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7. ¹H-NMR spectra (internal standard TMS) were recorded on a Varian EM 360-A (60 MHz) spectrometer. IR spectra were measured on a Perkin-Elmer 782 spectrometer and MS data were obtained using VG 12-250 mass spectrometer. **2e**: ¹H-NMR (CDCl₃/DMSO-d₆) δ 2.40 (s, 3H, Me), 7.75 (d, 1H, *J*=9 Hz), 8.30 (dd, 1H, *J*=9, 3 Hz), 8.46 (d, 1H, *J*=3 Hz); IR (KBr) 3248, 2235 cm⁻¹; MS (*m/z*) 221 (P⁺), 194 (P⁺-HCH). **2f**: ¹H-NMR(CDCl₃/DMSO-d₆) δ 2.36 (s, 3H, Me), 7.52-8.15 (m, 3H); IR (KBr) 3240, 2246 cm⁻¹; MS (*m/z*) 221 (P⁺), 206 (P⁺-Me), 194 (P⁺-HCN). **2g**: ¹H-NMR (CDCl₃/DMSO-d₆) δ 7.24-7.60 (m, 6H), 8.40 (dd, 1H, *J*=9, 2 Hz), 8.91 (d, 1H, *J*=2 Hz); IR (KBr) 3270, 2220 cm⁻¹; MS (*m/z*) 283 (P⁺) 256 (P⁺-HCN). **2h**: ¹H-NMR (CDCl₃/DMSO-d₆) δ 7.05-7.82 (m, 4H), 7.95-8.30 (m, 2H), 8.73 (d, 1H, *J*=2 Hz), 10.32 (s, 1H); IR (KBr) 3395, 3250, 2220 cm⁻¹; MS (*m/z*) 251 (P⁺), 224 (P⁺-HCN).

A Convenient Preparation of Enamines with N,N'-Sulfinyldiamines

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Following the first publication on alkylation and acylation of enamine in 1954 by Stork¹, utilization of enamines in a variety of reactions such as electrophilic substitution and addition, oxidation and reduction, cycloaddition expanded rapidly.² These useful enamines are usually prepared from the corresponding carbonyl compounds and secondary amines; effective methods are based on the concept of convenient removal of water produced by carbonyl-amine condensation. The usual auxiliary reagents for dehydration are K₂CO₃,³ CaO³, TsOH⁴, Dowex-50 resin⁵, BF₃·OEt₂⁶, AcOH⁷, MgSO₄,⁸ CaH₂,⁹ TiCl₄¹⁰ and molecular sieves¹¹.

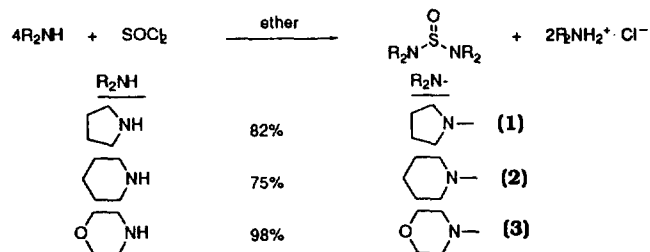
Other methods which chemically convert water to something else during the reaction have been introduced: it was shown that a mixture of tris(pyrrolidiny)borane, a ketone, pyrrolidine and a catalytic amount of TsOH in refluxing benzene for about 30 min gives the corresponding pyrrolidine enamines in good yield.¹² The same reasonings have been applied to tris(dimethylamino)arsine, and tin, silicon, germanium and titanium amides of M(NR₂)₄.^{13,14} However, a competing reaction is the formation of metal enolates.¹⁴

Table 1. Reactions of N,N'-Sulfinyldimorpholine **3** with Aldehydes and Ketones

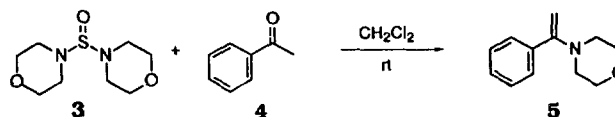
Entry	Carbonyl compounds	Reagent 3 (equiv)	Morpholine (extra equiv)	Enamine products yield(%) ^a
1	acetophenone	1.0	0	68
2	propiophenone	1.0	0	47
3	cyclohexanone	1.0	0	73
4	3-phenylpropanal	1.0	0.1	72
5	4-phenylbutanal	1.0	0.1	79
6	4-phenylbutanal	1.0	0.1	(83.0) ^b
7	4-phenylbutanal	1.0	1.0	(83.4) ^c
8	4-phenylbutanal	2.0	0.1	(86.1) ^c
9	4-phenylbutanal	3.0	0.1	(88.3) ^c

^a Isolated but unoptimized yields of the products, whose identity was confirmed by spectral analysis and/or independent synthesis. The yields in parenthesis refer to yield by HPLC. ^b HPLC condition (254 nm, flow rate 2 ml/Min, C 18 column, MeCN : H₂O = 7 : 3). ^c HPLC condition (254 nm, flow rate 2 ml/min, C18 column, MeOH : AcOH : H₂O = 50 : 1 : 49).

Our research was aimed at finding out a new and versatile process for enamine formation under mild condition by indirect dehydrative reactions of N,N,N',N'-tetraalkylsulfinyldiamines derived from secondary amines such as pyrrolidine, piperidine and morpholine¹⁵.



Thus, to a solution of 4 equiv of a secondary amine such as pyrrolidine, piperidine and morpholine in ether, SOCl₂ was added dropwise at 0°C, which was stirred at rt for 3 h. After filtration and evaporation of ether, unreacted SOCl₂ and amine, liquid product was obtained in almost quantitative yields after distillation. But in the case of the reaction product with morpholine, the liquid soon changed to crystalline solid, which had a long shelf life. Because of this crystallinity of N,N'-sulfinyldimorpholine **3** and ease of its isolation and handling, N,N'-sulfinyldimorpholine was selected as a model enamination reagent. Thus, N,N'-sulfinyldimorpholine **3** (1.0 equiv) was treated with acetophenone in methylene chloride at room temperature. After washing the ethereal solution with aqueous NaHCO₃ and drying with Na₂SO₄, morpholine enamine of acetophenone was obtained in 68% yield after vacuum distillation.



Consequently, reactions with some selected carbonyl compounds using N,N'-sulfinyldimorpholine were carried out, the

Table 2. Preparation of Enamines with Enamination Reagents Prepared *in situ* and with Preformed Reagents.

Entry	Amine	Carbonyl compounds	Enamine yield(%)	
			<i>in situ</i> method	Preformed reagent
1	morpholine	acetophenone	67	68
2	morpholine	propiophenone	46	47
3	morpholine	cyclohexanone	74	73
4	morpholine	2-chloroacetophenone	46	43
5	morpholine	phenylacetaldehyde	66 ^b	18
6	morpholine	3-phenylpropanal	72 ^b	72 ^b
7	morpholine	diphenylacetaldehyde	68 ^b	
8	morpholine	2-phenylpropanal	62 ^b	
9	morpholine	4-phenylbutanal	79 ^b	79 ^b
10	piperidine	acetophenone	78	
11	piperidine	propiophenone	60	
12	piperidine	cyclohexanone	72	
13	piperidine	2-chloroacetophenone	60	
14	piperidine	phenylacetaldehyde	71 ^b	
15	piperidine	3-phenylpropanal	57 ^b	
16	piperidine	diphenylacetaldehyde	73 ^b	
17	piperidine	2-phenylpropanal	72 ^b	
18	piperidine	4-phenylbutanal	69 ^b	
19	pyrrolidine	acetophenone	87	
20	pyrrolidine	propiophenone	66	
21	pyrrolidine	cyclohexanone	85	
22	pyrrolidine	2-chloroacetophenone	66	
23	pyrrolidine	phenylacetaldehyde	81 ^b	
24	pyrrolidine	2-phenylpropanal	60 ^b	
25	pyrrolidine	3-phenylpropanal	40 ^b	
26	pyrrolidine	4-phenylbutanal	35 ^b	
27	pyrrolidine	diphenylacetaldehyde	78 ^b	

^aIsolated but unoptimized yield. The identity of the products was confirmed by spectral analysis and/or independent synthesis.

^bWith an additional excess (0.1 eq) of amine.

results of which are summarized in Table 1.

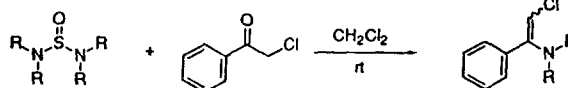
As shown in Entry 6, 8 and 9 in Table 1, an excess amount (100-200%) of **3** to aldehyde made only 2-3% increase in yield. Thus, it is assumed that the reactivity is more dependent on the character of carbonyl compound than that of enamine reagent. In the presence of the enamination reagent **3** alone, all the aldehydes examined in Table 1 did not react under the same reaction condition for enamination of ketones. Change of reaction temperature and solvents exerted virtually no effect at all. But addition of a catalytic amount (0.1 equiv) of morpholine to the reaction mixture in methylene chloride did bring about a rapid start of reaction within 5 min. But as shown in Entry 7, and excess amount of morpholine rather than a catalytic amount had no effect on yields (see Table 1).

It was found that, among the many solvents such as diethyl ether, acetonitrile and methylene chloride tried in the reaction of acetophenone and morpholine, methylene chloride was found to be the solvent of choice for this reaction.

Because the stoichiometric addition of 4 equiv of amine

and 1 equiv SOCl₂ gave almost quantitative yields of N,N'-sulfinyldiamines as mentioned earlier, it occurred to us that these enamination reactions of carbonyl compounds should be possible using the reagent prepared *in situ*. The differences in yields between the two reactions are almost unnoticeable. Additionally, with this *in situ* method, one does not have to worry about the preparation and handling of the preformed reagents. It should be noted additionally that a slight excess of the amines should be maintained throughout the *in situ* preparation and the reaction of the reagent. Otherwise, a non-characterizable mixture resulted. Thus, a combination of 4.1 equiv of an amine and thionyl chloride was normally used.

Under reaction conditions of direct dehydrative enamine formation from 2-chloroacetophenone with secondary amines, substitution occurs preferentially rather than enamination. But in the reaction with the *in situ* or preformed reagents, there formed only enamine product (Entry 4, 13, and 22).



And apparently there is inherent chemoselectivity of enamination by these reagents in that there was absolutely no reaction occurred with ethyl phenylacetate, phenylacetamide and benzyl cyanide under the same conditions with aldehydes and ketones.

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Analysis of Insecticides and Fungicides Employing Supercritical CO₂ and Modifiers

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During its relatively short existence, supercritical fluid ch-

romatography (SFC) has become an attractive alternative to GC and LC in certain industrially important applications. SFC gives the advantage of high efficiency and allows the analysis of non-volatile or thermally labile mixtures. Some applications of SFC to the separation of pesticides and fungicides are featured in this paper, along with representative chromatograms. Pesticide analysis has received much attention because of the environmental impact of pesticides and fungicides and the need to monitor their levels and those of their metabolites in complex sample matrices such as foods. GC often is the analytical method of choice because of the availability of sensitive, selective detectors (FPD, NOD, ECD). However, difficulties arise when the solutes cannot be analyzed by GC because of thermal instability. HPLC is not helpful either, because such compounds cannot be detected easily at trace levels by a UV detector or one of the other HPLC detectors. In these cases, SFC is an alternative to GC or HPLC for the analysis of pesticides. The SFC analysis of some polar pesticides using mass spectrometry as a detector has previously been reported¹. Thermally labile carbamate pesticides were also separated by capillary SFC².

The ability to analyze moderately polar compounds with supercritical CO₂ is demonstrated in this paper; however, modifiers must be used. One of the most difficult problems with SFC is how polar substrates can be analyzed. Using the classification scheme of eluents by Snyder³, carbon dioxide shows a polarity similar to that of hexane. The solvent power of the eluents used in SFC may be enhanced by adding a second eluent, the so-called 'modifier' to the basic mobile phase. Separations are often performed by SFC where

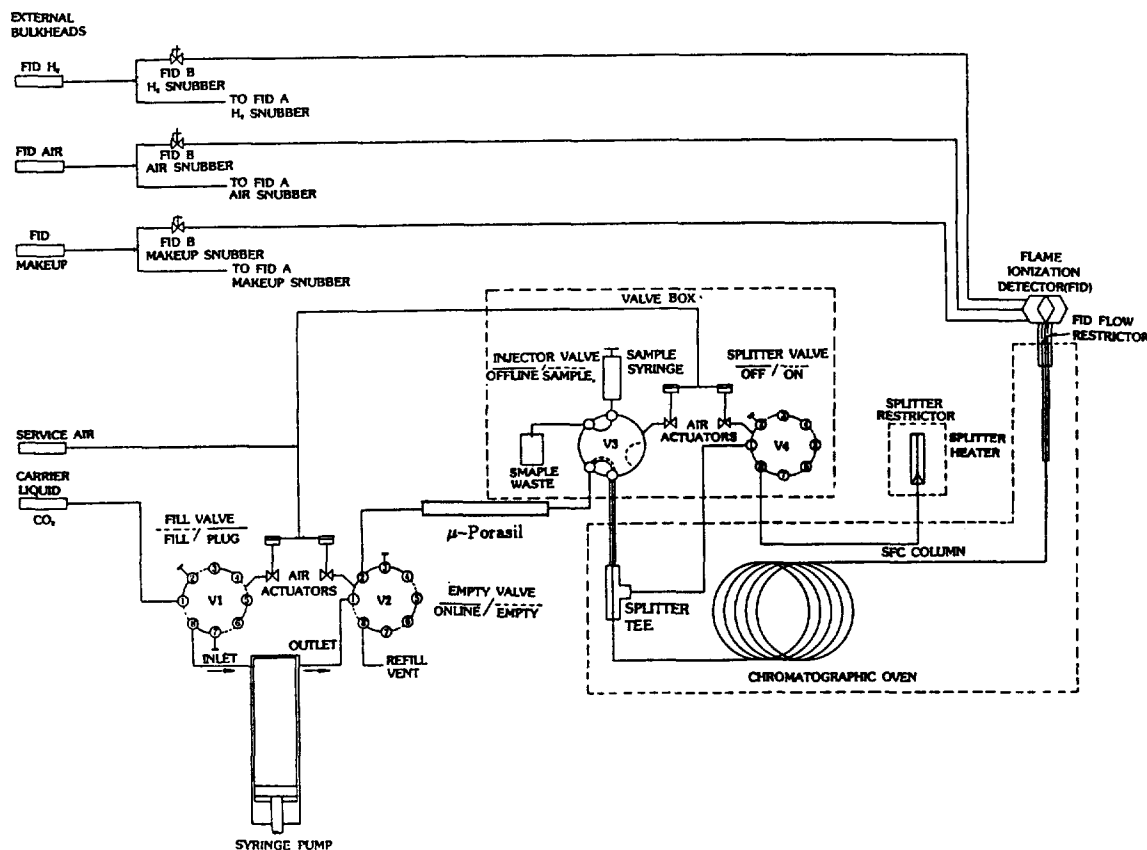


Figure 1. Overall system diagram for adding polar modifier to supercritical fluid mobile phase.