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Studies on the catalysis of the reaction of organotin phenoxides with bis(2,2,2-trichloroethyl) azodicarboxylate by lithium perchlorate

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Organotin phenoxides, which are distinctly more active than the corresponding phenols, react at room temperature with bis(2,2,2-trichloroethyl) azodicarboxylate to produce para-substituted phenolic hydrazides in high yields. Copyright © 2004 John Wiley & Sons, Ltd.

KEYWORDS: organotin phenoxides; bis(2,2,2-trichloroethyl) azodicarboxylate; lithium perchlorate; phenolic hydrazides

INTRODUCTION

Diprotected monosubstituted hydrazine derivatives are versatile intermediates in the synthesis of aromatic amines,[1] aryl hydrazines,[2,3] substituted hydrazine derivatives,[4–6] azatides (as important peptidomimetics),[7–9] and β-strand mimics.[10] These products are used in the preparation of a wide variety of biologically and industrially valuable compounds.[4–6,11,12] Monosubstituted hydrazines are also intermediates in the preparation of heterocyclic compounds such as pyrazoles,[13] indazoles,[14] imidazolinones,[15] and cinnolines.[16] Moreover, 2-heteroaryl hydrazines[17] are interesting synthetic targets due to their efficiency as ligands for a variety of metal complexes.[18–20] Diprotected aryl hydrazines are generally prepared by electrophilic amination[1,14,21–26] of electron-rich arens utilizing dialkyl azodicarboxylates or via the reaction of *tert*-butyl carbazates with boronic acids catalysed by cuprous chloride at room temperature.[27] Previously,[26] we have shown that organotin phenoxides react with diethyl azodicarboxylate (DEAD) in diethyl ether in the presence of lithium perchlorate ($LiClO_4$) to give the corresponding ring-aminated phenols. Phenols do not react with DEAD under these conditions. Leblanc and co-workers[1] have shown that the reactions of electron-rich arens with bis(2,2,2-trichloroethyl) azodicarboxylate in diethyl ether and acetone are strongly catalysed by lithium perchlorate (3 M solutions of $LiClO_4$ in Et_2O and acetone). A number of reactions have recently been shown to be surprisingly susceptible to such catalysis (typically, 5 M solutions in diethyl ether).[28–34] Davies[35] has proved that *O*-metallation of alcohols and enols raises their reactivity towards electrophiles such as aldehydes and alkyl or acyl halides. Therefore, we assumed that the polarity of the $M^{\delta+}-O^{\delta-}-Ar$ bond would be expected to promote the reaction with enophiles such as bis(2,2,2-trichloroethyl) azodicarboxylate. We have decided to use organotin phenoxides (n-Bu_3SnOAr) because of the pronounced polarity of the Sn–O bond and simplicity of their preparation. Although bis(2,2,2-trichloroethyl) azodicarboxylate is more expensive and less stable than DEAD, it is also more reactive in reactions with electron-rich arens. Therefore, we assume that its application may sometimes be an alternative to DEAD.

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RESULTS AND DISCUSSION

We have studied the reactions of different phenols **1a–d** and corresponding tin phenoxides **2a–d** with bis(2,2,2-trichloroethyl) azodicarboxylate carried out in 5 M solution of $LiClO_4$ in diethyl ether (Fig. 1). Previous studies with this azo enophile were carried out at elevated temperatures.[1] However, it is known that heating of solution of $LiClO_4$ in Et_2O or acetone may be hazardous. We hoped that the use of more concentrated solutions of $LiClO_4$ would enable us to carry out reactions with bis(2,2,2-trichloroethyl) azodicarboxylate at room temperature. The addition products **4a–b** obtained by us were isolated by chromatography on silica. The yields of this reaction for different phenolic

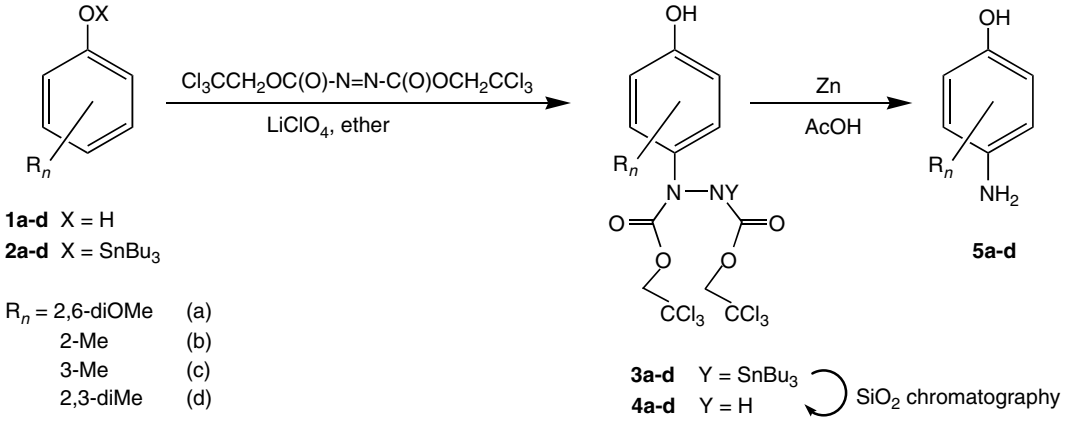

Figure 1. Synthesis of 4-hydroxysubstituted phenylhydrazides **4**.

substrates **1** and **2** are collected in Table 1. The newly obtained data show that the use of bis(2,2,2-trichloroethyl) azodicarboxylate may sometimes lead to better results than has been observed for DEAD.[26] For example, we found that no reaction occurred between 2-methylphenol (**1b**) and DEAD in 5 M solution of $LiClO_4$ in Et_2O at room temperature.[26] Also 2,6-dimethoxyphenol (**1a**) and the tributyltin phenoxide (**2a**) obtained from it do not react with DEAD under these conditions.

The aryl hydrazides **4a–d** prepared during the present study were easily converted in high yields to their corresponding anilines **5a–d** by reduction with zinc dust in acetic acid. They were identified by comparison with the literature ^{1}H NMR data for corresponding aminophenols. All the reactions studied were catalysed by $LiClO_4$, which we believe play, two roles in the present reaction, i.e. the activation of the azo compound and the stabilization of the intermediate complex. The 1.42×10^{-3} M solution of bis(2,2,2-trichloroethyl) azodicarboxylate in diethyl ether exhibits an absorption maximum at 143 nm. An increase in the concentration of $LiClO_4$ in Et_2O results in a decrease in the molar absorptivity at 243 nm. For example, its ratio in the solution of $LiClO_4$ in Et_2O changes from approximately 1.1 to 1.6 with increasing concentration of $LiClO_4$ in the range 1–1.9 mol dm^{-3}. This seems to reflect the decreasing lowest unoccupied molecular orbital of the azo compound by association with aggregates of $LiClO_4$.

The results obtained (Table 1) also indicate that *O*-metallation of the phenols (**1**) studied strongly promotes the reaction with bis(2,2,2-trichloroethyl) azodicarboxylate.

Table 1. Catalytic amination of different phenolic substrates **1** and **2** to addition products **4**[a]

Substrate	Yield (%)	^{1}H NMR data for hydrazides **4** in $CDCl_3$ (ppm)
1a	0	**4a**: 3.83 (6H, s), 4.80 (4H, s), 6.73 (2H, s), 8.00 (1H, br s, NH)
2a	60	
1b	60	**4b**: 2.19 (3H, s), 4.79 (4H, s), 6.71 (1H, d, J = 8.4 Hz), 7.10 (1H, dd, J = 8.4 and 2.1 Hz), 7.23 (1H, m), 7.92 (1H, br s, NH)
2b	100	
1c	70	**4c**: 2.21 (3H, s), 4.81 (4H, s), 6.71 (1H, d, J = 8.5 Hz), 7.14 (1H, dd, J = 8.5 and 2.4 Hz), 7.26 (1H, m), 7.59 (1H, br s, NH)
2c	100	
1d	40	**4d**: 2.03 (6H, s), 4.75 (4H, s), 6.58 (1H, d, J = 9.1 Hz), 7.21 (1H, d, J = 9.1 Hz), 7.92 (1H, br s, NH)
2d	100	

[a] Reaction time: 48 h, $Cl_3CCH_2O_2CN{=}NCO_2CH_2CCl_3$ 1.2 equivalents.

EXPERIMENTAL

UV spectra were recorded on a Specord spectrometer (Carl Zeiss, Jena, Germany) using 10 mm cells. NMR spectra were recorded using a Varian Gemini 200BB spectrometer operating at 4.7 T. The tributyltin phenoxides (**2**) studied were prepared by the azeotropic dehydration of appropriate parent phenols (**1**) and bis(tributyltin) oxide in toluene.[36]

Typical examples of the reactions studied are as follows: tributyl-2,6-dimethoxyphenyloxytin (**2a**; 222 mg, 0.5 mmol) and bis(2,2,2-trichloroethyl) azodicarboxylate (Aldrich, 228 mg, 0.6 mmol) were added to 5 M solutions of $LiClO_4$ in diethyl ether (1 cm^3). The progress of the reaction was monitored by thin-layer chromatography (SiO_2, using light petroleum–ethyl acetate (3/1, v/v) as eluent) and by ^{1}H NMR spectroscopy

which showed that *N*-(4-hydroxy-3,5-dimethoxy-1-phenyl)-*N′*-tributylstannyl-*N*,*N′*-dicarboxylic acid bis(2,2,2-trichloroethyl) ester (**3a**) was formed in 60% yield.

Column chromatography of the tributylstannyl intermediate **3a** on silica (Aldrich, 70–230 mesh) gave *N*-(4-hydroxy-3,5-dimethoxy-1-phenyl)-hydrazine-*N*,*N′*-dicarboxylic acid bis(2,2,2-trichloroethyl) ester (**4a**) as an oil, the reduction of which with zinc dust (1.0 equivalent, by weight) in acetic acid led to 4-amino-2,6-dimethoxyphenol (**5a**). It was identified by comparison of its ^{1}H NMR spectra with the literature data.[37] All other oily products **4b–d** were characterized by their chemical shift values (Table 1), and analogously identified as the corresponding aminophenols **5**. 4-Amino-3-methylphenol (**5c**) is a commercial compound whose spectrum is available in the Aldrich catalogue.[38] Also, the ^{1}H NMR spectra of 4-amino-2-methylphenol (**5b**) and 4-amino-2,3-dimethylphenol (**5d**) have been published elsewhere.[39–41]

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