

Reactions of *N*-acylhydrazones with thionyl chloride

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Dedicated to Professor A. Varvoglis on the occasion of his 65th birthday

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Abstract

N-Acylhydrazones of *o*-hydroxyaryl ketones react with thionyl chloride to give *N*-arylhydrazonoyl chlorides in good yields.

Keywords: *N*-Acylhydrazones, thionyl chloride, imidoyl chlorides, *o*-hydroxyaryl ketones, hydrazonoyl chlorides

Introduction

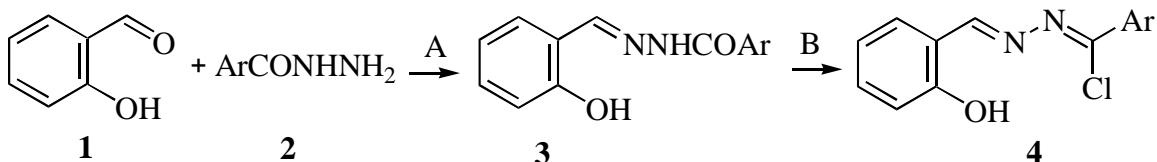
Imidoyl halides are very useful reagents in organic synthesis.¹ *N*-Arylhidrazonoyl halides are important members of this family. They have attracted a lot of interest in recent years mostly because of their synthetic usefulness. Several reviews presenting their chemistry appeared in the literature.¹⁻⁴ There are also some references about their structure. The presence of C=NNH moiety at the molecule gives the possibility of formation of (*E*) and (*Z*) isomers. It has been confirmed by spectroscopic studies^{5,6} as well as X-ray diffraction analysis⁶⁻⁸ that hydrazonoyl halides exist as (*Z*) isomers. Furthermore, it is known that (*Z*) isomers are thermodynamically more stable.⁹

Our continuous interest¹⁰⁻¹² in the use of *N*-acylhydrazones of aromatic aldehydes and ketones as starting materials for new molecules led us to investigate their reaction with thionyl chloride as a possible route to the synthesis of *N*-arylhydrazonoyl chlorides.

Results and Discussion

Commercially available salicylaldehyde **1** was reacted with hydrazide **2**, obtained also commercially, to prepare hydrazones **3** in very good yields according to the literature method.¹⁰

Reaction of **3** with thionyl chloride in benzene at room temperature yielded *N*-arylhydrazonoyl chlorides **4** in 58-70 % yield (Scheme 1). The products were identified by their NMR and MS spectra and elemental analysis.

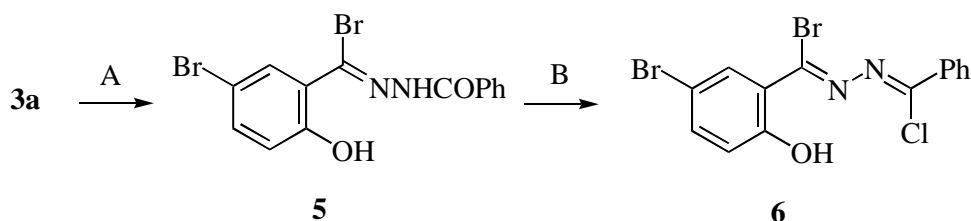


a: Ar=Ph b: Ar=*o*-HOC₆H₄ c: Ar=*o*-O₂NC₆H₄

A: propanol-2/reflux/24 h/82-90% B: SOCl₂/benzene/reflux/ 2 h/ 58-70%

Scheme 1

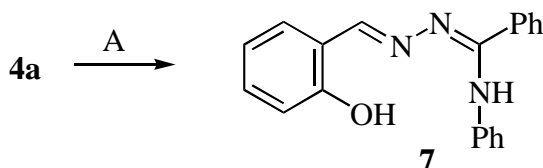
Subsequently, the brominated hydrazone **5** was prepared by treatment of salicylic aldehyde benzoyl hydrazone **3a** with bromine according to the literature method.¹⁰ The reaction of **5** with thionyl chloride afforded the bis-imidoyl dihalide **6** in good yield (Scheme 2).



A: Br₂/AcOH /NaOAc/25°C, 2h/67% B: SOCl₂ /benzene/reflux, 2h/70%

Scheme 2

Furthermore, treatment of **4a** with aniline in dimethylformamide led to the formation of derivative **7**, in 83% yield (Scheme 3). The anilino-derivative **7** was formed as a mixture of two isomers as it is indicated by the ¹H and ¹³C NMR spectra.



A: PhNH₂ /DMF/25 °C, 24h/83%

Scheme 3

Finally, attempts to perform the thionyl chloride reactions with *N*-benzoylhydrazone of *o*-hydroxy-acetophenone, with *N*-benzoyl hydrazone of *o*-amino-acetophenone as well as with *N*-carbonylethoxy hydrazone of *o*-amino-acetophenone were unsuccessful. They all gave complicated mixtures. In contrast, it is known that *N*-carbonylethoxy hydrazone of acetophenone and *o*-hydroxy-acetophenone afford 4-phenyl-1,2,3-thiadiazole and 4-(*o*-hydroxyphenyl)-1,2,3-thiadiazole respectively in good yields.^{13,14}

Experimental Section

General Procedures. Melting points were determined using a Kofler apparatus and are uncorrected. ¹H NMR (300 MHz) and ¹³C NMR (75 MHz) spectra were recorded on a Varian Unity Plus spectrometer. MS were measured on a Platform II spectrometer. Thionyl chloride, hydrazine hydrate, ketones and acylhydrazides were all purchased from Aldrich. *N*-Acylhydrazones was prepared according to the literature methods.^{11,15}

General procedure for the reaction of hydrazones with thionyl chloride

Thionyl chloride (2.5 mL) was added dropwise to a solution of *N*-acylhydrazone **3** or **5** (5 mmol) in benzene (10 mL). The reaction mixture was refluxed for 2 hours. The solvent was then evaporated and the residue was subjected to column chromatography (silica gel, 70-230 mesh) and it was eluted with petroleum ether/chloroform 5:1 to afford the pure products **4a-4c** and **6**.

***N*-Salicyliminophenylmethanehydrazonoyl chloride (4a).** Yellow solid; mp 122-124 °C; yield 70%; ¹H NMR (CDCl₃) δ 6.63-7.09 (m, 2H), 7.39-7.54 (m, 5H), 7.56-8.15 (m, 2H), 8.76 (s, 1H), 12.40 (s, 1H); ¹³C NMR (DMSO-*d*₆) δ 117.5, 118.7120.5, 129.2, 129.7, 132.3, 133.2, 133.6, 134.8, 159.9, 164.5; MS m/z (EI+): 258 (M), 223; Anal. Calcd for C₁₄H₁₁ClN₂O: C, 64.99; H, 4.28; N, 10.82; Cl, 13.70. Found: C, 64.79; H, 4.28; N, 10.86; Cl, 13.63.

***N*-Salicylimino-*o*-hydroxyphenylmethanehydrazonoyl chloride (4b).** Yellow semi-solid; yield 65%; ¹H NMR (DMSO-*d*₆) δ 6.87-6.97 (m, 4H), 7.25-7.39 (m, 1H), 7.41-7.44 (m, 1H), 7.52-7.54 (m, 1H), 7.87-7.89 (m, 1H), 8.67 (s, 1H), 11.8 (br, 1H), 12.05 (s, 1H); ¹³C NMR (DMSO-*d*₆) δ 114.0, 114.9, 115.7, 117.1, 117.5, 117.8, 127.1, 127.9, 130.1, 132.4, 147.4, 156.0, 157.5, 163.0; MS m/z (ES+): 274 (M); Anal. Calcd for C₁₄H₁₁ClN₂O₂: C, 61.21; H, 4.03; N, 10.20; Cl, 12.90. Found: C, 61.14; H, 4.12; N, 10.26; Cl, 12.75.

***N*-Salicylimino-*o*-nitrophenylmethanehydrazonoyl chloride (4c).** Yellow semi-solid; yield 58%; ¹H NMR (DMSO-*d*₆) δ 7.30-7.32 (m, 1H), 7.48-7.55 (m, 2H), 7.70-7.96 (m, 4H), 8.10-8.15 (m, 1H), 8.42-8.44 (s, 1H), 12.06 (s, 1H); ¹³C NMR (DMSO-*d*₆) δ 124.1, 125.1, 127.3, 129.4, 131.7, 132.8, 133.0, 133.6, 134.5, 134.9, 145.1, 148.2, 162.0; MS m/z (ES+): 303 (M); Anal. Calcd for C₁₄H₁₀ClN₃O₃: C, 55.36; H, 3.32; Cl, 11.67; N, 13.84. Found: C, 55.15; H, 3.32; Cl, 11.66; N, 13.79.

***N*-2-Hydroxy-5-bromophenylbromoimidoyl-phenylmethanehydrazonoyl chloride (6).** Yellow solid; mp 165-166 °C; yield 70%; ¹H NMR (DMSO-*d*₆) δ 7.52-7.63 (m, 3H), 7.91-7.93 (m, 2H),

8.04-8.07 (m, 2H), 8.98 (s, 1H), 12.53 (s, 1H); ^{13}C NMR (DMSO_{d6}) δ 110.6, 111.4, 120.0, 128.5, 129.0, 132.3, 132.9, 134.2, 138.0, 148.0, 155.1, 164.1; MS m/z (ES $^{+}$): 417 (M $^{+}$ 1); Anal. Calcd for $\text{C}_{14}\text{H}_9\text{Br}_2\text{ClN}_2\text{O}$: C, 40.37; H, 2.18; N, 6.72. Found: C, 40.22; H, 2.31; N, 6.68.

Procedure for the reaction of 4a with aniline. A mixture of imidoyl chloride **4a** (5 mmol) and aniline (5 mmol) in dimethylformamide (10 ml) was stirred at room temperature for 24 hours. The white precipitate was filtered and dried in vacuum to afford the pure product **7** as a mixture of two isomers.

[Phenyl-[(N-salicylimino)-imino]-methyl]-aniline (7). White solid; yield, 83%; ^1H NMR (DMSO_{d6}) δ 6.86-7.00 (m, 7H), 7.26-7.73 (m, 15H), 7.91-8.07 (m, 6H), 8.63 (s, 1H), 8.95 (s, 1H), 11.11 (s, 1H), 11.26 (s, 1H), 11.36 (s, 1H), 12.11 (s, 1H); ^{13}C NMR (DMSO_{d6}) δ 117.1, 117.2, 117.4, 118.6, 119.3, 120.0, 120.3, 120.4, 122.0, 128.3, 129.2, 129.7, 130.2, 131.5, 132.2, 132.6, 133.1, 133.5, 133.9, 134.7, 146.7, 149.0, 158.2, 159.8, 163.5, 164.4; MS m/z (AP $^{+}$): 316 (M $^{+}$ 1); Anal. Calcd for $\text{C}_{20}\text{H}_{17}\text{N}_3\text{O}$: C, 76.17; H, 5.43; N, 13.32. Found: C, 76.08; H, 5.70; N, 13.32.

Acknowledgements

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