

# SYNLETT Spotlight 73

## Trimethylsilyldiazomethane

Compiled by Neil S. Hodnett



This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Neil Hodnett was born in Chichester in 1977 and began his studies at the University of Bristol (UK) in 1995. He received his MSci in 1999, after spending a lively year at the Université de Montpellier II (France) as part of the *Socrates* exchange program. He enjoyed Bristol so much he decided to stay and is about to complete a PhD, under the supervision of Dr Guy C. Lloyd-Jones (Bristol), to develop a novel method for screening racemic catalysts based on kinetic resolution.

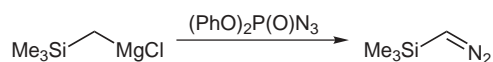
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### Introduction

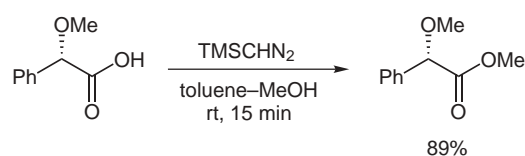
The commercially available reagent trimethylsilyldiazomethane<sup>1</sup> can be used as a stable and safe alternative to diazomethane in one-carbon homologations, as in the Arndt–Eistert reaction,<sup>2</sup> the homologation of carbonyl compounds<sup>3,4</sup> and O-methylation of carboxylic acids, phenols and alcohols. Additionally, the reagent can serve as a C–N–N synthon for the preparation of azoles.

Trimethylsilyldiazomethane is prepared as a hexane solution by diazo-transfer reaction between diphenyl phosphorazidate and the Grignard reagent prepared from chloromethyltrimethylsilane (Scheme 1).<sup>5</sup>

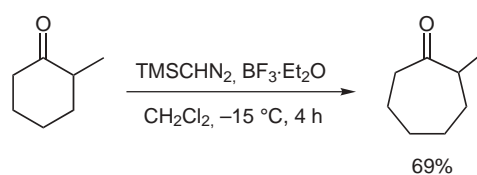


### Abstracts

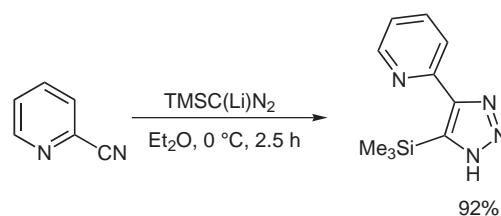
(A) Trimethylsilyldiazomethane (TMSCHN<sub>2</sub>) reacts rapidly with carboxylic acids in benzene or toluene in the presence of methanol, at room temperature, to afford the methyl esters in very high yields.<sup>6</sup> This method is particularly useful in quantitative analysis of fatty acids by gas chromatography.<sup>7</sup>



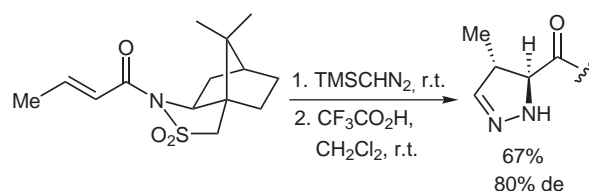
(B) Both cyclic and acyclic ketones react with TMSCHN<sub>2</sub> in the presence of boron trifluoride etherate to give the ring or chain homologated ketones. The steric bulk of the trimethylsilyl group promotes regioselective methylene insertion.<sup>8</sup>



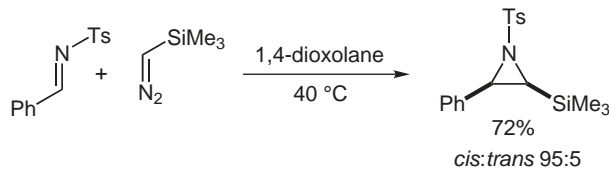
(C) While TMSCHN<sub>2</sub> will only react with activated nitriles, its lithium salt, TMS(Li)N<sub>2</sub>, reacts smoothly with aromatic, heteroaromatic and aliphatic nitriles to give the corresponding 4-substituted 5-trimethylsilyl-1,2,3-triazoles.<sup>9</sup> Reaction of TMS(Li)N<sub>2</sub> with  $\alpha,\beta$ -unsaturated nitriles can also afford pyrazoles in some cases.<sup>10</sup>



(D) TMSCHN<sub>2</sub> has been employed in asymmetric dipolar cycloadditions with chiral acrylates, to afford optically active  $\Delta^2$ -pyrazolines.<sup>11</sup> The cycloadditions proceed in high yield with a high degree of diastereoselectivity. This methodology has also been applied to the synthesis of the indolizidine metabolite stelletamide A.<sup>12,13</sup>



(E) TMSCHN<sub>2</sub> reacts directly with *N*-sulfonyl imines to furnish *C*-silylaziridines in good yields and high *cis*-stereoselectivities.<sup>14,15</sup> The resulting products undergo substitution of the silyl group with high diastereoselectivity and ring opening by nucleophiles with complete regioselectivity.



## References

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