

A Novel Synthesis of Unsymmetrical α -Amino Sulfides *via* the Sm/ZnCl₂ System in THF–Water†

Yunfa Zheng,^a Genliang Lu^b and Yongmin Zhang^{*b}

^aDepartment of Chemistry, Lishui Teachers College, Lishui 323000

^bDepartment of Chemistry, Zhejiang University (Xixi Campus), Hangzhou 310028

Unsymmetrical α -amino sulfides are synthesized in moderate to good yields *via* the reactions of 1-(α -aminoalkyl)benzotriazoles with sodium alkylthiosulfates promoted by the Sm/ZnCl₂ system in THF–water.

Benzotriazole methodology has been already come a long way and in the last decade, benzotriazole has been found to be an excellent synthetic auxiliary in many useful synthetic transformations.^{1–5} Because the benzotriazolone anion is a good leaving group, it may be used in place of a halogen in many reactions. The use of benzotriazole as a synthetic auxiliary has a number of significant advantages. For example, it is readily available and quite cheap; in addition it is acidic with a pK_a of *ca.* 8, which enables easy separation and recovery. Many types of compounds have been synthesized *via* the benzotriazole auxiliary.⁵

Although α -amino sulfide (N,S-acetal) structures in five- or six-membered rings are very common in heterocyclic chemistry and are readily available,⁶ open chain hemithioaminals have been relatively little explored. Aminomethyl phenyl sulfides are useful precursors in the preparation of (aminomethyl)trialkylstannanes.^{7,8} Some methods have been reported for the preparation of hemithioaminals, for example, condensation of thiophenols with secondary amines and formaldehyde,⁹ reactions of *N*-[1-(benzotriazol-1-yl)alkyl]amine with sodium salts of thiols,¹⁰ *etc.* However, these methods require the use of metallic sodium, alkaline media and thiophenols. Here we wish to report that unsymmetrical α -amino sulfides can be synthesized in moderate to good yields *via* the reactions of 1-(α -aminoalkyl)benzotriazoles with sodium alkylthiosulfates promoted by the Sm/ZnCl₂ system in THF–water in moderate to good yields.

The products and yields are listed in Table 1. The reactions were conducted in air and at room temperature in THF–H₂O (4:1). 1-(α -Aminoalkyl)benzotriazoles are very easy to prepare¹¹ and in view of the easily available starting material, high yields, mild and neutral reaction conditions as well as simple operation, we believe that the present procedure provides a useful method for the synthesis of unsymmetrical α -amino sulfides.

Experimental

Typical Procedure.—2 mmol Sm powder, 2 mmol ZnCl₂, 8 ml THF, 2 ml H₂O, 2 mmol RNH₂CH₂Bt and 2 mmol RSSO₃Na were placed in a 50 ml three-necked flask and the mixture stirred at room temperature for 4 h. The mixture was extracted with Et₂O. After drying over MgSO₄, the solvent was evaporated *in vacuo* and the product isolated by preparative TLC on silica gel using light petroleum (bp 35–60°C)–diethyl ether (15:1) as eluent. The products were characterized by their ¹H NMR, IR and mass spectra.

- Oil; $\nu_{\max}/\text{cm}^{-1}$ 3440 (NH); δ_{H} 0.8–1.7 (m, 7H), 2.61 (t, 2H), 3.82 (s, 1H, NH), 4.19 (s, 2H), 6.8–7.2 (m, 5H); m/z 195 (M⁺).
- Oil; $\nu_{\max}/\text{cm}^{-1}$ 3435 (NH); δ_{H} 0.8–1.8 (m, 18H), 2.60 (t, 2H), 3.78 (s, 1H, NH), 4.40 (q, 1H), 6.7–7.2 (m, 5H); m/z 265 (M⁺).
- Oil; $\nu_{\max}/\text{cm}^{-1}$ 3438 (NH); δ_{H} 0.8–1.8 (m, 22H), 2.65 (t, 2H), 3.75 (s, 1H, NH), 4.45 (q, 1H), 6.7–7.2 (m, 5H); m/z 321 (M⁺).
- Oil; $\nu_{\max}/\text{cm}^{-1}$ 3440 (NH); δ_{H} 0.8–1.7 (m, 19H), 2.60 (t, 2H), 3.76 (s, 1H, NH), 4.20 (s, 2H), 6.7–7.2 (m, 5H); m/z 307 (M⁺).
- Oil; $\nu_{\max}/\text{cm}^{-1}$ 3440 (NH); δ_{H} 0.8–1.7 (m, 7H), 2.11 (s, 3H), 2.63 (t, 2H), 3.80 (s, 1H, NH), 4.07 (s, 2H); 6.4–7.3 (m, 4H); m/z 209 (M⁺).
- Oil; $\nu_{\max}/\text{cm}^{-1}$ 3435 (NH); δ_{H} 0.8–1.8 (m, 14H), 2.15 (s, 3H), 2.60 (t, 2H), 3.70 (s, 1H, NH), 4.18 (q, 1H), 6.3–7.3 (m, 4H); m/z 251 (M⁺).
- Oil; $\nu_{\max}/\text{cm}^{-1}$ 3438 (NH); δ_{H} 0.8–1.8 (m, 18H), 2.18 (s, 3H), 2.58 (t, 2H), 3.75 (s, 1H, NH), 4.18 (q, 1H), 6.3–7.3 (m, 4H); m/z 279 (M⁺).
- Oil; $\nu_{\max}/\text{cm}^{-1}$ 3440 (NH); δ_{H} 0.8–1.7 (m, 7H), 2.53 (t, 2H), 4.05 (s, 1H, NH), 4.11 (s, 2H), 6.6–7.4 (m, 4H); m/z 229 (M⁺).
- Oil; $\nu_{\max}/\text{cm}^{-1}$ 3435 (NH); δ_{H} 0.8–1.8 (m, 10H), 2.50 (t, 2H), 4.05 (s, 1H, NH), 4.13 (q, 1H), 6.6–7.4 (m, 4H); m/z 243 (M⁺).
- Oil; $\nu_{\max}/\text{cm}^{-1}$ 3430 (NH); δ_{H} 0.8–1.8 (m, 11H), 2.50 (t, 2H), 3.98 (s, 1H, NH), 4.10 (s, 2H), 6.6–7.4 (m, 4H); m/z 257 (M⁺).
- Oil; $\nu_{\max}/\text{cm}^{-1}$ 3434 (NH); δ_{H} 0.8–1.7 (m, 15H), 2.55 (t, 2H), 4.05 (s, 1H, NH), 4.08 (s, 2H), 6.6–7.4 (m, 4H); m/z 285 (M⁺).

Table 1 Synthesis of unsymmetrical α -amino sulfides

Entry	R ¹	R ²	R	Yield ^a (%)
1	Ph	H	<i>n</i> -C ₄ H ₉	86
2	Ph	Me	<i>n</i> -C ₈ H ₁₇	82
3	Ph	Me	<i>n</i> -C ₁₀ H ₂₁	80
4	Ph	H	<i>n</i> -C ₁₀ H ₂₁	88
5	<i>o</i> -MeC ₆ H ₄	H	<i>n</i> -C ₄ H ₉	90
6	<i>o</i> -MeC ₆ H ₄	Me	<i>n</i> -C ₈ H ₁₃	85
7	<i>o</i> -MeC ₆ H ₄	Me	<i>n</i> -C ₄ H ₁₇	85
8	<i>o</i> -ClC ₆ H ₄	H	<i>n</i> -C ₄ H ₉	78
9	<i>o</i> -ClC ₆ H ₄	Me	<i>n</i> -C ₄ H ₉	80
10	<i>o</i> -ClC ₆ H ₄	H	<i>n</i> -C ₆ H ₁₃	76
11	<i>o</i> -ClC ₆ H ₄	H	<i>n</i> -C ₈ H ₁₇	76

^aIsolated yields of oils based on sodium alkylthiosulfates.

* To receive any correspondence.

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