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Efficient Synthesis of Alkyl β-Diketimines

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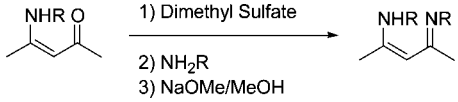


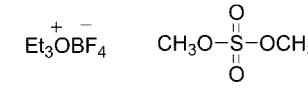
A general synthesis for the preparation of alkyl *N*,*N*′-β-diketimines has been developed. The method reported here demonstrates the use of dimethyl sulfate for conversion of enaminoketones to β-diketimines. The reaction can be performed without solvent, providing good yields.

We present in this Note the synthesis of alkyl β-diketimine compounds using dimethylsulfate. Our group required a general and efficient synthesis of *N*,*N*′-dialkyl-β-diketimines for use as ligands in electronic materials. These β-diketimine compounds are versatile as ancillary ligands for organometallic or inorganic compounds.[1]

There has been a revival of interest in β-diketimines in the past several years.[2] However, much of this work has been accomplished using aryl β-diketimines. The corresponding aryl β-diketimine is typically prepared under forcing conditions that are not conducive to volatile primary alkyl amines.[3] There have been few reports regarding the synthesis of alkyl β-diketimines since McGeachin's publication over 40 years ago.[4] Our focus is to provide a new commercially viable route to alkyl β-diketimines.

We desired conditions that would be safe, cost-effective, and amenable to large scale production, consistent with electronic grade materials. We describe the development and optimization of this synthetic process. The alkyl β-diketimines **5a**−**g** were prepared in a straightforward manner.

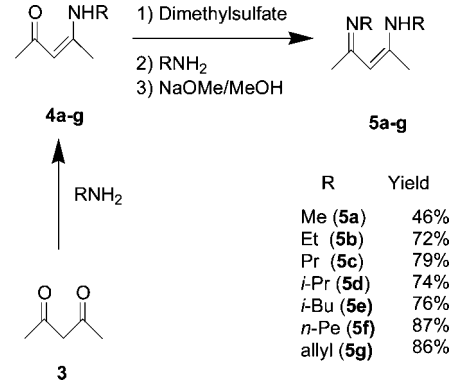
During substitution of 2,4-pentanedione (**3**) using primary alkyl amines, only the first condensation step proceeds at an observable rate. In compound **4**, conversion of the carbonyl to an imino group requires the use of a strong Lewis acid. Triethyloxonium tetrafluoroborate reagent (**1**), commonly referred to as Meerwein's salt, is often used to convert **4** to **5**.[5] We found that commercial sources of triethyloxonium tetrafluoroborate were unreliable and produced a mixture of products.[6] In our hands, Meerwein's reagent provides favorable results only when prepared immediately prior to use. Despite this improvement, there still remained the need to replace triethyloxonium tetrafluoroborate due to cost and potential safety issues.



1 **2**

FIGURE 1. Meerwein's salt (**1**) and dimethyl sulfate (**2**).

SCHEME 1. Preparation of Alkyl β-Diketimines (5a−g) under Solvent-Free Conditions



Our focus shifted to identifying a suitable replacement. Dimethyl sulfate (**2**) is a strong electrophile for activating oxygen as a leaving group and has been used extensively in commercial applications.[7] Moreover, industrial use of dimethylsulfate for O-alkylation has been reported by our company.[8] The difficulties associated with the conversion of **4** to **5** results from the recalcitrant nature of enaminoketone **4**, an extended amide. Therefore, a highly reactive reagent such as dimethyl sulfate was required.

Compound **4** is treated with dimethylsulfate and let stand at ambient temperature. Unless the enaminoketone **4** is a solid, there is no need for a solvent. The primary amine is then added dropwise to the reaction flask. In the same pot, the resulting salt is treated with a sodium methoxide solution to liberate β-diketimine **5**. Filtration and removal of methanol provides a crude mixture of **5** and unreacted or restored **4**. Residual volatile amine byproduct are removed with the solvent under vacuum. The desired compound is easily isolated by fractional distillation. The overall yields of compounds **5b**−**g** are between 72−87% (Scheme 1). Compound **5a** proved difficult to isolate, decom-

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(1) (a) Bradley, A. Z.; Thorn, D. L. U.S. Patent 7,388,113, 2008. (b) Bradley, A. Z.; Thompson, J. S.; Park, K.-H.; Marshall, W. J.; Dobbs, K. D. *Organometallics* **2006**, *25*, 2712. (c) Park, K.-H.; Bradley, A. Z.; Thompson, J. S.; Marshall, W. J. *Inorg. Chem.* **2006**, *45*, 8480.

(2) Bourget-Merle, L.; Lappert, M. F.; Severn, J. R. *Chem. Rev.* **2002**, *102*, 3031.

(3) Holm, R. H.; Parks, J. E. *Inorg. Chem.* **1968**, *7*, 1408.

(4) McGeachin, S. G. *Can. J. Chem.* **1968**, *46*, 1903.

(5) (a) Meerwein, H. *Org. Synth.* **1966**, *46*, 113. (b) Merriman, G. In *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; Wiley: New York, 1995; Vol. 3, p 2132. (c) Perst, H. In *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; Wiley: New York, 1995; Vol. 3, p 5105.

(6) The material obtained from commercial suppliers was discolored and gave an unacceptable degree of variability.

(7) Kirk, R. E. In *Encyclopedia of Chemical Technology*; Othmer, D. F., Ed.; Wiley: New York, 1983; Vol. 22, p 236.

(8) (a) Bensen, R. E.; Cairns, T. L. *J. Am. Chem. Soc.* **1948**, *70*, 2115. (b) Caprolactam reactivity parallels that of related open chain amides.

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posing during distillation. The starting material (**4**) can be collected as the higher boiling fraction or recovered from the still pot.

The need for new materials to facilitate future electronic technology applications has created a challenging synthetic opportunity. We have developed a scalable and cost-effective synthesis of β-diketimine ligands. We have extended the use of dimethylsulfate to the synthesis of *N*,*N*′-dialkyl-β-diketimines and established a viable protocol for a cost-effective preparation, allowing suitable quantities of material for product sampling and testing. We have found that dimethyl sulfate reduces variability, achieving consistent results in multiple batch runs over the course of several years, thus controlling impurities and eliminating wasteful batch processes. By using a variety of alkyl amines, we have demonstrated the general use of this method to prepare alkyl β-diketimine ligands.

Experimental Section

Two representative β-diketimine ligand preparations, demonstrating the use of primary amines, are given below. NMR spectra were recorded and chemical shifts were reported in ppm by reference to deuterated solvent. All of the β-diketimines in this work are known compounds; their NMR spectra are consistent with the chemical literature.[1,2,4]

***N*,*N*′-Diethyl-2,4-pentanediketimine (5b).** A 250 mL round bottom flask was charged with 4-(ethylamino)-3-pentene-2-one (30.0 g, 237 mmol) and dimethylsulfate (30.0 g, 238 mmol). The reaction solution was stirred and then allowed to stand (12 h) at ambient temperature to give a viscous oil. A 2 M solution of ethylamine in THF (150 mL) was added with vigorous stirring. The solution was stirred (1 h) until it solidified. The intermediate salt can be isolated or used directly.

A solution of NaOMe (12.8 g, 237 mmol) in MeOH (40 mL) was added to the intermediate salt (vida supra), and the mixture was stirred (1 h) at ambient temperature. The solvent was removed in vacuo to give an oil that was extracted with pentane, filtered and concentrated to give a crude yellow oil. The product, *N*,*N*′-diethyl-2,4-pentanediketimine, was isolated by fractional distillation to give a yellow oil (28.6 g, 72% yield). ^{1}H NMR (C_6D_6): δ 11.4 (s br, 1H) 4.56 (s, 1H), 3.10 (q, 4H, J = 7.1 Hz), 1.69 (s, 6H), 1.15 (t, 6H, J = 7.1 Hz). ^{13}C NMR (C_6D_6): δ 160.1, 94.9, 91.5, 19.5, 17.2.

***N*,*N*′-Diisobutyl-2,4-pentanediketimine (5e).** A 250 mL round bottom flask was charged with 4-(isobutylamino)-3-pentene-2-one (36.9 g, 237 mmol) and dimethylsulfate (30.0 g, 237 mmol). The reaction solution was stirred (5 min) and then allowed to stand (without stirring) overnight. The yellow mixture became orange and viscous. Isobutyl amine (18 g, 246 mmole) was added (exothermic) with vigorous stirring via addition funnel. The solution was stirred (1 h) until it solidified. The intermediate salt was not isolated and was directly converted to the free amine.

A solution of NaOMe (12.8 g, 237 mmol) in MeOH (ca. 40 mL) was added to the intermediate salt and stirred for 1 h. The solvent was removed in vacuo to give an oil that was extracted with pentane, filtered and concentrated to give a crude yellow oil. The product was isolated by fractional distillation to give a yellow oil (35.4 g, 72% Yield). ^{1}H NMR (C_6D_6): δ 11.4 (s br, 1H) 4.68 (s, 1H), 3.07 (d, 4H, J = 6.5 Hz), 1.93 (m, 2H), 1.83 (s, 6H), 1.08 (d, 12H, J = 7.0 Hz). ^{13}C NMR (C_6D_6): δ 160.3, 95.3, 55.3, 30.9, 21.3, 19.9.

Safety. Dimethylsulfate is safely used in many commercial processes. See http://www.dupont.com/dms/ for more information.

Supporting Information Available: Proton NMR spectra of compounds **5a**−**g**. This material is available free of charge via the Internet at http://pubs.acs.org.

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