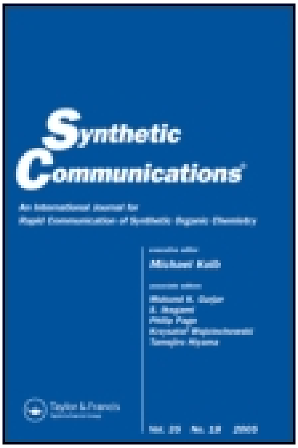

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Ram N. Ram [a] & Arif Ali Khan [a]
[a] Department of Chemistry, Indian Institute of Technology, Delhi, Hauz Khas, New Delhi, 110016, India

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A SIMPLE METHOD FOR THE PREPARATION OF N-SULFONYLIMINES BY DIRECT CONDENSATION OF *p*-TOLUENESULFONAMIDE WITH DIARYL KETONES

Ram N. Ram* and Arif Ali Khan

Department of Chemistry, Indian Institute of Technology,
Delhi, Hauz Khas, New Delhi-110016, India

ABSTRACT

Diaryl ketones condense with *p*-toluenesulfonamide in refluxing 1,2-dichloroethane in the presence of $TiCl_4$/$Ti(O\text{-}iPr)_4$ or $TiCl_4$/Et_3N to give N-sulfonylimines in generally good yields.

N-sulfonylimines are useful precursors for the preparation of important synthetic intermediates such as oxaziridines[1] and aziridines,[2] as well as for the synthesis of compounds of medicinal importance.[3,4] N-sulfonylimines also serve as heterodienes and heterodienophiles in [4 + 2] cycloaddition reactions.[5] Direct condensation of primary sulfonamides with aldehydes in the presence of some dehydrating agents ($TiCl_4$, 4-A Molecular sieves, $MgSO_4$, $AlCl_3$) is documented in the literature.[1,6–10] However, to the best of our knowledge, only a few reports are available

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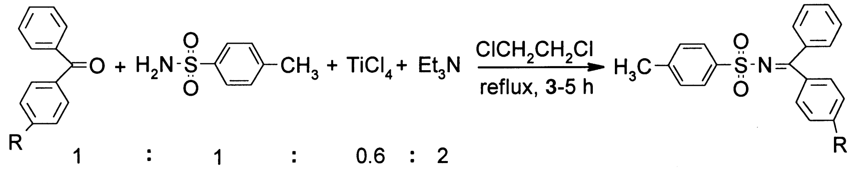
* Corresponding author. E-mail: rnram@chemistry.iitd.ernet.in

for the preparation of N-sulfonylimines of hindered non-enolizable ketones. None of these methods involves direct condensation of sulfonamides with diaryl ketones. The N-sulfonylimines of such ketones have been prepared by in situ generation of their oxime O-sulfinyl derivatives[11] and their subsequent homolytic rearrangement to sulfonylimines by the reaction of *p*-toluenesulfonamide–$AlCl_3$ complex[12] with Ph_2CCl_2 in dichloroethane, and by the reaction of a few diaryldiazomethanes with N,N-dichloroarenesulfonamides or with chloramine B or chloramine T.[13,14] Herein, we report two simple methods for the direct condensation of *p*-toluenesulfonamide with diaryl ketones affording N-sulfonylimines in generally good to excellent yields.

In **Method I**, equimolar proportions of *p*-toluenesulfonamide and ketone are heated at reflux for 15–20 h in dichloroethane in the presence of a mixture of $TiCl_4$ and $Ti(O\text{-}iPr)_4$, taken in 0.5 and 0.2–0.3 molar proportions, respectively, giving N-sulfonylimines in moderate to good yields (35–76%).

In **Method II**, the reactants in the molar ratio as given by equation (1) are heated at reflux for 3–5 h in dichloroethane. This method is superior to the first, as the reaction time is only 3–5 h, giving the products in higher yields (71–97%)[15] (Table 1).



Equation 1

These methods also worked well with aromatic aldehydes; however, enolizable ketones gave a number of unidentified products. These reactions have been carried out in different solvents (e.g., benzene, chloroform, carbon tetrachloride and a mixture (1:1) of $CHCl_3$ and CCl_4). In all these cases the N-sulfonylimines obtained were in syrupy form and took 15–30 days to crystallize. However, these compounds were obtained as solids after final work-up when prepared by Method II using 1,2-dichloroethane as the reaction medium, and can easily be recrystallized from a suitable solvent. All the N-sulfonylimines were characterized by ^1H and ^{13}C NMR, mass and IR spectral studies.

Table 1. Synthesis of N-Sulfonylimines from Diaryl Ketones

		Reflux Time (h)		Yield of N-Sulfonylimine (%)	
S.No.	Ketone	Method I	Method II	Method I	Method II
1	R[a] = H	20	5	76	83
2	= Br	15	3	61	73
3	= OMe	15	3	60	71
4	= Me	15	4.5	56	73
5	= NO_2	17	3	62	83
6	= Ph	20	5	70	97
7	Chalcone	17	4.5	35[b]	75
8	9-Fluorenone	18	5	52[b]	82

[a] See equation 1.
[b] In this method, the reaction developed a dark brown color, which was removed by treatment with animal charcoal, resulting in lower yields.

EXPERIMENTAL

Melting points are uncorrected. *p*-Nitrobenzophenone[16] and $Ti(O\text{-}iPr)_4$[17] were prepared by the reported procedures. All the other reagents were commercially available and were used as received except triethyl amine, which was dried before use by heating at reflux over calcium hydride for 2 h and distilled. The solvents were freshly distilled before use. IR spectra were recorded as KBr discs using a Nicolet 460 FT-IR spectrophotometer and NMR spectra were recorded in $CDCl_3$ on a Brucker 300 MHz DPX spectrometer with TMS as the internal standard. Mass spectra were recorded on Jeol SX-102 spectrometer at RSIC, CDRI Lucknow.

General Procedure

Method I

Diaryl ketone (5 mmol) and *p*-toluenesulfonamide (5 mmol) were dissolved in freshly distilled 1,2-dichloroethane (20 mL). To this solution $TiCl_4$ (2.5 mmol) and $Ti(O\text{-}iPr)_4$ (1.50 mmol) were successively added. The reaction mixture was heated at reflux for 15–20 h. After completion of the reaction (marked by a single spot of N-sulfonylimine on TLC), the reaction mixture was cooled to room temperature and then washed with dil. HCl, followed by saturated $NaHCO_3$ and water. The dichloroethane solution was dried (anhydrous Na_2SO_4) and evaporated on a rotary evaporator to give light yellow/brown syrup, which solidified on standing at room temperature for 15–30 days. The solid N-sulfonylimines were further purified by recrystallization.

Method II

p-Toluenesulfonamide (5 mmol) and ketone (5 mmol) were dissolved in dichloroethane and $TiCl_4$ (2.5 mmol) was added with stirring, followed by dropwise addition of triethyl amine (10 mmol). The reaction mixture was heated at reflux for 3–5 h. The progress of the reaction was monitored by TLC. Usual work-up after the completion of the reaction yielded N-sulfonylimines in high yields.

Analytical and Spectral Data of N-Sulfonylimines (1–8)

1: Colorless crystals (benzene) m.p. 102°–104°C (lit.,[11] 102°C); IR (cm^{-1}) $\nu_{C=N}$ 1601, $\nu_{O=S=O}$ $1318_{(asym)}$, $1158_{(sym)}$; $^{\delta}H$: 2.43 (3H, s, CH_3), 7.25–7.83 (14H, m, aromatic); $^{\delta}C$: 21.45 (CH_3), 127.26, 128.04, 129.28, 129.64, 138.56, 143.23 (aromatic), 178.65 (C = N); *m*/*z*: 335 (M^+, 20%), (calc. 335.42), 272 (27%), 180 (100%), 155 (23%).

2: Colorless crystals (dichloroethane) m.p. 98°–100°C; IR (cm^{-1}) $\nu_{C=N}$ 1586, $\nu_{O=S=O}$ $1325_{(asym)}$, $1154_{(sym)}$; $^{\delta}H$: 2.43 (3H, s, CH_3), 7.25–7.83 (13H, m, aromatic); $^{\delta}C$: 21.48 (CH_3), 127.27, 128.18, 129.35, 131.40, 138.29, 143.45 (aromatic), 177.37 (C = N); *m*/*z*: 415, 413 (M^+, 54%, 58%), (calc. 413.32, 415.32), 351, 349 (33%, 46%), 259, 257 (59%, 54%), 155 (49%).

3: Light yellow crystals (dichloroethane) m.p. 94°–96°C; IR (cm^{-1}) $\nu_{C=N}$ 1594, $\nu_{O=S=O}$ $1303_{(asym)}$, $1151_{(sym)}$; $^{\delta}H$: 2.43 (3H, s, CH_3), 3.86 (3H, s, -OCH_3), 6.87–7.83 (13H, m, aromatic); $^{\delta}C$: 21.42 (CH_3), 55.43 (OCH_3), 113.61, 126.31, 126.67, 127.11, 127.81, 129.21, 129.49, 130.87, 132.74, 136.42, 138.80, 143.00, 143.18 (aromatic), 178.08 (C = N); *m*/*z*: 365 (M^+, 72%), (calc. 365.45), 301 (11%), 210 (100%), 155 (5%).

4: Light yellow crystals (dichloroethane) m.p. 82°–84°C; IR (cm^{-1}) $\nu_{C=N}$ 1585, $\nu_{O=S=O}$ $1326_{(asym)}$, $1154_{(sym)}$; $^{\delta}H$: 2.41, 2.42 (6H, $2CH_3$), 7.19–7.84 (13H, m, aromatic); $^{\delta}C$: 21.44, 21.55 ($2CH_3$), 127.21, 127.93, 128.83, 129.24, 138.78, 143.11 (aromatic), 178.74 (C = N); *m*/*z*: 349 (M^+, 74%), (calc. 349.45), 285 (38%), 194 (91%), 155 (35%).

5: Yellow crystals (ethyl acetate) m.p. 137°–138°C; IR (cm^{-1}) $\nu_{C=N}$ 1593, $\nu_{O=S=O}$ $1324_{(asym)}$, $1151_{(sym)}$; $^{\delta}H$: 2.45 (3H, s, CH_3), 7.25–7.85

(13H, m, aromatic); $^{\delta}$C: 21.51 (CH$_3$), 123.15, 127.33, 128.56, 129.50, 129.99, 133.95, 137.74, 143.95 (aromatic), 175.81 (C$=$N); *m*/*z*: 380 (M$^+$, 21%), (calc. 380.42), 316 (8%), 225 (14%), 155 (64%).

6: Yellow crystals (benzene) m.p. 108°–111°C; IR (cm^{-1}) $\nu_{C=N}$ 1612, $\nu_{O=S=O}$ 1306$_{(asym)}$, 1148$_{(sym)}$; $^{\delta}$H: 2.43 (3H, s, CH$_3$), 7.25–7.85 (18H, m, aromatic); $^{\delta}$C: 21.47 (CH$_3$), 126.70, 127.16, 127.28, 128.05, 128.17, 128.89, 129.30, 130.61, 138.63, 139.72, 143.22 (aromatic), 178.36 (C$=$N); *m*/*z*: 411 (M$^+$, 100%), (calc. 411.52), 347 (17%), 256 (70%), 155 (11%).

7: Light yellow crystals (ethyl acetate) m.p. 150°–152°C (lit.,[11] 152°–153°C); IR (cm^{-1}) $\nu_{C=N}$ 1612, $\nu_{O=S=O}$ 1314$_{(asym)}$, 1146$_{(sym)}$; $^{\delta}$H: 2.41 (3H, s, CH$_3$), 7.03–8.00 (16H, m, aromatic and alkenic); $^{\delta}$C: 21.47 (CH$_3$), 127.15, 128.29, 128.66, 128.98, 129.37, 129.99, 131.00, 131.76, 134.56, 138.77, 143.36, 148.66 (alkenic and aromatic), 177.51 (C$=$N); *m*/*z*: 361 (M$^+$, 8%), (calc. 361.46), 206 (100%), 204 (69%).

8: Orange needles (dichloroethane) m.p. 182°–184°C (lit.,[16] 184°–186°C); IR (cm^{-1}) $\nu_{C=N}$ 1607, $\nu_{O=S=O}$ 1316$_{(asym)}$, 1151$_{(sym)}$; $^{\delta}$H: 2.46 (3H, s, CH$_3$), 7.45–8.01 (12H, m, aromatic); $^{\delta}$C: 21.50 (CH$_3$), 120.15, 126.54, 126.97, 128.76, 129.38, 134.67, 138.88, 143.46 (aromatic), 172.36 (C$=$N); *m*/*z*: 333 (M$^+$, 38%), (calc. 333.40), 269 (28%), 177 (13%), 155 (39%).

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