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A NEW DEHYDROGENATION REACTION OF INDOLINES TO INDOLES _VIA_ AZASULFONIUM SALTS

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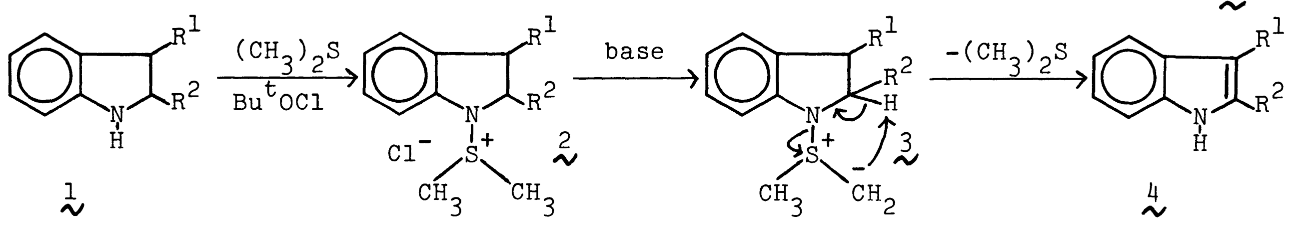
Indolines (1) have been converted to the corresponding azasulfonium salts (2) and the subsequent intramolecular base catalyzed abstraction of the hydrogen at C-2 gave indoles (4) in good yields.

We have reported a facile reduction of indoles to indolines with pyridine-borane without affecting other functional groups,[1)] and applied this reaction to the introduction of a methoxyl group to the benzene ring of indolines[2)] and to the reductive modification of peptides containing tryptophyl residues.[3)] On the course of this study, we required a mild, general, and high yield method for the dehydrogenation of indolines to indoles. Of the several methods available for the dehydrogenation of indolines to indoles,[4)] active MnO_2, $CuCl_2$-pyridine, chloranil, and Pd/C are most commonly used. However, many of these methods suffer from carefully controlled conditions, lack of generality, or low yield in the case of the dehydrogenation of a functionalized indoline.

We report here a facile dehydrogenation of indolines to indoles _via_ azasulfonium salts (2)[5)] generated with indolines, dimethyl sulfide, and _tert_-butyl hypochlorite. 2 has acidic hydrogens on the carbons adjacent to the sulfur due to the inductive effect of the positive sulfur. Bases such as sodium ethoxide or triethylamine abstract a proton from the methyl attached to sulfur to give the ylide (3).



Intramolecular attack of the nucleophilic end of 3 to the hydrogen of C-2 yields an indolenine derivative, which is converted to 4 by proton transfer. A Sommelet-Hauser type rearrangement[6)] was not observed because 7-(thiomethoxymethyl)indolines are not detected in the reaction mixture. A typical procedure is as follows: _Tert_-butyl hypochlorite (3.9 mmol) in CH_2Cl_2 (10 ml) was added dropwise to a vigorously stirred mixture of indoline (1a) (3 mmol), dimethyl sulfide (4.5 mmol), and triethylamine (3 mmol) in CH_2Cl_2 (10 ml) at -65 °C for 1 hr. After the reaction mixture was stirred for 2 hr at -65 °C, sodium ethoxide solution [prepared from Na (15 mmol) and ethanol (5 ml)] was added for 10 min, and the stirred reaction mixture was allowed to warm up to room temperature for 2 hr. After usual work-up of the reaction mixture, the solution was extracted with CH_2Cl_2 (30×2 ml) and the combined CH_2Cl_2 extracts were washed with water (20 ml) and dried over anhydrous

Na_2SO_4. After evaporation of CH_2Cl_2, the residue was purified by column chromatography [SiO_2, benzene-hexane (1:1) for elution] to give indole (**4a**) in 82% yield. The results are presented in the table. 2,3-Dihydro-L-tryptophan derivatives (**1f** and **g**) were oxidized to **4f** and **g** by this procedure without racemization (optical purity≧95% in both cases). It was recently reported[7] that a N-chloroindoline derivative was dehydrochlorinated to a indole derivative accompanying with considerable amounts of nuclear chlorinated indolines. We examined this reaction for the dehydogenation of indoline (**1a**) and large amounts of nuclear chlorinated products were obtained. The characteristic feature of our method is that the procedure is simple (a one-pot reaction) and the reaction conditions are mild enough to be applicable to indolines with functionality which would be sensitive to elevated temperature, acids, or strong bases.

Table. Dehydrogenation of Indolines (**1**) to Indoles (**4**)[a]

1		Yield of (**4**) (%)
a	$R^1=R^2=H$	82
b	$R^1=CH_3$, $R^2=H$	91
c	$R^1=H$, $R^2=CH_3$	69
d	$R^1-R^2=(CH_2)_4$	63
e	$R^1=(CH_2)_2NHBz$, $R^2=H$	74^b
f	$R^1=CH_2CH(NHAc)CO_2Et$, $R^2=H$	$63^{c,d}$
g	Z-L-Ala-2,3-dihydro-L-Trp-OMe	$61^{c,e}$

a) Indolines (**1**) were prepared by the literature method,[1] and all products were identified by the mixed melting point measurements with the authentic samples. b) A mixture of CH_2Cl_2-$(CH_2OMe)_2$ (1:1) was used as solvent. c) Et_3N was used as base. d) $[\alpha]_D^{24}$ +48.0° (c=0.5, $CHCl_3$). Lit.[8] $[\alpha]_D^{20}$ +50° (c=0.5, $CHCl_3$). e) $[\alpha]_D^{21}$ +49.2° (c=0.5, $CHCl_3$). Authentic **4g**: mp 138-139 °C; $[\alpha]_D^{21}$ +52.0° (c=0.5, $CHCl_3$); Anal. Calcd for $C_{23}H_{25}N_3O_5$: C, 65.23; H, 5.95; N, 9.92. Found: C, 65.22; H, 5.83; N, 9.90.

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