-up with Na_2SO_3 was accomplished as usual. The basic extract gave 283 mg of colorless solid. This was recrystallized (acetone–Skellysolve "B") to give 63 mg (7%) of β-ketoamide **7b**. The residue from the filtrate was recrystallized from chloroform to give 209 mg (18%) of **25** as colorless needles: mp 162–163°; ir (KBr) 3455, 3360, 3285, 1660, 1510, 1480, 1215, 1105–1020, 770, and 710 cm^{-1}; nmr (DMSO-d_6) τ 9.07 (t, J = 7 Hz, 3), 7.73 (q, J = 7 Hz, 2), 2.45 (s, 5), 1.02 (br s, 1), and 0.50 (br s, 1); *m/e* (%) M^+ 239 (54.3), 238 (26.5), 224 (80.3), 220 (15.6), 219 (16.3), 218 (28.5), 204 (6.8), 173 (6.1), 159 (10.2), 146 (6.1), 115 (20.4), and 105 (100). The acidic extract gave 688 mg (54%) of oxathiazine **4b**.

D. 2b (2.13 g, 735 mmol) was dissolved in 20 ml of ether and 2 ml of H_2O was added. The mixture was allowed to stand for 2 hr, and the precipitated product was then filtered, yield 1.24 g (89%) of 2-benzoylbutyramide (**7b**), mp 150–151°.

Nmr Studies of Keto–Enol Equilibria. 1,3-Diphenyl-2-propanone (**1d**, 2.10 g, 10 mmol) was dissolved in 5 ml of dry CCl_4, and CSI (0.85 ml, 9.8 mmol) was added. After 64 hr (no CSI left in solution) the mixture was diluted with 5 ml of CCl_4. The nmr at this time showed starting ketone **1d** (12%), β-ketoamide **2d** (33%; τ 6.45 (s, CH_2), 5.23 (s, CH), and −0.3 (br s, NH)), and enol amide **2'd** (55%); τ 6.75 (s, CH_2), 1.85 (br s, NH), and −2.16 (br s, OH). The enol **2'd** thus makes up 63% of the keto–enol mixture.

To phenyl-2-propanone (**1c**) (1.34 g, 10 mmol) in 10 ml of dry CCl_4 was added CSI (9.8 mmol). At 25 hr reaction time, the nmr showed **1c** (20%; amide **2c** (31%; τ 7.97 (s, CH_3), 5.25 (s, CH), and −0.30 (br s, NH)), and enol **2'c**, (49%; τ 8.18 (s, CH_3), 1.73 (br s, NH) and −2.90 (br s, OH)). Enol **2'c** was present to the ex-

tent of 61%. If the reaction was allowed to proceed further, the mixture began to separate into two phases and some decomposition set in.

To propiophenone (**1a**) (134 mg, 1 mmol) in 1 ml of dry CCl_4 in an nmr tube was added CSI (0.085 ml, 0.98 mmol). After 45 hr the mixture began separating into two phases. Nmr at 42 hr showed **1a** (43%), amide **2a**, (47%; τ 8.49 (d, J = 7 Hz, CH_3), 5.42 (q, J = 7 Hz, CH), and *ca.* −0.80 (NH)), and enol **2'a** (10%; τ 7.92 (s, CH_3), and −1.00 to −0.80 (OH and NH)). The enol form **2'a** was thus present to the extent of 18%.

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Unsaturated Carbenes from Primary Vinyl Triflates. II.[1] Spin Multiplicity via Stereochemistry of Addition to Olefins

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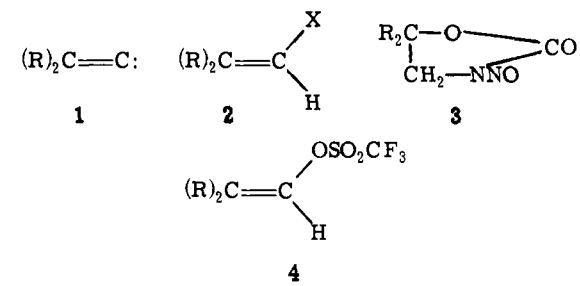
Abstract: The stereochemistry of addition of isopropylidenecarbene, generated from primary vinyl triflates, to olefins was investigated. Addition was found to be more than 98% stereoselective to *cis*- and *trans*-2-methoxy-2-butene and stereospecific to *cis*- and *trans*-2-butene indicating that the nascent carbene is a singlet. Dilution experiments with *trans*-2-butene and perfluorocyclobutane as the inert diluent strongly suggest that the singlet is also the ground state of such unsaturated carbenes.

It is well known[2] that carbenes can exist in both the singlet and triplet state depending upon both the nature of the particular carbene as well as its mode of generation. Methylene itself has been shown[3] to possess a triplet ground state in agreement with recent theoretical calculations.[4]

In recent years, besides continued developments in normal carbene chemistry,[2] there have been increasing reports and interest in unsaturated carbenes (**1**). Such species have been generated from primary vinyl halides[5] (**2**) and RLi, base decomposition of N-nitrosooxazolidones[6] (**3**), and most recently from primary vinyl triflates[1] (**4**) and *t*-BuOK. Despite this surgence of interest in unsaturated carbenes, very little is known about their spin multiplicity. Recent theoretical calculations by Dewar and coworkers[7] using the MINDO/2 procedure as well as earlier calculations by Gleiter and Hoffmann[8] predict the singlet to be the ground state for methylenecarbene itself (**1**; R = H). However, outside of a brief mention by Newman[6d] of the stereochemistry of addition of isopropylidenecarbene (**1**; R = CH_3) as generated from nitrosooxazolidone to *cis*- and *trans*-4-methyl-2-pentene, with little or no experimental detail given, there are no experimental data on the spin multiplicity of these species. Therefore, we undertook and report in this paper a detailed investigation of the spin multiplicity of unsaturated carbenes (**1**) as generated[1] from primary vinyl triflates (**4**) and determined by the stereospecificity of addition to olefins.



1 **2** **3**

4