Pergamon

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Synthesis of a Sterically Congested Diazirine: 2-Azi-camphane

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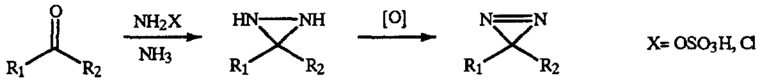
Abstract: The synthesis of 2-azi-camphane has been achieved despite the fact that the spirocyclic carbon center is sterically congested. Although the yield is somewhat low, the highly pure diazirine can be used as a precursor for the burgeoning class of sterically congested carbenes.

Diazirines[1] are increasingly popular carbene[2] precursors. Upon photolysis or thermolysis, they usually[2a] eliminate molecular nitrogen to form these highly reactive, divalent carbon species. In contrast to other carbene precursors such as diazo compounds,[3] many of the diazirines are relatively stable and can be stored for longer periods of time without decomposition. And even small, explosive diazirines can be preserved in solution. Therefore, for most synthetic and academic applications, diazirines are the reagents of choice. Their only limitation, thus far, has been their availability.

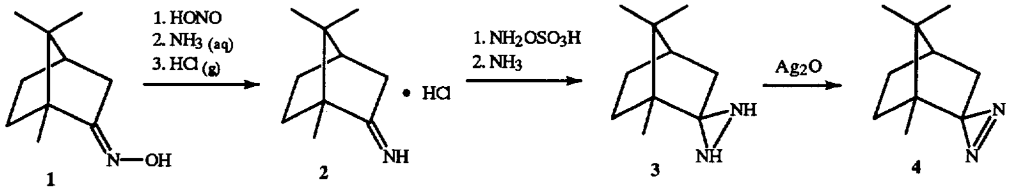
3,3-Dialkyldiazirines are almost exclusively synthesized according to the Schmitz diaziridine reaction.[4] This involves the reaction of a ketone or its Schiff's base derivative with ammonia and an electrophilic aminating agent such as hydroxylamine-*O*-sulfonic acid or chloramine. The diaziridine obtained can be oxidized to the corresponding diazirine as shown in Scheme 1. The crucial step, however, is the formation of the three-membered ring which depends mostly on the reactivity of the ketone's carbonyl center.[5] For cyclic ketones[6], just one α-alkyl substituent[1c] lowers the yield of diaziridines somewhat and α,α-dialkyl substitution prevents the reaction altogether.[5a] In this case, the electrophilic aminating agent reacts faster with the large excess of ammonia present under Schmitz conditions than with the sterically hindered ketone. Furthermore, direct alkylation of diazirines would be difficult since the initial deprotonation step leads to vinyl anions.[7]



Scheme 1. Synthesis of 3,3-dialkyldiazirines from their corresponding ketones

In this report, we present the preparation of the sterically congested diazirine deriving from camphor. Camphor is rather unreactive and the diaziridine is unobtainable[8] through the standard procedure.[4] Therefore, the simultaneous presence of ammonia and electrophilic aminating agent during the diaziridine-ring-forming step needed to be eliminated. This difficulty was circumvented by using camphor imine hydrochloride (**2**) instead of camphor itself. Imines of sterically hindered ketones are easily obtained by nitrosation of their oximes with subsequent ammonolysis,[9] as depicted in Scheme 2.

When camphor oxime (**1**) was treated in this manner, the imine hydrochloride **2**[8] was isolated in 57% yield. Next, **2** was reacted with hydroxylamine-*O*-sulfonic acid to give diaziridine **3** after subsequent neutralization with ammonia. Oxidation of **3** with silver oxide provided sterically congested 2-azi-camphane (**4**) in 15% yield from **2**. Unlike 2-diazo-camphane,[10] which is extremely unstable,[10a] diazirine **4** is thermally enduring and can even be sublimed at 110-125°C. Though the yield is somewhat low, finally, the first successful method leading to sterically congested α,α-dialkyl substituted diazirines has been achieved.



Scheme 2. Preparation of imine hydrochlorides from oximes of sterically hindered ketones and subsequent modified Schmitz reaction.

Method and Analysis:[8] To a stirred solution of camphor imine hydrochloride (1.88 g, 10 mmol) at −78°C in methanol (20 mL), NH_2OSO_3H tech. (1.25 g, 10 mmol) was added over 10 min. After 30 min, the mixture was stored in the freezer at −20°C overnight. A slow stream of ammonia was bubbled in at −50°C for 1 h. After warming up to r.t., the solvent was subjected to rotary evaporation. The solid residue was triturated thrice with ether (50 mL) in a sintered funnel. To a stirred solution of the total filtrate at r.t., freshly prepared Ag_2O (2.32 g, 10 mmol) was added over 5 min. The filter flask was fitted with a rubber stopper and a silicone oil bubbler. After 18 h, during which a silver mirror formed, anhydr. Na_2SO_4 was added and the solvent was filtered through a sintered funnel and then evaporated. (All unwanted silver residues can be digested by $50\%(^{w}/_{w})$ HNO_3.) The solid residue was purified by flash column chromatography (silica gel 60, 230–400 mesh / pentane) from the camphor oxime side product to yield the title compound as a white solid (0.247 g, 1.5 mmol) in 15% yield.
m.p.= 110–125°C (sublimes); $\bar{v}_{max}$ /cm^{-1} (CCl_4) 1390, 1452, 1564, 1604, 1665, 2874, 2956; δ_H /ppm (360 MHz, $CDCl_3$) 0.18 (3H, s) 0.84 (1H, d, J= 13.9 Hz) 0.87 (3H, s) 1.16 (3H, s) 1.35–1.58 (3H, m) 1.73–1.90 (3H, m); δ_C /ppm (90 MHz, $CDCl_3$) 10.1 (q), 19.2 (q), 19.6 (q), 28.0 (t), 31.6 (t), 37.2 (t), 39.8 (s), 45.0 (d), 46.1 (s), 48.2 (s); m/z (EI) 136($[M-N_2]^+$), 121, 105, 93, 79, 67, 53, 41, $C_{10}H_{16}N_2$ requires 164.1313.

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