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## Mercuration demercuration of Aliphatic Isocyanates: a New Mild Route to Primary Amines

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Abstract: Aliphatic isocyanates react with mercury acetate in THF/H<sub>2</sub>O and successively with sodium boro hydride to give aliphatic primary amines in good yields in short reaction times with high stereo control.

The hydrolysis of isocyanates represents a key step in the synthesis of primary amines<sup>1</sup> but sterically hindered precursors require long reaction times, high temperatures or the use of strong acid or bases<sup>2</sup>. During our studies on the synthesis of aminoalcohols having the ephedrine structure, we synthetized the diastereomerically pure trans 2-phenyl-3-isocyanatotetrahydrofuran (1)<sup>3</sup>. Attempts to interconvert 1 into the corresponding trans 2-phenyl-3-aminotetrahydrofuran (2), employing acid conditions<sup>2c</sup> (TFAA, 35 °C, 56 h), gave 2 in a 20% yield along with products derived from the tetrahydrofurane ring opening. On the other hand, basic reaction conditions cannot be used because the isomerization of the C<sub>3</sub> of 1, due to the high acidity of the proton in æ position to the isocyano group takes place. We recently have found very mild reaction conditions to operate the isocyanate—amine functional group interconversion, employing mercury acetate (Scheme and Table). In a typical run 0.01 mol of the substrate in 40 ml of a 50% THF/H<sub>2</sub>O solution was added with 0.01 mol of Hg(OAc)<sub>2</sub> in 40 ml of the same solvent. After 45 min. NaBH<sub>4</sub> (0.02 mol.) in a 5% NaOH solution (50 ml) were slowly added.



 $R-N=C=O \xrightarrow{1)Hg(OAc)_2,THF/H_2O} R-NH_2$ 

After the complete formation of  $Hg^0$ , the mixture was extracted with diethyl ether and, after the usual workup gave the crude amine. The reaction is not affected by steric hindrance and is completely stereospecific: in particular compounds 6 and 8 have the same optical purity as the precursors employed. The low yield obtained with 12 (10%, run 6) can be explained by the high tendency of the isocyanate 11 to dimerize in the reaction conditions employed<sup>4</sup>.



Run	Substrates	Products	Yields %
1	NCO O Ph	CO Ph 2	80 <sup>(a)</sup>
2			(b) 100
3	NCO	NH <sub>2</sub> 6	100 <sup>(c)</sup>
4	T NCO 7	NH <sub>2</sub> 8	90 <sup>(d)</sup>
5		NH <sub>2</sub> 10	(b) 100
6		NH <sub>2</sub> 12	10 <sup>(d)</sup>

Notes: a) The stereochemistry was evaluated by <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy:<sup>b</sup>) The precursor was prepared from the corresponding acyl chloride with noted procedures<sup>2d</sup>: <sup>c</sup>) The substrate was obtained starting from the (+)(S) 2-methylbutanoic acid chloride and sodium azide<sup>2c</sup>: <sup>d</sup>) The precursor is commercially available:

The products were characterized by  ${}^{1}$ H and  ${}^{13}$ C NMR, FT-IR spectroscopy and Mass spectrometry. The yields were evaluated on the recovered materials. The reaction can be explained through the formation of the isocyanate mercurial, (I) able to undergo reduction to amine, performed by NaBH<sub>4</sub>.

## **References and Notes**

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3.) The synthesis of 1 should be published elsewhere.

4.)R. E. Buckles, L. A. McCrue, Macromol. Chem., 77, 185 (1964).

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