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NOTE

N-Methyl-*N*-*p*-toluenesulfonylformamide: A Stable and Convenient *N*-formylating Agent

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N-Methyl-*N*-*p*-toluensulfonylformamide prepared by the reaction of *N*-methyl-*p*-toluenesulfonamide and formic acid, is demonstrated to be an effective *N*-formylating agent.

Formylation is a very important process in organic synthesis. An excellent review describes the numberous formylating methods and formylating agents available[1]. Typical *N*-formylation agents are formic halides, anhydrides and esters, formic acid and *N*-formyl derivatives. Formylation reactions employing formyl halides or anhydrides are difficult to carry out due to the instability of these reagents. Isopropenyl formate is a fast formylating reagent, but its preparation involves a multistep synthesis[2]. Other reagents require the use of expensive catalysts[3]. *N*-Formyl derivatives have been extensively used for the formylation of amines, amides, imines and alcohols[4]. Commercially available *N*-formylimidazole is an effective formylating agent, but it is extermely hygroscopic, becoming liquid in air within several minutes[5]. 4-Formyl-2-methyl-1,3,4-thiadiazoline-5-thione selectively formylates primary and secondary amines under neutral conditions, but it can be troublesome to isolate from 2-methyl-1,3,4-thiadiazoline-5-thione[4-f].

We now describe the previously unreported use of the stable, non-hygroscopic and easily accessible *N*-methyl-*N*-*p*-toluenesulfonylformamide as a convenient *N*-formylating agent. *N*-Methyl-*N*-*p*-toluenesulfonylformamide was previously made by Treppendahl and Jakobsen from *N*-methyl-*p*-toluenesulfonamide and refluxing formic acid[6]. *N*-Methyl-*N*-*p*-toluenesulfonylformamide formylates a variety of amines in good yields (Scheme 1 and Table 1).

$$\underset{(1)}{\mathrm{Ts-NCH_3(CHO)}} + \underset{(2)}{\mathrm{HNR_1R_2}} \rightarrow \underset{(3)}{\mathrm{R_1R_2NCHO}} + \underset{(4)}{\mathrm{Ts-NHCH_3}}$$

As demonstrated in Table-1, *N*-methyl-*N*-*p*-toluenesulfonylformamide can formylate both aliphatic and aromatic amines in good yields at the indicated temperature and in an appropriate solvent.[†]

[†] A solution of amine **2** (15 mmol) was added dropwise to a solution of **1** (2.8 g, 14 mmol) in appropriate solvent (40 mL) at indicated temperature (Table-1). After completion of the reaction, the solvent was evaporated and CH_2Cl_2 was added to residue and solution was washed with NaOH (1N, 20 mL). The organic layer was dried and solvent removed to afford pure *N*-formamide **3** (Table-1).

TABLE-1
N-FORMAMIDES **3** PREPARED

Entry	R_1	R_2	Solvent	Temp. (°C)	Time (h)	Yield (%)
1	Et	Et	CH_2Cl_2	30	0.5	80
2	Me	Me	CH_2Cl_2	30	0.7	73
3	$PhCH_2$	H	THF	40	1.0	66
4	Ph	H	THF	65	2.0	57
5	1-Naphthyl	H	THF	65	2.5	47
6	$2\text{-}NO_2C_2H_4$	H	Xylene	138	6.0	32
7*	$-CH_2COOH$	H	THF	65	3.0	44

*: Amino acid was dissolved in NaOH and then was added to THF.

As shown in Table 1 aliphatic amines are formylated faster than aromatic amines. Even deactivated aromatic amine such as 2-nitroaniline is formylated by this reagent to corresponding formamide on heating.

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