

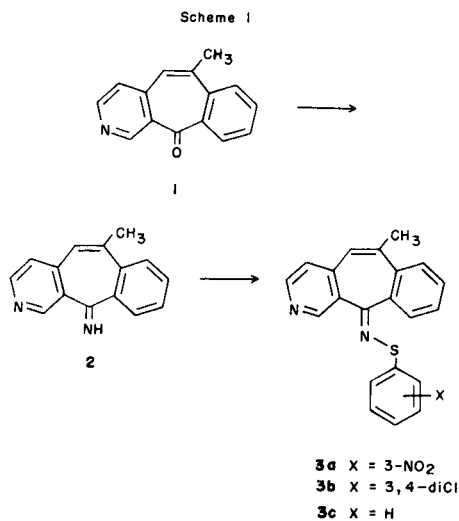
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Efficient, high-yield syntheses of *N*-diarylmethylene sulfenamides (sulfenimines) have been developed under mild laboratory conditions. Diaryl ketones have been shown to form ketimines readily by condensation with ammonia in the presence of titanium tetrachloride.

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In our program to prepare various substituted imino-bridged heterocycles [4] we needed a route to tertiary carbinamines. The route to such products reported by Davis [5] utilizing *N*-alkylidenearenesulfenamides as starting materials appeared attractive. However, the intermediates of importance to us would be derived from diaryl ketones and the reported sequence was not applicable to compounds of this type. Previous attempts to generate these type products met with failure [6]. We thus began an investigation to develop a method of synthesis of such compounds and study their use as intermediates to tertiary carbinamines in which two of the substituents are aryl functions.

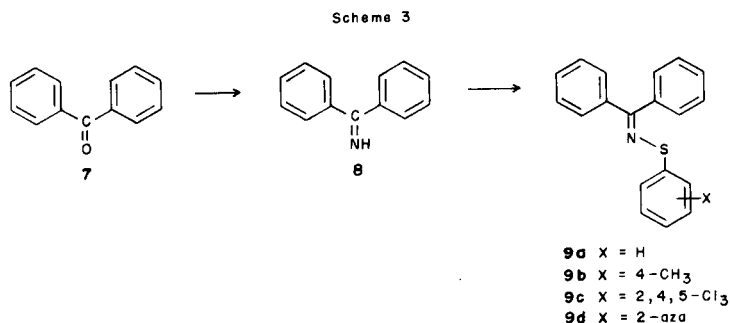
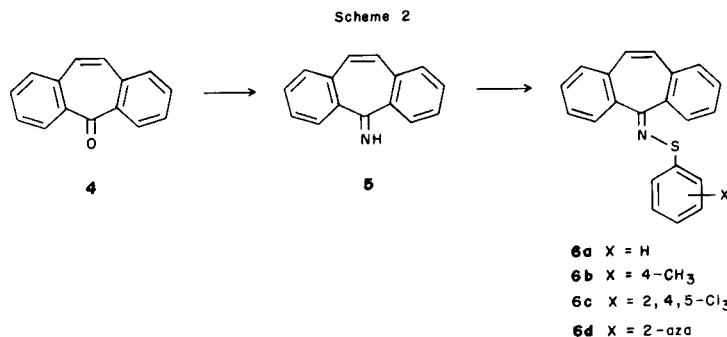


The reported explanation for the failure to prepare such products was based on their proposed mechanism of formation [6]. The ketones in this report, **1**, **4**, and **7**, also failed to condense with sulfenamides under a variety of dehydrating conditions. We felt that if the imines of diaryl ketones could be generated easily, they would be of great value in the synthesis of the desired sulfenimines. The reported preparations of ketimines derived from ammonia and an appropriate ketone usually involve the use of extraordinarily high temperatures and complex reaction condi-

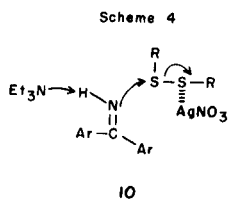
tions [7]. We looked for a more useful, convenient laboratory preparation of such products. Although titanium tetrachloride is a powerful dehydrating agent and acid catalyst for the generation of enamines and ketimines from organic amines and carbonyl compounds [8], we could find no report of its use with ammonia. We found that ketimines from three different diaryl ketones were formed readily in toluene. For example, after addition of ammonia through an inlet tube to a cold (0°) mixture of **1** [1] and titanium tetrachloride in toluene, no reaction was observed (tlc) while the mixture was maintained at 0°, even with periodic additional passage of ammonia through the mixture. However, as the reaction was allowed to warm to 25°, a transformation of the ketone to a single new product was observed. Workup by addition of aqueous carbonate solution allowed isolation of the product **2** to be achieved without decomposition. Similar reactions with **4** and **7** generated **5** and **8** in equally good yield. Warming of the reaction mixtures to 30-60° increased the conversion rate with no deleterious effect upon the yields.

With these imines in hand we turned our attention to the preparation of the sulfenimide derivatives **3**, **6** and **9**. Based on the concept of amine exchange [7] our initial idea was to heat the preformed imine **2** with a suitable sulfenamide under vacuum to assist in removal of ammonia. This procedure worked well for the preparation of **3a** and **3b** from 3-nitro- and 3,4-dichlorobenzenesulfenamide, respectively [6]. However, the scope of this reaction was severely limited due to the scarcity of stable sulfenamides.

Although Davis indicated that the desired products could be prepared from an appropriate ketimine and a sulfonyl chloride [9], we desired more readily available substrates than sulfonyl halides. Many disulfides are commercially available, and even though Davis reported that attempts to form sulfenimines from ketimines and disulfide/silver nitrate solutions failed [6], we searched for experimental conditions that would facilitate this transformation. The initial reaction of the anion of **2**, generated by methyl lithium at -60°, with diphenyl disulfide in the presence of silver nitrate did give the desired product **3c**, albeit in low yield. In additional experiments with several of



the ketimines, disulfides and silver nitrate in methanol, the sulfenimides were generated with a maximum yield in the 45-50% range. We felt that this was the result of a second molecule of the ketimine functioning as a proton acceptor during the transformation depicted in Scheme 4,



thus limiting the yield. Addition of an equivalent of triethylamine provided isolated yields of approximately 90% using stoichiometric quantities of the other reagents. It was found that the phenyl and tolyl disulfides underwent smooth reaction with each of the ketimines **2**, **5**, and **8** at ambient temperature, whereas 2,4,5-trichlorophenyl disulfide underwent a very slow condensation. The disulfide in this case did not readily dissolve, limiting the formation of the silver complex. When the disulfide and silver nitrate were refluxed in methanol prior to the addition of the other reagents, the reaction proceeded as rapidly as the more soluble disulfides. The 2,2'-dipyridyl disulfide initially also gave poor isolated yields. Complexation of the silver nitrate with the pyridyl nitrogen atoms may have accounted for this result, since yields were increased to comparable values obtained for other products when more than two equivalents of silver nitrate were used.

We have succeeded in providing an efficient synthesis

of sulfenimines from diaryl ketones through the readily accessible ketimine intermediates. The result of our investigation into the use of these type derivatives for the preparation of tertiary carbinamines will be included in our next communication.

EXPERIMENTAL

Melting points were taken on a Thomas-Hoover melting point apparatus in open capillaries and are uncorrected values. ¹H nmr spectra were recorded on a Varian T-60 spectrometer using TMS as an internal standard. Mass spectra were run on an AEI MS 902 by Mr. Shoji Date and microanalyses were performed under the direction of Dr. William C. Randall.

6-Methylbenzo[5,6]cyclohepta[1,2-c]pyridin-11-imine (2).

Titanium tetrachloride (3.30 ml, 5.7 g, 0.030 mole) was added to a solution of **1** [**1**] (4.2 g, 0.019 mole) in toluene (150 ml). The resulting dark red slurry was cooled to 0-5° and gaseous ammonia was bubbled into the stirred mixture for 20 minutes. The cooling bath was removed and the reaction was stirred at 25° overnight. The red-orange mixture was added to saturated aqueous sodium carbonate (250 ml) and stirred for 1 hour. The layers were separated and the toluene solution was washed with saturated aqueous sodium carbonate (75 ml) and saturated sodium chloride (75 ml). The original aqueous wash was extracted with ethyl acetate (2 × 100 ml) and the organic layers were combined, washed with saturated sodium chloride solution and dried (sodium sulfate). After filtration and removal of the solvent, trituration of the residue with hexane produced an off-white solid, 3.3 g, mp 154-164°. Recrystallization from acetonitrile gave material with mp 165-167°; mw (Rast): 217 (220.26 calcd.); ¹H nmr (deuteriochloroform): δ 2.37 (s, 3H, =C-CH₃), 6.79 (s, 1H, H₄-C=), 7.08 (d, J = 2.5 Hz, 1H, H₃), 7.3-7.7 (m, 4H, H₇₋₁₀), 8.56 (d, J = 2.5 Hz, 1H, H₂), 8.87 (br s, 1H, =NH), 9.9 (s, 1H, H₁).

Anal. Calcd. for C₁₅H₁₂N₂: C, 81.79; H, 5.49; N, 12.72. Found: C, 81.64; H, 5.47; N, 12.61.

Dibenzo[*a,d*]cyclohepten-5-imine (4).

Using titanium tetrachloride (34.5 g, 0.182 mole), dibenzo[*a,d*]cyclohepten-5-one (**4**) (25 g, 0.123 mole) and toluene (750 ml) and following the

procedure described above, there was obtained 20.6 g, mp 60-62°, of a white solid after trituration with petroleum ether (30-60°); ¹H nmr (deuteriochloroform): δ 6.86 (s, 2H, olefin bridge), 7.20-7.53 (m, 6H, aromatic), 7.57-7.83 (m, 2H, aromatic), 9.00 (br s, 1H, =NH).

Anal. Calcd. for C₁₅H₁₁N: C, 87.77; H, 5.40; N, 6.82. Found: C, 87.44; H, 5.47; N, 6.67.

Benzophenonimine (8).

Following the procedure for **2** and using titanium tetrachloride (13.8 g, 0.073 mole), benzophenone (**7**) (9.1 g, 0.05 mole) and toluene (300 ml) there was obtained a clear, colorless oil, 7.8 g, bp 110-120° (bp₃ 127°) [10]; ¹H nmr (deuteriochloroform): δ 7.03-7.82 (m, 10H, aromatic), 9.35 (br s, 1H, =NH); ir (neat film): 3230 cm⁻¹ (=NH).

N-(6-Methylbenzyl[5,6]cyclohepta[1,2-*a*]pyridin-11-ylidene)-3-nitrobenzenesulfenamide (**3a**).

A mixture of **2** (0.13 g) and 3-nitrobenzenesulfenamide [**6**] (0.1 g) was heated to 90° under vacuum overnight. Addition of acetonitrile (3 ml) to the cooled mixture deposited 0.10 g of an off-white solid, mp 172-174°; ms: m/e = 373 (mw calcd. = 373.42).

Anal. Calcd. for C₂₁H₁₅N₃O₂S: C, 67.54; H, 4.05; N, 11.25. Found: C, 67.18; H, 3.97; N, 11.08.

N-(6-Methylbenzo[5,6]cyclohepta[1,2-*c*]pyridin-11-ylidene)-3,4-dichlorobenzenesulfenamide (**3b**).

A mixture of **2** (1 g) and 3,4-dichlorobenzenesulfenamide [**6**] (0.88 g) was heated to 90° under vacuum for 24 hours. After cooling, the residue was dissolved in hot acetonitrile (5 ml) and cooled, yield 1.6 g, mp 124.5-126.5°. Recrystallization from acetonitrile gave 1.24 g of an off-white solid, mp 127.5-129.5°; ms: m/e = 396 (mw calcd. -Cl³⁵ = 396).

Anal. Calcd. for C₂₁H₁₄Cl₂N₂S: C, 63.48; H, 3.55; N, 7.05; Cl, 17.85. Found: C, 63.56; H, 3.55; N, 7.02; Cl, 17.94.

N-(6-Methylbenzo[5,6]cyclohepta[1,2-*c*]pyridin-11-ylidene)benzenesulfenamide (**3c**).

Methyl lithium (1.8 ml, 1.4 *M* in THF) was added dropwise to a solution of **2** (0.5 g, 0.002 mole) in THF (15 ml) at -60°. After complete addition, diphenyl disulfide (0.55 g, 0.0025 mole) in THF (10 ml) was added, followed by silver nitrate (0.42 g, 0.0025 mole) in THF (15 ml)-DMF (10 ml). The mixture was stirred at this temperature for 2 hours then treated with dilute sodium hydroxide solution and extracted with ethyl acetate. The organic layer was washed with 5% sodium hydroxide (2 × 100 ml), saturated sodium chloride (100 ml) and dried (sodium sulfate). The residue after evaporation of the solvent was subjected to thick-layer chromatography (silica, chloroform/ethyl acetate 1:1, v/v). The band corresponding to the desired material (R_f ~ 0.65) was scraped and extracted with ethyl acetate. The residual oil after evaporation of the solvent crystallized from acetonitrile to give 0.15 g of white crystals, mp 137.5-139.5°.

Anal. Calcd. for C₂₁H₁₆N₂S: C, 76.80; H, 4.91; N, 8.53. Found: C, 76.92; H, 4.85; N, 8.55.

N-(Dibenzo[*a,d*]cyclohepten-5-ylidene)phenylsulfenamide (**6a**).

Diphenyl disulfide (1.4 g, 0.0064 mole) was added to a solution of silver nitrate (1.1 g, 0.0065 mmole) in methanol (25 ml). A fluffy white precipitate formed to which was added **5** (1.0 g, 0.0049 mole) and triethylamine (0.51 g, 0.005 mole). The heterogeneous mixture was stirred overnight, diluted with ether (75 ml) and filtered. The filtered solid was washed with methanol and ether and the combined filtrates were concentrated under reduced pressure. The residue was dissolved in ether, washed with water and dried (sodium sulfate). After evaporation of the ether, the residual white powder was chromatographed over silica gel (75 g) eluting with toluene-hexane (1:3) to give 1.36 g (88%) of white solid, mp 133-134°.

Anal. Calcd. for C₂₁H₁₅NS: C, 80.48; H, 4.82; N, 4.47; S, 10.23. Found: C, 80.47; H, 4.99; N, 4.58; S, 10.32.

N-(Dibenzo[*a,d*]cyclohepten-5-ylidene)-4-methylphenylsulfenamide (**6b**).

The procedure above was followed using tolyl disulfide (1.57 g, 0.0064 mole). A yellow solid was obtained from the extraction that was recrystallized from ethanol to give 1.34 g (84%) of yellow crystals, mp 140-142°.

Anal. Calcd. for C₂₂H₁₇NS: C, 80.70; H, 5.23; N, 4.28; S, 9.79. Found: C, 80.57; H, 5.38; N, 4.23; S, 9.70.

N-(Dibenzo[*a,d*]cyclohepten-5-ylidene)-2,4,5-trichlorophenylsulfenamide (**6c**).

The procedure above was followed using 2,4,5-trichlorophenyl disulfide (2.71 g, 0.0064 mole). On completion of the additions, a thick mixture developed that was difficult to stir. The mixture was then heated under reflux for 4 hours and stirred overnight. The workup, substituting chloroform for ether, gave a yellow solid that was recrystallized from ethyl acetate to give 1.72 g (84%), mp 207-210°. Recrystallization from acetonitrile gave material with mp 213-214°.

Anal. Calcd. for C₂₁H₂₁Cl₃NS: C, 60.52; H, 2.90; N, 3.36; S, 7.69; Cl, 25.52. Found: C, 60.39; H, 2.99; N, 3.30; S, 7.84; Cl, 25.28.

N-(Dibenzo[*a,d*]cyclohepten-5-ylidene)-2-pyridylsulfenamide (**6d**).

The procedure above was followed, using 2,2'-dipyridyl disulfide (1.4 g, 0.0064 mole) silver nitrate (2.2 g, 0.013 mole) and triethylamine (0.65 g, 0.0065 mole). The product from the usual workup was chromatographed over silica gel (75 g), eluting with chloroform saturated with gaseous ammonia, diluted 1:3 with chloroform to give 1.24 g (81%, of white solid, mp 185-187°). Recrystallization from ethanol gave material with mp 186.5-189°.

Anal. Calcd. for C₂₀H₁₄N₂S: C, 76.40; H, 4.49; N, 8.91; S, 10.20. Found: C, 76.48; H, 4.52; N, 8.89; S, 10.27.

N-(Diphenylmethylene)phenylsulfenamide (**9a**).

A mixture of **8** (1 g, 0.0055 mole), diphenyl disulfide (1.56 g, 0.0072 mole), silver nitrate (1.22 g, 0.0072 mole), and triethylamine (0.55 g, 0.0055 mmole) in methanol was treated as described above. The usual workup and purification on silica gel eluting with toluene-hexane (1:3) gave 1.43 g of a yellow oil that solidified on standing. Trituration with ethanol gave 1.3 g (82%), based on purity of starting imine **8** as 90%, of white crystals, mp 69.5-72°.

Anal. Calcd. for C₁₉H₁₅NS: C, 78.86; H, 5.22; N, 4.84; S, 11.08. Found: C, 78.90; H, 5.35; N, 5.00; S, 11.20.

N-(Diphenylmethylene)-4-methylphenylsulfenamide (**9b**).

A mixture of **8** (1.0 g, 0.0055 mole), tolyl disulfide (1.76 g, 0.0072 mole), silver nitrate (1.22 g, 0.0072 mole) and triethylamine (0.74 g, 0.0074 mole) in methanol was treated as described above. The yellow solid from the extraction was recrystallized from ethanol to give 1.30 g (87%), based on purity of starting imine **8** as 90%, of white crystals, mp 97-98°.

Anal. Calcd. for C₂₀H₁₇NS: C, 79.17; H, 5.65; N, 4.62; S, 10.57. Found: C, 78.71; H, 5.90; N, 4.51; S, 10.42.

N-(Diphenylmethylene)-2,4,5-trichlorophenylsulfenamide (**9c**).

A mixture of 2,4,5-trichlorophenyl disulfide (3.04 g, 0.0072 mole) and silver nitrate (1.22 g, 0.0072 mole) in methanol (25 ml) was refluxed for 1 hour. The imine **8** (1.0 g, 0.0055 mole) and triethylamine (0.74 g, 0.0074 mmole) were added and the reaction mixture was treated as described above. The product was extracted with chloroform and recrystallized from acetonitrile to give 1.63 g (83%), based on purity of starting imine **8** as 90%, of tan needles, mp 155-157.5°.

Anal. Calcd. for C₁₉H₁₂Cl₃NS: C, 58.11; H, 3.08; N, 3.57; S, 8.16; Cl, 27.08. Found: C, 57.73; H, 3.05; N, 3.42; S, 8.28; Cl, 27.59.

N-(Diphenylmethylene)-2-pyridylsulfenamide (**9d**).

A mixture of **8** (1.0 g), 2,2'-dipyridyl disulfide (1.57 g, 0.0072 mole), silver nitrate (2.45 g, 0.0144 mole) and triethylamine (0.74 g) was treated as described above. After 24 hours, the mixture was added to 50 ml of 5% sodium hydroxide solution and extracted with ether. The organic layer

was dried (sodium sulfate) and concentrated to a white solid that was recrystallized from ethanol to give 1.27 g (87%), based on purity of starting imine **8** as 90%, of fluffy white needles, mp 137.5-138.5°.

Anal. Calcd. for C₁₈H₁₄N₂S: C, 74.45; H, 4.86; N, 9.65; S, 11.04. Found: C, 74.52; H, 5.02; N, 9.72; S, 10.86.

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