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A NOVEL, SIMPLE SYNTHESIS OF AMINOADAMANTANES

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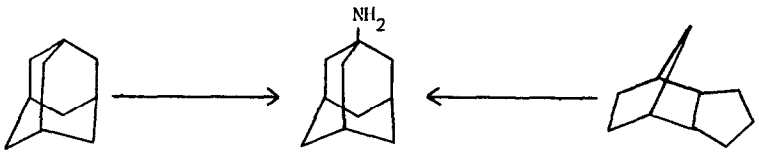
This communication deals with a novel, simple synthesis of aminoadamantanes from adamantanes or adamantane precursors by amination with trichloramine and aluminum halide. In addition, evidence pertinent to the mechanistic aspects is presented. Earlier work has shown that simple t-alkanes, such as methylcyclohexane, undergo amination in this system to yield the corresponding t-carbinamines(1).

Adamantane(I) in the presence of trichloramine and aluminum chloride in methylene chloride solvent (NCl_3:$AlCl_3$:$C_{10}H_{16}$ = 1:2:1.5 molar ratio) gave a nearly quantitative yield of 1-aminoadamantane(II)(2)(yields are based on trichloramine). The general procedure described earlier(1) was used except that acid treatment of the reaction mixture during work-up was carried out under more vigorous conditions. With a molar ratio of 1:2:1, essentially the same results were obtained.



I II III

Various saturated tricyclic hydrocarbons containing ten or more carbon atoms are

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known to rearrange to adamantane or its alkyl derivatives under the influence of aluminum halides(3,4). We found that 1-aminoadamantane (60% yield) is formed in one step from trichloramine, aluminum chloride, and tricyclo[5.2.1.$0^{2,6}$]decane(III) (1:2:1.5 molar ratio). Use of the aluminum bromide-t-butyl bromide catalyst system(5) (NCl_3:$AlBr_3$:$C_{10}H_{16}$:t-BuBr = 1:2:1.5:0.036 molar ratio) increased the yield to 86%.

Previous routes to 1-aminoadamantane starting from adamantane produce yields from 60-65% in procedures involving a number of steps(2,6). Furthermore, the yield from III (5,7) in a multistep sequence is no more than 30%. The advantages of the trichloramine-aluminum halide method are clearly evident.

According to our working hypothesis(1), amination of t-alkanes by this procedure involves carbonium ion formation via hydride abstraction followed by combination with a nitrogen-containing nucleophile(8). Cation generation from adamantane has been observed in Lewis acid systems(9). Apparently, the same carbonium ion is selectively attacked in the case of the adamantane precursor. In contrast with prior investigations involving other t-alkanes(1), the product at the end of the adamantane reaction was in the form of the N,N-dichloro derivative. The difference in behavior presumably stems from the inability of adamantane to generate, in an accompanying reaction, olefinic material which can convert the N,N-dichloro form to the amine in the presence of acid(8). The authentic substance was prepared for comparison (infrared and mass spectra) from 1-aminoadamantane hydrochloride and calcium hypochlorite.

It is apparent that the presence of trichloramine facilitates rearrangement or diminishes undesirable side reactions. To our knowledge this amination method comprises the first example of introduction of a functional group during rearrangement to the adamantane nucleus.

Extensions of this technique to other substrates in this series proved to be rewarding. 1,3-Dimethyladamantane on amination with trichloramine and aluminum chloride

(NCl_3:$AlCl_3$:$C_{12}H_{20}$ = 1:2:1.5 molar ratio) gave 1-amino-3,5-dimethyladamantane (70-75% yield)(2). Perhydroacenaphthene, which is known to rearrange to 1,3-dimethyladamantane (5), afforded a 73% yield of the same amine after initial exposure to aluminum chloride at 100° for 24 hr., followed directly by treatment with trichloramine at 0° ($C_{12}H_{20}$:$AlCl_3$:NCl_3 = 1.7:2:1 molar ratio). A 35% yield was realized from the one-step procedure. Prior synthesis(2) of this amine from 1,3-dimethyladamantane by a more involved pathway proceeded in 63% yield. Starting from precursor(5), the best yield one obtains is about 40% in several steps.

By-product amines were present in some of the amination reactions.

1-Aminoadamantane (adamantylamine)(10) is of physiological interest as an antiviral agent.

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