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UNUSUAL DEGREE OF SELECTIVITY IN DIAMANTANE DERIVATIZATIONS

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Abstract: Direct, selective functionalization of diamantane to 1- and 4-aminodiamantanes was obtained with $NCl_3/AlCl_3$. 1- and 4-diamantanethiols were prepared from their respective bromides without rearrangement.

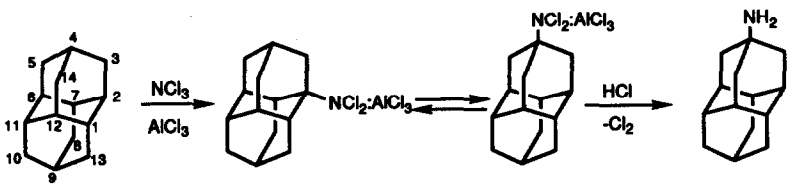
Diamantane's rigid skeleton may offer opportunities in the preparation of new types of polymers, liquid crystals, and thin films (Langmuir-Blodgett or self-assembled monolayers). Furthermore, because the tertiary C-H bonds on diamantane are unactivated and nearly equivalent, diamantane may be a good model for selective functionalization of unactivated C-H bonds, a topic of increasing interest. Diamantane was intensively studied following the development of its efficient synthesis from norbornadiene,[1] and a new procedure promises to make it even more readily available.[2] In general, the 1-substituted derivatives are kinetic products, and difficultly separable mixtures of 1- and 4- derivatives are formed under thermodynamic conditions.[3] Only one previous functionalization -- to 4-acetyldiamantane -- favored the 4-isomer.[4]

In direct aminations, diamantane is more reactive toward $NCl_3/AlCl_3$[5] than adamantane, and selective amination requires carefully controlled conditions. Many reaction conditions were investigated: solvents and concentrations (CH_2Cl_2, $CF_2ClCFCl_2$, $ClCH_2CH_2Cl$ and their combinations; 0.1-0.3 M initial diamantane concentration, 0.60 M initial NCl_3 concentration), temperature (from -30°C to 25°C), normal and inverse addition (NCl_3 vs. diamantane), and the relative quantity of catalyst (diamantane:$AlCl_3$ ratios from 5:4 to 1:4). Addition of NCl_3/CH_2Cl_2 to diamantane and $AlCl_3$ gave the greatest yields with controlled selectivity to the 1- or 4- positions. Under equilibrium conditions, the ratio of 4-:1-amino- diamantane is greater than 20:1, an extremely unusual degree of selectivity.[6,7]

Unlike adamantane, which is inert to further attack by NCl_3, under more forcing conditions and excess $NCl_3/AlCl_3$, diamantane undergoes additional substitution to form diamino and aminochloro derivatives. These compounds were always formed as a complex mixture and no attempts were made to isolate them. Their molecular formulas were assigned by high resolution GC/MS, but it was not possible to unambiguously assign isomers.

Steric factors appear to play the determining role in the selectivity to the 4-position. From models, it is unlikely that the steric requirements of NCl_2 on a diamantane intermediate would be sufficient to yield of 4-amino:1-amino ratio of >20. Therefore, it is likely that $AlCl_3$ remains complexed to the diamantane-NCl_2 intermediate and in doing so leads to the

observed thermodynamic mixture which strongly favors 4-substitution. Weak or reversible complexation of dervitiving agents may be a valuable tool for selective functionalization of hydrocarbons, a usually difficult task plagued by side reactions.

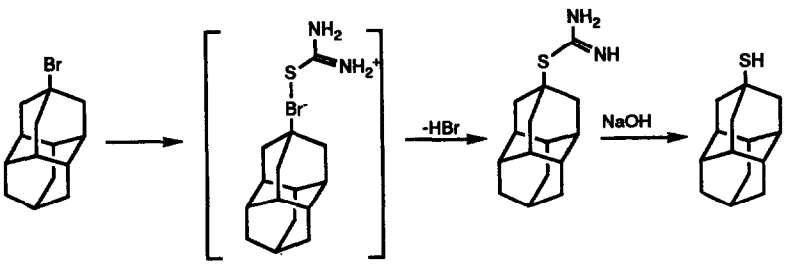


Reaction of tetrahydro-Binor-S, a diamantane precursor, with $NCl_3/AlCl_3$ yielded a complex mixture not containing 1- or 4-aminodiamantane. This observation is evidence against the rearrangement of the diamantane skeleton itself as a mechanism of 1- to 4- isomerization.

Disubstitution of the diamantane skeleton, generally by dibromination, leads to a mixture from which the 4,9 derivative can be recovered by crystallization. Conversion of the dibromide to other derivatives is a reasonable, but time-consuming procedure, and a one-step synthesis of diamino derivatives would be extremely useful. Since diamination of adamantane was unsuccessful under the conditions that led to mixtures of diamino- and aminochloro-diamantanes, it is clear that the first functionalization deactivates the skeleton toward electrophilic attack. The disubstituted diamantane products only formed under conditions under which the 1- to 4- rearrangement has been observed to occur, and therefore it is reasonable to postulate that this rearrangement, which places the functional group at one end of the molecule, facilitates reaction at the distant 9-position.

Reaction of purified 1- or 4- bromodiamantane[1,3] with thiourea at room temperature for 1 hour gave the corresponding isothiouronium salts which were directly hydrolyzed with NaOH to the respective low odor thiols.[8,9]

The mechanism of the reaction between diamantane bromides and thiourea is somewhat problematic. An S_N2 displacement with inversion is clearly impossible, and the absence of isomerized products (e.g., 4-Br to 1-SH) argues against the presence of free diamantane cations. Nucleophilic attack by sulfur on bromine, followed by ligand-ligand coupling and loss of bromide, is consistent with the observations.



In conclusion, direct mono-amination of diamantane with $NCl_3/AlCl_3$ can be controlled to give high selectivity to either 1- or 4-aminodiamantane, but diamination does not occur cleanly with this reagent under more forcing conditions. The corresponding 1- and 4-diamantanethiols may be prepared by from thiourea and the corresponding bromides in two steps.

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(6) **4-Aminodiamantane**. Diamantane, 0.47 g (2.5 mmol) was dissolved in 25 mL of dry 1,2-dichloroethane at 25°C and the solution was cooled to -10°C. Aluminum trichloride, 0.365 g (2.75 mmol) was added, slow nitrogen purging was started, and the solution was further cooled to -25°C. A solution of NCl_3 (4.61 mL of a 0.60 M CH_2Cl_2 solution, 2.75 mmol) was added via syringe pump over 1 h at -25°C, the mixture was allowed to warm to -10°C over 30 m, and stirred at this temperature for 1 h. The reaction is quenched by the rapid addition of 20 mL of cold 18% HCl under vigorous N_2 purging to remove the Cl_2 that is generated. The resulting aqueous layer was collected, washed once each with 15 mL CH_2Cl_2 and ether, made basic (pH 9) with 50% NaOH, extracted 3 times with 20 mL CH_2Cl_2, and dried over Na_2SO_4. Solvent evaporation yielded 0.22 g (37% yield) of a white, slightly air sensitive solid which was 84% pure by GC analysis (retention time 5.59 min on 10 m DB-1 capillary column at 150°C). Further attempts at purification failed; a major contaminant (11%, retention time 11.45 min) was determined to be an aminochlorodiamantane by high resolution GC/MS. The structure of this compound was unambiguously assigned by comparison of its ^{13}C spectrum with that of 4-diamantanol. ^{13}C NMR ($CDCl_3$) δ 36.43 ($C_{1,7,11}$), 39.05 ($C_{2,6,12}$), 46.71 ($C_{3,5,14}$), 45.91 (C_4), 37.42 ($C_{8,10,13}$), 25.68 (C_9); ^1H NMR ($CDCl_3$) δ 1.54-2.14 (m); mass spectrum m/z (rel

intensity) 204 (7), 203 ($M^{+\cdot}$, 52), 187 (10), 107 (5), 106 (100); high resolution mass spectrum, found 203.1750, calc. for $C_{14}H_{21}N$ 203.1674.

(7) **1-Aminodiamantane.** This product is the principle product (up to a ratio of 1-amino:4-amino = 7:1) in reactions run with a diamantane:$AlCl_3$ ratio of 5:4. This known compound can also be prepared in 3 steps from diamantane[1] and was identified by GC/MS: retention time 5.77 min; mass spectrum m/z (rel intensity) 203 ($M^{+\cdot}$, 28), 187 (24), 186 (100), 130 (51), 129 (39), 106 (13), 95 (39), 94 (68); high resolution mass spectrum, found 203.1687, calc. for $C_{14}H_{21}N$ 203.1674.

(8) **1-Diamantanethiol.** S-(1-diamantyl)isothiuronium bromide was prepared by a modification of the methods used for the synthesis of 1-adamantane-thiol.[10,11] A mixture of 1-bromodiamantane 1.336g (5 mmol), thiourea 0.76 g (10 mmol), and 2.5 mL of 48% HBr was stirred at 25°C in 5 mL of acetic acid for 20 hours, refrigerated and the resulting acetone-insoluble crystals (isothiuronium bromide) were stirred with 5 mL of 5% aqueous NaOH for 64 h at 25°C. The resulting mixture was acidified to pH 2 with conc HCl, extracted 3 times with 25 mL CH_2Cl_2, and dried over K_2CO_3. Solvent removal under vacuum yielded a white, slightly odorous crystal, 0.86 g (78%), m.p. 225-228°C. ^{13}C NMR ($CDCl_3$) δ 51.26 (C_1), 39.35 ($C_{2,12}$), 34.02 ($C_{3,14}$), 25.56 (C_4), 38.43 (C_5), 36.50 (C_6), 44.46 ($C_{7,11}$), 37.77 ($C_{8,10}$), 29.40 (C_9), 50.07 (C_{13}); ^1H NMR ($CDCl_3$) 1.2-2.5 (m); GC, retention time 8.93 min; mass spectrum, m/z (rel intensity) 220 (3, $M^{+\cdot}$), 188 (17), 187 (100, $M^{+\cdot}$), 145 (9), 131 (12), 105 (14), 95 (6), 91 (8); high resolution mass spectrum, obs. 220.1355, calc. for $C_{14}H_{20}S$ 220.1286.

(9) **4-Diamantanethiol.** This compound was prepared from 1.336 g (5 mmol) of 4-bromodiamantane by the same method to yield 0.73 g (66%) of a more odorous white crystal identified as 4-diamantanethiol, which was free of detectable 1-diamantanethiol by GC (retention time 8.38 min), m.p. 62-63°C. ^{13}C NMR ($CDCl_3$) δ 35.98 ($C_{1,7,11}$), 39.33 ($C_{2,6,12}$), 37.41 ($C_{8,10,13}$), 48.26 ($C_{3,5,14}$), 25.52 (C_9), 41.71 (C_4); ^1H NMR ($CDCl_3$) δ 1.62-1.88 (m); mass spectrum, m/z (rel intensity) 220 (4, $M^{+\cdot}$), 188 (16), 187 (100, $M^{+\cdot}$-SH), 159 (7), 145 (8), 151 (13), 105 (9); high resolution mass spectrum, obs. 220.1351, calc. for $C_{14}H_{20}S$ 220.1286.

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