A Convenient Synthesis of Ketenimines from Thioamides with Haloiminium Salts

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Received 19 October 1999; revised 28 December 1999

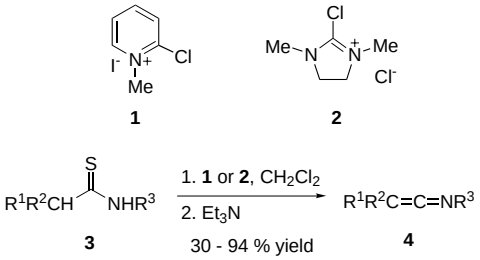
Abstract: Ketenimines were conveniently synthesized from *N*-monosubstituted thioacetamides with dehydrating agents such as 2-chloro-1,3-dimethylimidazolinium chloride or 2-chloro-1-methylpyridinium iodide.

Key words: ketenimine, thioamide, dehydrating agent, haloiminium salt, elimination

Since Staudinger[1] first reported about ketenimines in 1919, development in the chemistry of these moieties can be known from some reviews.[2] As stated in the reviews, most studies of these compounds have been done in the last three decades only. Various types of cyclic reactions using ketenimines were reported[2,3] and ketenimines have become interestingly useful in the synthesis of heterocycles. In the literature, various synthetic methods of ketenimines were reported as described in reviews.[2,4] Although thioamides were employed as starting materials for ketenimine preparation,[4] there was a disadvantage in comparison to other synthetic methods. HgO[5] or phosgene[6] had to be used for elimination of hydrogen sulfide, otherwise ketenimines could not be isolated in pure state.[7]

2-Halogenated pyridinium salts, especially 2-chloro-1-methylpyridinium iodide (**1**), were known to act as dehydrating agents, and condensation easily proceeded using these reagents[8] in the absence of strong acids or bases. 2-Chloro-1,3-dimethylimidazolinium chloride (DMC, **2**) could be also used as a dehydrating agent[9] like 2-halopyridinium salts. The reagents **1** and **2** were employed for the synthesis of heterocumulenes such as isothiocyanates and carbodiimides by elimination of hydrogen sulfide from dithiocarbamates[10] and *N*,*N'*-disubstituted thioureas,[11] respectively. Therefore, we applied the method using these reagents for thioacetamides to synthesize ketenimines.

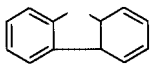
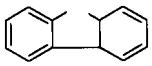
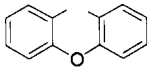
When triethylamine was added to the mixture of *N*,2,2-triphenylthioacetamide (**3a**) and 2-chloro-1,3-dimethylimidazolinium chloride (**2**), the color of the solution changed to yellow. After 2 h the product was isolated and purified by chromatography. It showed a strong peak around 2000 cm^{-1} in the IR spectrum and physical data[12] satisfied the structure of *N*-phenyldiphenylketenimine (**4a**). A similar treatment was carried out for various thioacetamides and the results are shown in the Table. The reactions of thioacetamides with 2-chloro-1-methylpyridinium iodide (**1**) also gave ketenimines (Entries 2 and 5), but the yields were inferior to those obtained with **2**. Elimination of hydrogen sulfide from thioacetamides with **2** proceeded at room temperature (Entry 3). However, higher temperature afforded better yields of the ketenimines. The reaction of *N*-*t*-butyl-2,2-diphenylthioacetamide with **2** did not proceed to afford the corresponding ketenimine due to sterical hindrance around the nitrogen atom, and the starting thioacetamide was recovered (Entry 10).



Scheme

Next, the synthesis of less stable ketenimines was investigated. Di- or monoaryl substituted thioacetamides were treated with **2** and triethylamine at lower temperature than those used for the syntheses of triaryl substituted ketenimines **4a-f**. After removal of both the solvent and the solid byproducts, such as triethylamine hydrochloride and 1,3-dimethylimidazoline-2-thione, the structures of di- or monoaryl substituted ketenimines **4g-k** were confirmed by their ^{1}H NMR spectra. It was reported that the formed ketenimines were thermally unstable and that they easily polymerized or rearranged to nitrile compounds during purification.[13] Because isolation of ketenimines **4g-k** by chromatography or distillation was unsuccessful, the yields of **4g-k** were determined from their ^{1}H NMR spectra and it was shown that the ketenimines formed in good yields (Entries 11-15). However, elimination of hydrogen sulfide from aliphatic thioacetanilides failed, and aliphatic ketenimines could not be detected under these reaction conditions (Entries 16-18). The NMR spectral data of *N*-benzyl-2,2-diphenylketenimine (**4g**), which could rearrange to 2,2,3-triphenylpropionitrile, showed good agreement with the reported data of ketenimines and was greatly different from that of the nitrile.[13b] Furthermore, for the product **4k**, long range coupling was observed between the vinylic proton and the methylene protons of *N*-benzyl group.[13c] In these reactions, the only impurities ob-

Table Synthesis of Ketenimines (**4**) from Thioamides (**3**)[a]

Entry	R^1	R^2	R^3	Temp. (°C)	Time (h)	Product	Yield[c] (%)
1	Ph	Ph	Ph	reflux	2.5	**4a**	90
2[b]				reflux	2.5	**4a**	43
3	Ph	Ph	*p*-MeC_6H_4	r.t.	2.5	**4b**	52
4				reflux	2.5	**4b**	67
5[b]				reflux	2.5	**4b**	41
6	Ph	Ph	*p*-$MeOC_6H_4$	reflux	2.5	**4c**	30
7			Ph	reflux	2.5	**4d**	88
8			*p*-MeC_6H_4	reflux	2.5	**4e**	94
9			*p*-MeC_6H_4	reflux	2.5	**4f**	74
10	Ph	Ph	*t*-Bu	reflux	2.5		–
11	Ph	Ph	$PhCH_2$	0	3.5	**4g**	94
12	Ph	H	Ph	0	3.5	**4h**	94
13	Ph	H	*p*-MeC_6H_4	0	3.5	**4i**	87
14	Ph	H	*p*-$MeOC_6H_4$	0	3.5	**4j**	78
15	Ph	H	$PhCH_2$	0	3.5	**4k**	82
16	Me	Me	*p*-MeC_6H_4	0	3.5		–
17	Me	H	*p*-MeC_6H_4	0	3.5		–
18	H	H	*p*-MeC_6H_4	0	3.5		–

[a] Reaction conditions: **3** (1 mmol), **2**(1.5 mmol), Et_3N (4 mmol), CH_2Cl_2 (10 mL).
[b] **1** was used instead of **2**.
[c] Entries 1–9: yield of isolated product after chromatography; Entries 11–15: determined by ^1H NMR spectroscopy.

served in the NMR spectra were 1,3-dimethylimidazolidin-2-one and 1,3-dimethylimidazolidine-2-thione. These compounds are stable and do not disturb the following reactions where ketenimines are employed as starting materials.

In summary, ketenimines were synthesized from the corresponding thioacetamides in good yields under mild reaction conditions. There was no necessity in worrying about the rearrangement of ketenimines because the reactions proceeded at moderate temperatures.

Mps were determined on a Mettler FP90 microscopic plate, and uncorrected. ^1H NMR spectra were obtained with a Varian Gemini 300BB spectrometer and chemical shifts are reported in ppm relative to internal tetramethylsilane. ^{13}C NMR spectra were obtained with a JEOL LA-500 spectrometer and chemical shifts are reported in ppm relative to internal $CDCl_3$ (77 ppm). IR spectra were recorded on a JASCO FTIR-5300 spectrophotometer. HRMS spectra were obtained with a Hitachi M-80B mass spectrometer. Starting thioamides **3** were prepared from the corresponding amides with Lawesson's reagent.[14]

Syntheses of Triaryl Substituted Ketenimines 4a-4f; General Procedure

To the solution of thioamide **3** (1 mmol) in CH_2Cl_2 (10 mL), a dehydrating reagent (**1** or **2**, 1.5 mmol) was added. The mixture was refluxed for 30 min under N_2, Et_3N (4 mmol) was added and the mixture was further refluxed for 2 h. The solvent was evaporated under reduced pressure and the crude product was chromatographed on silica gel with a CH_2Cl_2/hexane (1:1) mixture as eluent. The product was further purified by recrystallization from an appropriate solvent (cf individual products).

***N*-(2,2-Diphenylethenylidene)aniline (4a)**
Mp 52-52.5 °C (from pentane) (Lit.[15]: 55-56 °C).

IR (KBr): ν_{max} = 1995, 1589, 1485, 760, 696 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 7.20-7.40 (m, 15H, ArH).

^{13}C NMR ($CDCl_3$): δ = 78.0, 124.0, 126.5, 127.8, 128.9, 129.6, 134.0, 140.6, 190.6.

Anal. Calcd. for $C_{20}H_{15}N$: C, 89.19; H, 5.61; N, 5.20. Found: C, 88.92; H, 5.45; N, 5.11.

4-Methyl-*N*-(2,2-diphenylethenylidene)aniline (4b)
Mp 44-44.5 °C (from pentane) (Lit.[16]: 82-84 °C).

IR (KBr): ν_{max} = 1995, 1597, 1493, 1188, 820, 760, 694 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.38 (s, 3H, CH_3), 7.22-7.37 (m, 14H, ArH).

Anal. Calcd. for $C_{21}H_{17}N$: C, 89.01; H, 6.05; N, 4.94. Found: C, 89.06; H, 6.02; N, 4.94.

4-Methoxy-*N*-(2,2-diphenylethenylidene)aniline (4c)
Mp 81-83 °C (from hexane) (Lit.[16]: 83-85 °C).

IR (KBr): ν_{max} = 1985, 1501, 1250, 1032, 839, 764, 694 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 3.81 (s, 3H, CH_3O), 6.90 (d, 2H, *J* = 8.8 Hz, ArH), 7.21-7.37 (m, 12H, ArH).

***N*-(9*H*-Fluoren-9-ylidenemethylene)aniline (4d)**
Mp 81-82 °C (from hexane) (Lit.[3a]: 85-85.5 °C).

IR (KBr): ν_{max} = 2016, 1588, 1476, 1449, 760, 725 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 7.32-7.44 (m, 9H, ArH), 7.59-7.62 (m, 2H, ArH), 7.88-7.91 (m, 2H, ArH).

4-Methyl-*N*-(9*H*-fluoren-9-ylidenemethylene)aniline (4e)
Oil (Lit.[3a] oil).

IR (KBr): ν_{max} = 2012, 1453, 820, 762, 727 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.37(s, 3H, CH_3), 7.21 (d, 2H, *J* = 8.8 Hz, ArH), 7.31-7.33 (m, 6H, ArH), 7.57-7.61 (m, 2H, ArH), 7.87-7.91 (m, 2H).

^{13}C NMR ($CDCl_3$): δ = 21.2, 74.0, 120.5, 121.8, 124.5, 125.4, 126.4, 130.3, 135.7, 135.8, 137.7, 139.0, 181.2.

HRMS: *m/z* Calcd. for $C_{21}H_{15}N$: 281.1204. Found: 281.1213.

4-Methyl-*N*-(9*H*-xanthen-9-ylidenemethylene)aniline (4f)
Mp 120-121 °C (decomp.) (from hexane).

IR (KBr): ν_{max} = 1993, 1483, 1447, 1302, 1262, 822, 752 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.38 (s, 3H, CH_3), 6.94-7.00 (m, 4H, ArH), 7.06-7.19 (m, 4H, ArH), 7.20 (d, 2H, *J* = 8.2 Hz, ArH), 7.29 (d, 2H, *J* = 8.2 Hz, ArH).

Anal. Calcd. for $C_{21}H_{15}NO$: C, 84.82; H, 5.08; N, 4.71. Found: C,. 85.00; H, 4.99; N, 4.63.

Syntheses of Ketenimines 4g-4k; General Procedure
To the solution of thioamide **3** (1 mmol) in CH_2Cl_2 (10 mL), DMC (**2**, 1.5 mmol) was added. The mixture was stirred for 30 min at 0 °C under N_2, Et_3N (4 mmol) was added and the mixture was further stirred for 3 h at 0 °C. The solvent was evaporated under reduced pressure and hexane was added to the crude reaction products. The precipitated $Et_3N{\cdot}HCl$ and 1,3-dimethylimidazolidine-2-thione were filtered off, and filtrate was evaporated under reduced pressure. The yield was determined by ^1H NMR spectroscopy.

***N*-(Benzyl)-*N*-(2,2-diphenylethenylidene)amine (4g)**
Oil (Lit.[13b]: oil).

IR (neat): ν_{max} = 2012, 1597, 1493, 1453, 760, 694 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 4.77 (s, 2H, CH_2), 7.14-7.35 (m, 15H, ArH).

^{13}C NMR ($CDCl_3$): δ = 56.9, 76.3, 125.9, 127.1, 127.7, 128.3, 128.5, 128.7, 134.5, 136.7, 188.0.

HRMS: *m/z* Calcd. for $C_{21}H_{17}N$: 283.1361. Found: 283.1334.

***N*-(2-Phenylethenylidene)aniline[13c] (4h)**
IR (neat): ν_{max} = 2016, 1591, 1487, 758, 693 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 5.23 (s, 1H, CH=C), 7.05-7.38 (m, 10H, ArH).

^{13}C NMR ($CDCl_3$): δ = 60.6, 123.7, 125.2, 125.5, 127.6, 128.8, 129.4, 132.4, 140.4, 190.7.

HRMS: *m/z* Calcd. for $C_{14}H_{11}N$: 193.0891. Found: 193.0887.

4-Methyl-*N*-(2-phenylethenylidene)aniline (4i)
IR (neat): ν_{max} = 2004, 1597, 1495, 822, 760, 691 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.36 (s, 3H, CH_3), 5.23 (s, 1H, CH=C), 7.07-7.29 (m, 9H, ArH).

^{13}C NMR ($CDCl_3$): δ = 21.0, 60.6, 123.6, 125.1, 125.4, 128.8, 130.0, 132.7, 137.6, 137.7, 190.0.

HRMS: *m/z* Calcd. for $C_{15}H_{13}N$: 207.1048. Found: 207.1074.

4-Methoxy-*N*-(2-phenylethenylidene)aniline (4j)
IR (neat): ν_{max} = 2004, 1601, 1458, 835, 762, 692 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 3.82 (s, 3H, CH_3O), 5.22 (s, 1H, CH=C), 6.89 (d, 2H, *J* = 9.1 Hz, ArH), 7.10-7.18 (m, 3H, ArH), 7.24-7.32 (m, 4H, ArH).

^{13}C NMR ($CDCl_3$): δ = 55.5, 60.8, 114.6, 125.0, 125.1, 125.4, 128.8, 132.8, 132.9, 159.2, 189.3.

HRMS: *m/z* Calcd. for $C_{15}H_{13}NO$: 223.0997. Found: 223.0994.

***N*-(Benzyl)-*N*-(2-phenylethenylidene)amine (4k)**
IR (neat): ν_{max} = 2022, 1597, 1453, 1331, 696 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 4.71 (d, 2H, *J* = 2.2 Hz, CH_2), 4.82 (t, 1H, *J* = 2.2 Hz, CH=C), 7.02-7.07 (m, 3H, ArH), 7.19-7.36 (m, 7H, ArH).

^{13}C NMR ($CDCl_3$): δ = 56.8, 58.6, 124.7, 125.1, 127.6, 128.0, 128.4, 128.7, 133.4, 136.9, 188.4.

HRMS: *m/z* Calcd. for $C_{15}H_{13}N$: 207.1048. Found: 207.1080.

Acknowledgement

2-Chloro-1,3-dimethylimidazolinium chloride (DMC) was kindly supplied by Shiratori Pharmaceutical Co., Ltd.

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Article Identifier:
1437-210X,E;2000,0,04,0517,0520,ftx,en;F06899SS.pdf