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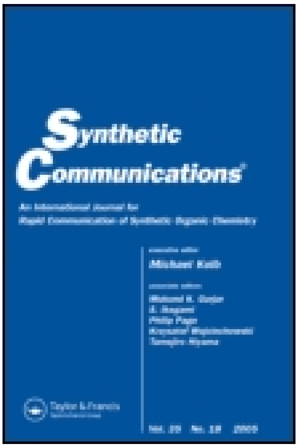

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One-Pot Synthesis of N-Alkyl Sulfonyl Hydrazones by Dialkyl Acetylenedicarboxylate-Mediated Reaction of Trialkylphosphites with Sulfonyl Hydrazones

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ONE-POT SYNTHESIS OF *N*-ALKYL SULFONYL HYDRAZONES BY DIALKYL ACETYLENEDICARBOXYLATE-MEDIATED REACTION OF TRIALKYLPHOSPHITES WITH SULFONYL HYDRAZONES

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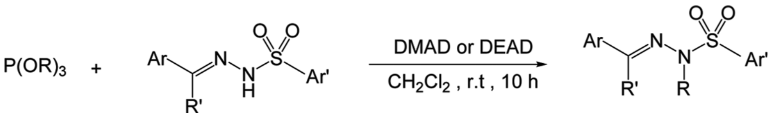
GRAPHICAL ABSTRACT



Abstract *Stable derivatives of* N-*alkyl sulfonyl hydrazone were obtained in excellent yields from the reaction between electron-deficient acetylenic ester compounds and sulfonyl hydrazones in the presence of trialkylphosphites in dichloromethan at room temperature.*

[Supplementary materials are available for this article. Go to the publisher's online edition of Synthetic Communications® *for the following free supplemental resource(s): Full experimental and spectral details.]*

Keywords Dialkyl acetylenedicarboxylate; *N*-alkyl sulfonyl hydrazone; sulfonyl hydrazone; trialkylphosphite

INTRODUCTION

The synthesis of sulfones has drawn much attention over the years because sulfones constitute useful building blocks in natural products and pharmaceutical compounds.[1–3] On the other hand, sulfonyl hydrazones exhibit interesting chemical properties and are useful intermediates in organic synthesis.[4–7] In this context, *N*-alkylated hydrazones are of interest because they have various applications in organic synthesis as useful precursors.[8–12] In accordance with that, interest in the development of new methods for their preparation continues unabated. Commonly, *N*-alkylation is achieved using alkyl halide, a base, and a phase-transfer catalyst.[13–15] Recently, acid-catalyzed reaction of tosylhydrazones can achieve *N*-alkylation of tosylhydrazones.[16] Of the previously reported methods of *N*-alkyl-

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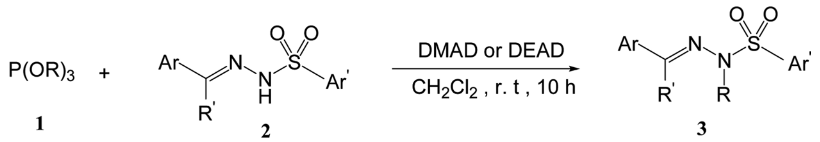


3	R	R'	Ar	Ar'	Yield %
a	Me	H	4-ClC$_6$H$_4$	4-MeC$_6$H$_4$	85
b	Me	H	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	80
c	Et	H	4-ClC$_6$H$_4$	4-MeC$_6$H$_4$	90
d	Et	H	Ph	4-MeC$_6$H$_4$	86
e	Et	H	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	77
f	Me	H	4-ClC$_6$H$_4$	Ph	85
g	Et	H	4-ClC$_6$H$_4$	Ph	83
h	Me	Me	Ph	4-MeC$_6$H$_4$	80
i	Et	Me	Ph	4-MeC$_6$H$_4$	83
j	Me	Me	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	87
k	Et	Et	Ph	Ph	85
l	Me	Me	4-NO$_2$C$_6$H$_4$	4-MeC$_6$H$_4$	80

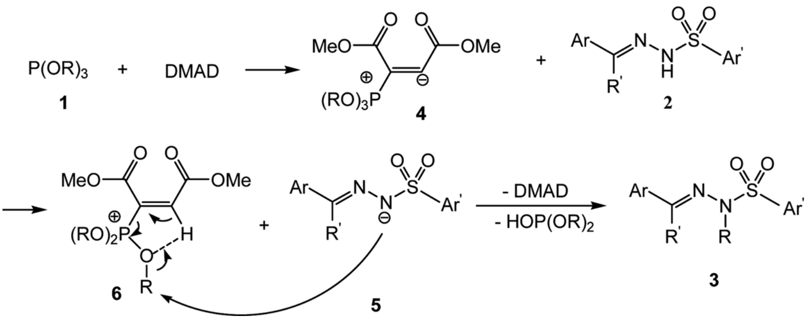
Scheme 1. Synthesis of *N*-alkyl sulfonyl hydrazones via one-pot reaction of sulfonyl hydrazone, trialkylphosphite, and dialkyl acetylenedicarboxylate.

ation of hydrazones, the reaction of tosylhydrazone as nucleophile in the Mitsunobu reaction is one of the most attractive routes because of its simplicity and the great diversity of alcohols.[17,18]

In the context of our interest in multicomponent reactions,[19] we observed the formation of *N*-alkyl sulfonyl hydrazones in good yield when sulfonyl hydrazones were reacted with zwitterion derived from trialkylphosphite and dialkyl acetylenedicarboxylate (Scheme 1). Under optimized conditions, studies on the development of substrate scope were then carried out. Various substituted sulfonyl hydrazones, which were prepared from ketones, arylbenzealdehydes, and relative sulfonyl hydrazides, were used as substrate. This method was proven to be general and efficient for preparing aranesulfonyl hydrazones.

RESULTS AND DISCUSSION

The products were separated by chromatography on a silica-gel column and supported by spectroscopic data. In the infrared (IR) spectrum of **3a** the vibrational stretching of the sulfonamide group was observed at 1353 and 1161 cm^{-1} as two strong absorptions. The methyl proton of tosyl resonated as sharp singlet at 2.41 while the proton of the *N*-Me displayed at 3.24 ppm. The hydrogen of imine bond appeared as a singlet at 7.52 ppm. The aromatic proton signals were visible as four doublets at δ 7.30, 7.79 ($J = 8.80$ Hz) and δ 7.36, 7.59 ($J = 6.80$ Hz). In the 100.6-MHZ ^{13}C NMR spectrum (CDCl$_3$), the peaks at $\delta = 141$ and 33.2 were discernible



Scheme 2. Proposed mechanism for the synthesis of *N*-alkyl sulfonyl hydrazones.

and due to the imine and *N*-methyl carbon, respectively. All other signals were also in good agreement with the proposed structure. Finally, the structure was confirmed by elemental analysis and mass spectra.

The following mechanistic postulate may be invoked to rationalize the reaction (Scheme 2). It is conceivable that the phosphite reacts with acetylenic ester to form the zwitterion **4** and subsequent protonation of the reactive 1:1 adduct by sulfonyl hydrazone **2**. Then the intermediate **6** with a hydrogenic bond reacts with sulfonyl hydrazone ion **5** by elimination of dimethyl acetylenedicarboxylate (DMAD) and dialkylphosphonate.

In conclusion, we have uncovered a novel, clean, and efficient synthesis of *N*-alkyl sulfonyl hydrazone by dialkyl actylenedicarboxylate–mediated reaction of trialkylphosphites with sulfonyl hydrazones. The mild experimental conditions used in this reaction are especially noteworthy.

EXPERIMENTAL

Trialkylphosphite and dialkyl actylenedicarboxylate were obtained commercially and used without further purification. Compounds **2** were prepared according to Ref. 20. Instruments used were as follows: mp, Electrothermal-9100 apparatus; IR spectra, Shimadzu-IR-460 spectrometer ($\bar{\nu}$ in cm^{-1}), ^1H and ^{13}CNMR spectra, Bruker DRX-400 Avance instrument at 400.1 and 100.6 MHz, resp. (δ in ppm, J in Hz); MS, Finnigan-MAT-8430EI-MS mass spectrometer at 70 eV in m/z (rel. %); and elemental analyses, Vario EL III CHNO elemental analyzer.

General Procedure for Preparation of *N*-Alkyl Sulfonyl Hydrazones (3a–3l)

A solution of dialkyl acetylenedicarboxylate (1 mmol) in 2 mL dry CH_2Cl_2 was added dropwise to a magnetically stirred solution of trialkylphosphite **1** (1 mmol) and sulfonyl hydrazone **2** (1 mmol) in 4 mL dry CH_2Cl_2 at room temperature over 10 min. The reaction mixture stirred for 10 h. The solvent was removed under reduced pressure, and the residue was separated by silica-gel (Merck 230–240 mesh) column chromatography using hexane–ethyl acetate mixture as eluent.

N′[1]-[(4-Chlorophenyl)methylene]-N[1],4-dimethyl-1-benzenesulfonohydrazide (3a)

White powder, mp: 152 °C, yield: 0.27 g (85%). IR (KBr): 2932, 1559, 1468, 1353, 1161, 1093, 929, 819, 676, 547. ^{1}H NMR (400.1 MHz, $CDCl_3$): $\delta_H = 2.41$ (3H, s, Me), 3.24 (3H, s, NMe), 7.30 (2H, d, $J = 8.8$ Hz, 2CH), 7.36 (2H, d, $J = 6.8$ Hz, 2CH), 7.52 (1H, s, CH), 7.59 (2H, d, $J = 6.8$ Hz, 2CH), 7.79 (2H, d, $J = 8.8$ Hz, 2CH). ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta_C = 21.5$ (Me), 33.2 (NMe), 128.1 (2CH), 128.3 (2CH), 128.9 (2CH), 129.5 (2CH), 132.7 (C), 133.4 (C), 135.7 (C), 141.8 (CH), 144.2 (C). EI-MS: 322 (M^+, 5), 277 (20), 167 (100), 152 (25), 132 (30), 111 (25), 84 (85), 65 (32). Anal. calc. for $C_{15}H_{15}ClN_2O_2S$ (322.80): C, 55.81; H, 4.68; N, 8.68. Found: C, 55.81; H, 4.50; N, 8.31.

Supplementary Material

Full experimental details and ^{1}H and ^{13}C NMR spectra can be found via the Supplementary Content section of this article's Web page.

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