DOI: 10.1002/adsc.200800787

Selective Preparation of Diamondoid Fluorides[1]

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Received: December 18, 2008; Published online: April 7, 2009

Dedicated to Armin de Meijere on the occasion of his 70th birthday.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.200800787.

Abstract: The selective fluorination of diamantane, triamantane, [121]tetramantane, and [1(2,3)4]-pentamantane bromides and alcohols was achieved by using the fluorinating agents silver fluoride (AgF) and diethylaminosulfur trifluoride (DAST). Various mono-, di-, tri- and even tetrafluorinated diamondoid derivatives were prepared and characterized. We were also able to prepare the amino fluoro and the fluoro alcohol derivatives of diamantane from the corresponding monoprotected diamondoid diols. These reactions can be carried out in a highly selective manner and proceed without isomerizations. The fluorinated, unequally disubstituted derivatives are valuable compounds for the exploration of electronic, pharmacological, and material properties of functionalized diamondoids.

Keywords: alkanes; cage compounds; diamondoids; fluorination; nanodiamonds

Introduction

Very recently the class of hydrocarbon cage compounds, the so-called diamondoids, has received renewed attention not only by organic chemists.[2] These nanometer-sized diamond-like molecules (nanodiamonds) resemble parts of the hydrogen-terminated diamond lattice (Figure 1) with the well-known adamantane (**1**) as their parent. While **1**[3] and diamantane (**2**)[4] (which are together with triamantane (**3**) called the lower diamondoids) were isolated from petroleum more than forty years ago, no diamondoids larger than [121]tetramantane[5] (**4**) could be prepared synthetically.[2] These so-called higher diamondoids remained a virtually unknown class of materials. The revival of diamondoids began in 2003 when Dahl et al. isolated and identified 21 different higher polymantanes *via* HPLC/MS techniques from petroleum.[6] Dahl et al. showed that higher diamondoids possess a variety of shapes (e.g., stick, pyramidal or disc-shaped[7]), and that some of them are even chiral [e.g., (*M*)-[123]tetramantane (**4a**), Figure 1]. With

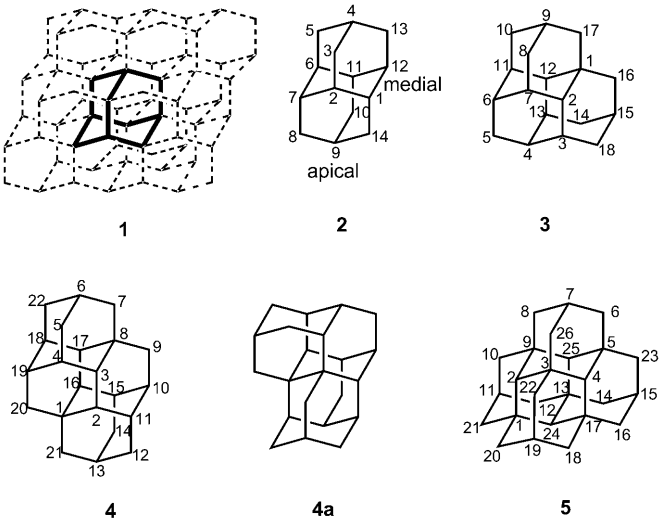


Figure 1. Diamondoids as part of the hydrogen-terminated diamond lattice: adamantane (**1**), diamantane (**2**), triamantane (**3**), [121]tetramantane (**4**), (*M*)-[123]tetramantane (**4a**), and [1(2,3)4]pentamantane (**5**).

these new compounds it was possible to show that derivatives (halides, alcohols, thiols, amines, etc.) can be prepared very selectively up to [1(2,3)4]pentamantane (**5**), the simplest centrosymmetric hydrocarbon with the (111) face of diamond, and [12312]hexamantane.[8–12] Diamondoids share some unique properties with hydrogen-terminated diamond such as a negative electron affinity (NEA) that was recently shown to exist for self-assembled-monolayers (SAMs) of thiol-diamondoids upon high-energy irradiation.[13] They are also used as sterically demanding ligands in N-heterocyclic carbene reactions.[14]

Recently we were able to demonstrate that the synthesis of unequally disubstituted diamantane derivatives, like amino alcohols and amino acids, is possible through the monoprotection of the corresponding diols by using fluorinated alcohols as solvent and reagent under acidic conditions.[15] This novel and currently only possibility of selectively preparing these unequally disubstituted derivatives encouraged us to synthesize difunctionalized diamondoids that also include fluorine substituents. Since it is known that the introduction of fluorine atoms into molecules can enhance or modify their properties or biological activities[16] we were particularly interested in the preparation of fluorinated unequally disubstituted polymantanes. These new compounds would make the use of diamondoids even more attractive (e.g., to tune the NEA effect,[13] for pharmacologically interesting diamondoid compounds[17,18] or as tags for structure determinations in highly symmetrical higher diamondoids).

While there are numerous fluorinated adamantane derivatives known in the literature only a few other fluorinated diamondoids have been synthesized and studied to date. Diamantane[19] (**2**) and triamantane[20] (**3**) were perfluorinated using elemental fluorine, while the selective mono- and difluorination has only been achieved for **2** by Olah and co-workers using either a nitronium tetrafluoroborate/pyridine polyhydrogen fluoride (PPHF) or a $NaNO_3$/PPHF mixture for diamantane bromides, chlorides, and **2** or pure PPHF for the conversion of alcohols.[21] Olah et al. also attempted to prepare 1,4,9-trifluorodiamantane (**13a**) by using the nitronium tetrafluoroborate/PPHF mixture but instead obtained the 1,4,7,9-tetrafluorodiamantane in 72% yield after 10 days reaction time.[22] Even though these reactions gave the corresponding diamantane fluorides in high yield, proper precautions must be taken when handling PPHF; additionally special laboratory equipment is required. Besides these fluorination methods, there are several other literature procedures for the preparation of fluorinated adamantanes. For example, the fluorination of **1** and its derivatives can be carried out directly using CF_3OF,[23] elemental fluorine,[24,25] $CsSO_4F$,[26] XeF_2,[27] chlorine trifluoride,[28] electrochemically,[29] iodine pentafluoride,[30] oxygen difluoride[31] or by the fluorinating agent Selectfluor™ (**6**) (Figure 2).[25] Other possibilities are the halogen exchange reaction using AgF[32] or the use of commercially available fluorinating agents for alcohols like DAST (**7**) (diethylaminosulfur trifluoride) or Deoxofluor (**8**) [bis(2-methoxyethyl)aminosulfur trifluoride].[18,33]

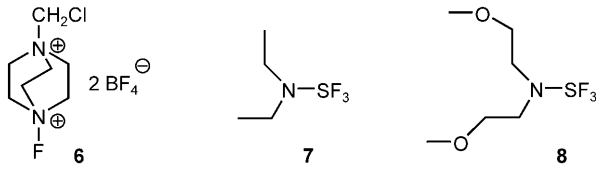


Figure 2. Examples of commercial available fluorinating agents: Selectfluor™ (**6**), DAST (**7**), and Deoxofluor (**8**).

Results and Discussion

Although there is a wide variety of fluorination methods for **1** (and **2)** we first utilized pure PPHF for the conversion of triamantan-9-ol (**18b**) which resulted in the corresponding fluoride **18a** in 47% yield. Even though this reaction is usable for the preparation of fluorides it requires a large excess of reagent, special equipment, and caution. While Olah et al. used the PPHF reagent in different variants to prepare **9a**, **10a**, **11a**, **12a**, 3-fluorodiamantane, and 1,4,7,9-tetrafluorodiamantane (*vide supra*), we decided to use the halogen exchange reaction with AgF for bromides and to work with DAST for the diamondoid alcohols. These two fluorinating reagents can be handled well in glassware and are commercially available.

As we showed earlier with our experimental and theoretical results[8,9] the bromination of **2** and other diamondoids mostly leads to medially substituted derivatives. For the preparation of mono- and bisapical bromides the use of Lewis acids is required and results in rearranged mixtures with low yields.[34] Therefore we developed a method to prepare the valuable mono- and bisapical alcohols from the corresponding diamondoids in high yields by using 100% nitric acid.[12] With these bromide and alcohol precursors we were able to prepare the corresponding diamantane fluorides **9a**–**12a** in high yields by using DAST and AgF (Table 1). The results from Table 1 show that both fluorinating reagents work very well and produce the desired fluorides without isomerizations; that is, both bromides and alcohols may be used as starting materials. We were also able to provide structural proof for all four derivatives by X-ray analyses (Supporting Information).

In the next step we tried to prepare the unknown 1,4,9-tri- and 1,4,6,9-tetrafluorinated derivatives of **2**.

Table 1. Yields, temperatures, times, solvents and equivalents of the fluorinating agents used for the synthesis of fluorinated diamondoids.

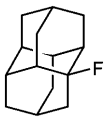
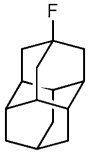
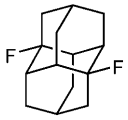
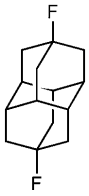
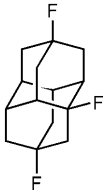
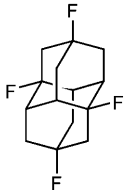
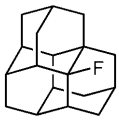
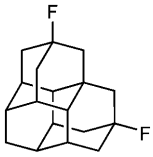
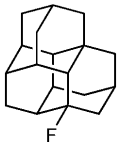
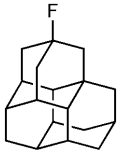
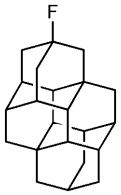
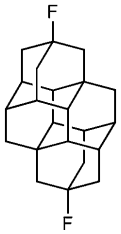
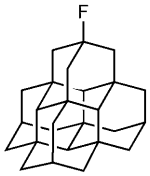
Entry	Product		Starting compound	Fluorinating agent	Equiv. of reagent	Solvent (anhydrous)	Time [h]	Temp. [°C]	Yield [%]
1		**9a**	bromide **9b**	AgF	4.3	cyclohexane	2	reflux	81
2			alcohol **9c**	DAST	1.6	CH_2Cl_2	1	0–5	90
3		**10a**	bromide **10b**	AgF	4.3	cyclohexane	2	reflux	91
4			alcohol **10c**	DAST	1.6	CH_2Cl_2	1	0–5	86
5		**11a**	dibromide **11b**	AgF	6.8	cyclohexane	2	reflux	85
6			dialcohol **11c**	DAST	3.4	CH_2Cl_2	1	0–5	94
7		**12a**	dibromide **12b**	AgF	6.8	cyclohexane	2	reflux	94
8			dialcohol **12c**	DAST	3.4	CH_2Cl_2	1	0–5	94
9		**13a**	tribromide **13b**	AgF	4.6	cyclohexane	3	reflux	86
10		**14a**	tetrabromide **14b**	AgF	8.4	cyclohexane	5.5	reflux	96
11		**15a**	bromide **15b**	AgF	1.7	cyclohexane	2	reflux	66
12		**16a**	dialcohol **16b**	DAST	4.9	CH_2Cl_2	1.5	0–5	81
13		**17a**	alcohol **17b**	DAST	3.3	CH_2Cl_2	1	0–5	95
14		**18a**	alcohol **18b**	DAST	3.4	CH_2Cl_2	1	0–5	71

Table 1. (Continued)

Entry	Product		Starting compound	Fluorinating agent	Equiv. of reagent	Solvent (anhydrous)	Time [h]	Temp. [°C]	Yield [%]
15		**19a**	alcohol **19b**	DAST	2.4	CH_2Cl_2	1	0–5	75
16		**20a**	dialcohol **20b**	DAST	5.8	CH_2Cl_2	1.5	0–5	96
17		**21a**	alcohol **21b**	DAST	6.3	CH_2Cl_2	1	0–5	65

Since it is possible to synthesize starting materials **13b** and **14b** from **2** with a bromine/$AlBr_3$ mixture[34] we used the halogen exchange reaction with AgF to prepare these novel compounds (for **14a** see X-ray structure in Figure 3). The results in Table 1 show that this fluorination method is very suitable to synthesize these derivatives in high yield but that an increasing number of substituents leads to longer reaction times (*vide infra*). The preparation of the equally tetrasubstituted derivatives of **2**[34,35] is less studied in comparison to **1**[36] and the synthesis of **14a** is interesting because it is not possible to prepare the corresponding tetraalcohol from **14b** through reaction in nitric acid (*vide infra*).[37] With these experiments we close the gap of the missing fluorinated diamantanes and turned our interest to the preparation of fluorinated higher diamondoids. Since in the case of **3** bromination reactions are only high yielding for the preparation of 2-bromotriamantane[9] (**15b**) we only prepared 2-fluorotriamantane (**15a**) from **15b**. For all other reactions of **3**, **4**, and **5** the corresponding alcohols[11,12] were used as the starting materials (Table 1). The preparation of these fluorides is also high yielding and isomerizations do not occur.

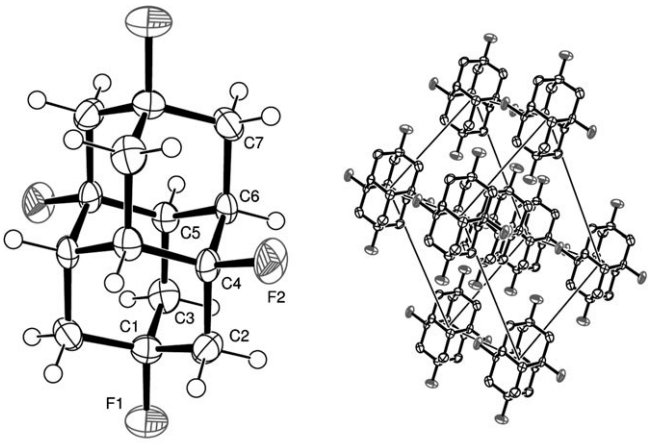
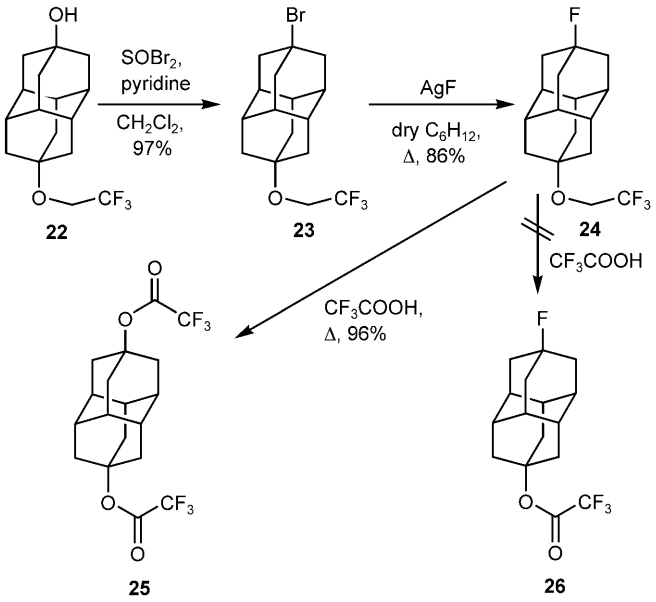


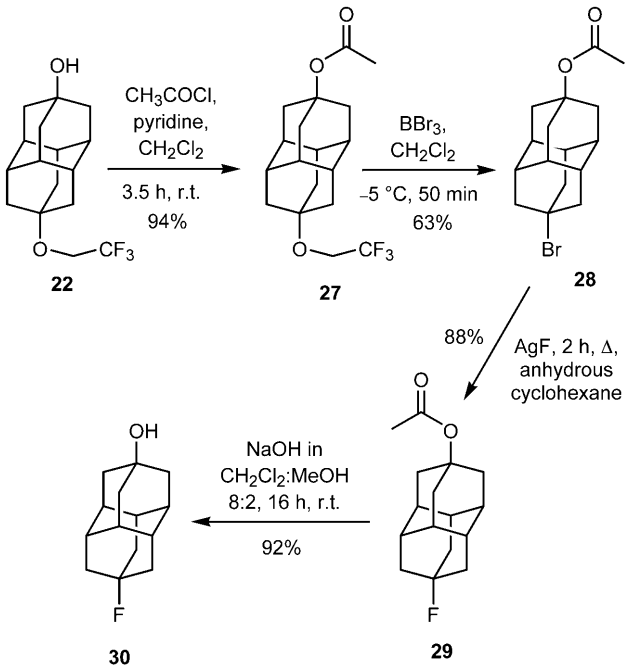
Figure 3. X-ray crystal structure and packing of tetrafluorinated diamantane **14a**. Hydrogen atoms are omitted in packing for clarity.

In the absence of fluorine decoupling the ^{13}C NMR resonance signals of the fluorinated compounds are split by multi-bond ^{19}F–^{13}C couplings (also holds for the later described unequally disubstituted fluoride derivatives). If two or more fluorine substituents replaced hydrogen atoms of the cage in compounds **11a**–**14a**, **16a**, and **20a** we observed for the signals of the fluorinated carbon atoms and the ^{13}C NMR resonance signals very complex splitting patterns due to the ^{13}C–^{19}F couplings (high order spin systems). For the correct ^{13}C NMR signal assignments it was not necessary to analyse the high order ^{13}C–^{19}F spin systems.

To emphasize the practicality of these fluorination methods we used **2** as our model compound to synthesize unequally disubstituted fluorinated diaman-



Scheme 1. Attempts to synthesize a diamantane fluoro alcohol which lead to the formation of the bis(trifluoroacetoxy) ester **25**.



Scheme 2. Synthetic pathway for the preparation of 9-fluorodiamantan-4-ol (**30**) from the fluoro monoether **22**.

tanes. In order to prepare a fluoro alcohol we used our monoprotection method starting from diamantan-4,9-diol.[15] 9-(2,2,2-Trifluoroethoxy)-diamantan-4-ol (**22**) was converted into the corresponding bromide **23** using $SOBr_2$ (Scheme 1). The halogen exchange reaction with AgF was carried out in 86% yield to give the fluoro ether **24**. At this point we used trifluoroacetic acid to convert the ether into a base-labile ester function; this reaction worked very well in our recent preparation of amino alcohols.[15] To our suprise the fluorine atom was also substituted by a trifluoroacetoxy group (Scheme 1); the cleavage of a fluorine adamantane bond is known in literature, like for the preparation of amides[38] or the brominolysis of fluoroadamantane.[39] Unfortunately other cleavage procedures (e.g., with concentrated acetic acid or diluted acetic acid even at elevated temperatures) were also not successful and the ether function was retained even though the fluorine atom was not touched. The use of 20% aqueous HCl at higher temperatures afforded only 4,9-dichlorodiamantane. All of these inefficacious results show that a strong acid is required to cleave the fluoro ether function which then unfortunately also cleaves the C–F bond. Also the use of NaI together with TMSCl gave no result. To bypass this problem we protected the remaining hydroxy group of monoether **22** with an acetoxy function to give the desired product **27** in high yield (Scheme 2).

Next we tried to cleave the ether function with BBr_3 in dichloromethane. This reaction proceeds at −5 °C and results in the formation of 4-acetoxy-9-bromodiamantane (**28**). We found that for this step the reaction temperature and time is crucial. If the excess of BBr_3 is too large or if the temperature is too high 4,9-dibromodiamantane (**12b**) forms as the only product. Even though the ether and ester (*vide infra*) cleavage can, in principle, also form the diamondoid hydroxy derivative we detected no product mixture in all experiments. Apparently the use of a strong Lewis acid like BBr_3 is needed to selectively cleave fluoro ether **27**. The halogen exchange reaction with AgF is straightforward and **29** could be hydrolyzed to the desired 9-fluorodiamantan-4-ol (**30**) by NaOH in a dichloromethane/MeOH mixture (Scheme 2). Structural proof of this compound was obtained from an X-ray measurement (Figure 4). The crystal structure of **30** shows interactions of the hydroxy hydrogens to the fluorine atom of the neighbour molecule.

In this context we envisioned to utilize the unexpected formation of compound **25** for the preparation of the unknown diamantan-1,4,6,9-tetraol (*vide supra*) by refluxing **14a** in trifluoroacetic acid. However, even after alkaline work-up we could only detect the starting material **14a**. This shows again that the reactivities of the bridgehead positions are controlled by substituents at the other bridgeheads and that the formation of **14a** (and all other fluorides from bromides) is driven by the withdrawal of the bromine with silver to form the precipitating AgBr.

After having succeeded in the preparation of the fluoro alcohol **30** we turned our interest to the synthesis of an amino fluoro derivative of **2**. We brominated our recently prepared diamantane amino alcohol **31**

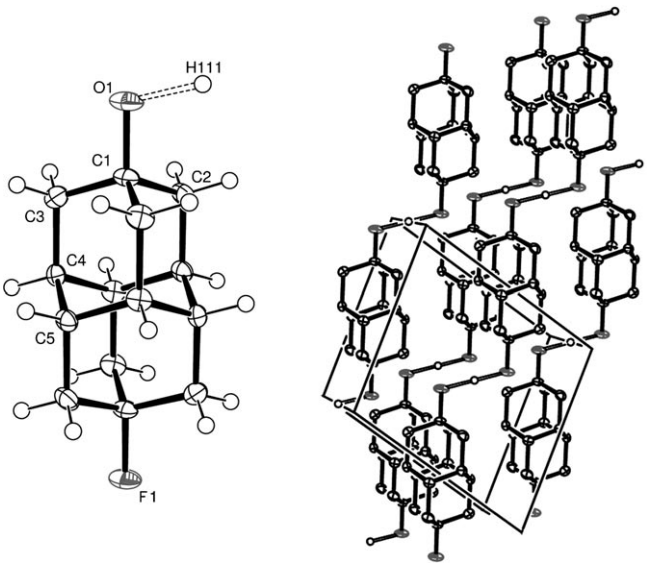
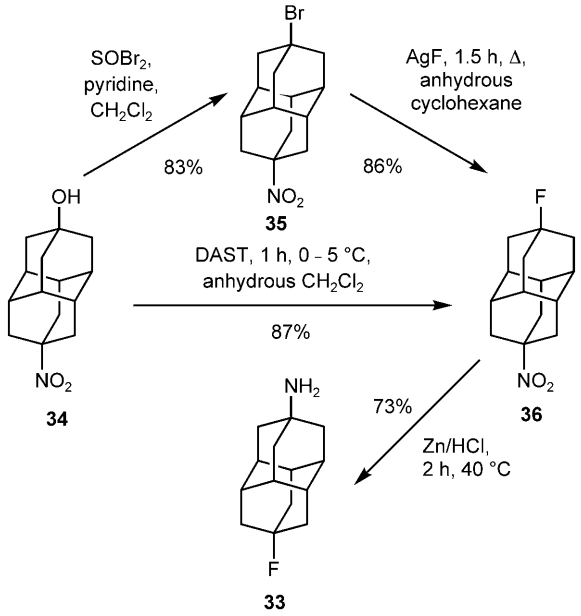


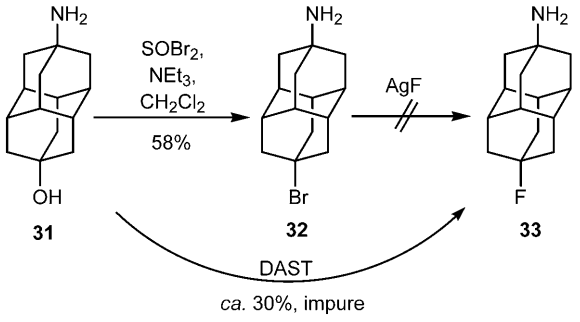
Figure 4. X-ray crystal structure and packing of 9-fluorodiamantan-4-ol (**30**) showing O–H–F interaction. C–H hydrogen atoms have been removed from packing for clarity.



Scheme 4. Preparation of 4-amino-9-fluorodiamantane (**33**) by exchanging the hydroxy group of the nitro alcohol **34** with $SOBr_2$/AgF or directly with DAST and by hydrogenating the nitro group using Zn/HCl.

to study the exchange reaction with AgF and attempted the direct fluorination using DAST (Scheme 3). Unfortunately, bromine exchange with AgF afforded just the starting compound. This reaction was not unexpected due to the strong complexation of the silver ions by the amino function. The direct conversion with DAST was low yielding due to the formation of the ammonium salt of HF and some persistent impurities that could not be removed from the crude product.

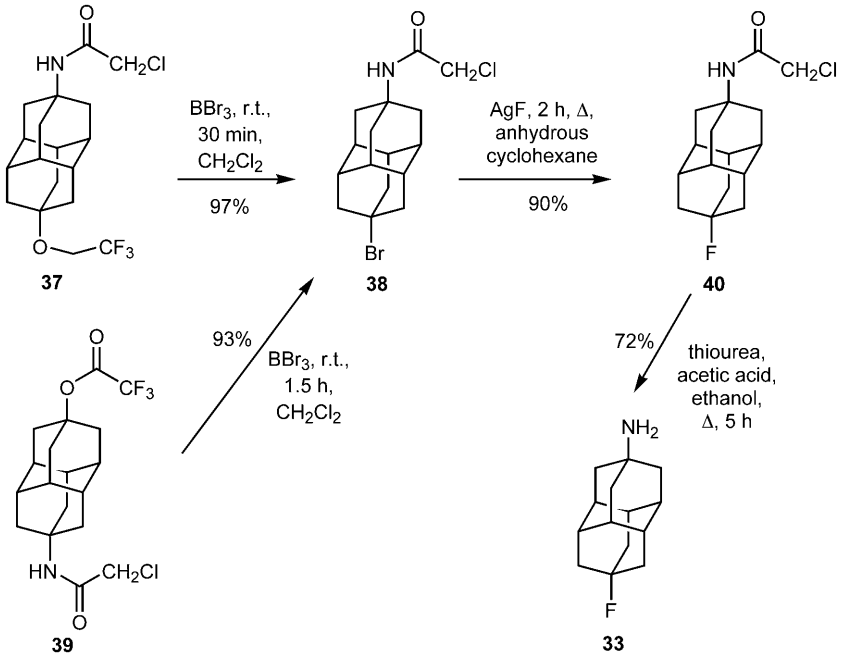
Being faced with the problem of the free amino function and with the knowledge that the introduction of this functional group is a rather difficult task we developed two different routes for the synthesis of compound **33**. Since the amino function of **31** can be oxidized by *m*-chloroperbenzoic acid (*m*-CPBA) to the corresponding nitro alcohol[15] **34** we converted the alcohol function either by bromination and treatment with AgF or by direct fluorination utilizing



Scheme 3. Attempted synthesis of diamantane amino fluoride **33** from the amino alcohol **31**.

DAST to afford 4-fluoro-9-nitrodiamantane (**36**) in high yields (Scheme 4). Next we reduced the nitro group by using a zinc/diluted HCl mixture at 40 °C and obtained the amino fluoride **33** with 73% yield (Scheme 4). In this case the reaction temperature was high enough to reduce the nitro group selectively with zinc while on the other hand it was low enough for leaving the carbon-fluorine bond untouched.

Since the synthesis of the **33** requires six steps starting from 9-(2,2,2-trifluoroethoxy)-diamantan-4-ol (**22**) we devised a route with fewer steps. Monoether **22** can be transferred *via* a Ritter-type reaction with chloroacetonitrile to 2-chloro-*N*-[9-(2,2,2-trifluoroethoxy)diamant-4-yl]acetamide (**37**).[15] By analogy to the synthesis of 9-fluorodiamantan-4-ol (**30**) we cleaved the trifluoroethoxy ether with BBr_3 in dichloromethane. Thereby we were able to isolate 2-chloro-*N*-[9-(bromo)diamantan-4-yl]acetamide (**38**) in 97% yield (Scheme 5). We also found that BBr_3 is not only capable of cleaving the fluorinated ether but that it can also cleave the ester of 9-(2-chloro-acetylamino)-diamantan-4-yl trifluoroacetic acid ester (**39**) in high yield (93%). Both reactions can be carried out at room temperature while the acetamide is not cleaved by BBr_3. The presence of different substituents at the cage did not seem to affect the course of the ether and ester cleavage since in all cases only the brominated derivatives were obtained. Brominated chloroacetamide **38** was then converted into fluorine derivative **40** with AgF. From our results of cleaving the ether function we knew that acetic acid is not strong



Scheme 5. 4-Amino-9-fluorodiamantane (**33**) synthesized through cleavage of the ether function of chloroacetamides **37** and **39** with BBr_3 and by cleaving the acetamide with thiourea in EtOH/acetic acid.

enough to cleave the C–F bond even at elevated temperatures. Therefore we could use our adaption[15] of the protocol of Jirgensons et al.[40] by converting the chloroacetamide into an amine by refluxing **40** with thiourea, acetic acid and ethanol. After work-up the crude product was purified *via* its hydrochloride salt to give the pure fluoro amine **33** with 72% yield (Scheme 5). This reaction shows that the cleavage of chloroacetamides is not only applicable for the preparation of amino alcohols[15] but also tolerates the fluorine atom even at elevated temperatures. With the second method we were able to reduce the number of steps from six to four and to increase the overall yield.

Conclusions

We utilized two different fluorination reactions (halogen exchange reaction with AgF and conversion of alcohols using DAST) for the preparation of fluorinated diamondoids. Thereby we could complete the series of fluorinated diamantane derivatives with the novel tri- and tetrafluorinated compounds **13a** and **14a**. We also extended these reactions to triamantane (**3**), [121]tetramantane (**4**), and [1(2,3)4]pentamantane (**5**). By using diamantane (**2**) as a model, we showed that the previously reported monoprotected diols can be selectively converted into unequally disubstituted derivatives such as the fluoro alcohol **30**. We were also able to prepare the amino fluoro diamantane derivative **33** by using two different synthetic pathways. No isomerizations were observed in these reactions. Further investigations of these new compounds will explore their biological behaviour (e.g., the influence of the fluorine substituent on certain properties like binding interactions, changes in reactivity or metabolic stability in comparison to the non-fluorinated compounds) and their use in material science applications (e.g., tuning of the NEA effect).

Experimental Section

General Remarks

All ^{1}H NMR spectra were recorded at 600 and 400 MHz, respectively, using Bruker AV 600 and AV 400 spectrometers. ^{13}C NMR spectra were taken at 150 and 100 MHz using the same instruments. The ^{19}F NMR spectra were measured on the AV 400 at 376 MHz. Chemical shifts are reported in ppm (δ scale) using TMS as internal standard or the solvent signal as secondary standard. For the ^{19}F NMR spectra $CFCl_3$ in $CDCl_3$ was used as internal standard. Structural assignments were made by 2D NMR spectra (COSY, HSQC, HMBC, TOCSY, HOESY). IR spectra were recorded as KBr pellets using a Bruker IFS 25. Melting points are not corrected and were measured with Büchi Dr. Tottoli Typ S or with the melting point meter KSP I N from Krüss. Elemental analyses were carried out using a Thermo Electron Flash EA 1112 Series. HR-MS were recorded using a Finnigan MAT 95 with the electron impact method (EI). HPLC purifications were performed using an HPLC Pump 64 by Knauer (detectors: RI by Knauer "Differential Refraktometer" and UV by LKB 2151 at 220 nm wavelength) using a RP-18 phase column. The X-ray crystallographic data were

collected on a STOE IPDS diffractometer equipped with a low temperature system (Karlsruher Glastechnisches Werk) and Mo-K_α radiation. All non-diamondoid chemicals were commercial and used as received. Cyclohexane, dichloromethane, and diethyl ether were dried according to standard procedures.[41] All reactions were carried out without an inert gas atmosphere. The brominated compounds **9b**, **10b**, **11b**, **12b**, **13b**, and **14b** were prepared by the procedure of Gund et al.[34] Also the compounds **9c**, **10c**, **11c**, **12c**, **13c**, **16a**, **17a**, **18a**, **19a**, **20a**, **21a**, **22**, **31**, **34**, **37**, and **39** were prepared using literature procedures.[11,12,15,37,42]

Procedures for the Preparation of Fluorinated Diamondoids 9a–21a

All of the following derivatives were prepared either by using AgF and/or DAST.

1-Fluorodiamantane (9a)

Using AgF: A brown suspension of **9b** (100 mg, 0.37 mmol) and AgF (200 mg, 1.58 mmol) in dry cyclohexane (6 mL) was refluxed for 2 h. After evaporation of the solvent the crude product was purified by column chromatography on silica gel (CH_2Cl_2, R_f: 0.69) to furnish the pure, colourless product **9a**; yield: 62.9 mg (81%).

Using DAST: **9c** (100 mg, 0.49 mmol) in dry dichloromethane (20 mL) was cooled in an ice bath at 0–5 °C. After the addition of DAST (0.1 mL, 0.76 mmol) the yellow solution was stirred for 1 h at the same temperature and then quenched with saturated $NaHCO_3$ solution (50 mL) and dichloromethane (20 mL) was added. After separation the aqueous solution was extracted twice with dichloromethane (40 mL each). The combined organic phases were washed with distilled water (40 mL) and dried over anhydrous Na_2SO_4. The obtained crude product was purified using column chromatography on flash silica gel (pentane, R_f: 0.22) to furnish pure **9a**; yield: 91 mg (90%); mp 255–258 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 2.20$–2.10 (m, 3H, H-3,9,13), 2.03 (br s, 2H, H-7,11), 1.89 (br s, 2H, H-2,12), 1.82–1.73 (m, 3H, H-4,14), 1.70–1.54 (m, 7H, H-5,6,8,10), 1.52–1.44 (m, 2H, H-3,13); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 94.9$ [C, $^1J(^{13}C,^{19}F) = 187.1$ Hz, C-1], 43.2 [CH_2, $^2J(^{13}C,^{19}F) = 18.1$ Hz, C-14], 41.8 [CH, $^2J(^{13}C,^{19}F) = 17.1$ Hz, C-2,12], 40.7 [CH, $^3J(^{13}C,^{19}F) = 8.1$ Hz, C-7,11], 37.6 (CH_2, C-5), 37.0 [CH_2, $^4J(^{13}C,^{19}F) = 2.0$ Hz, C-8,10], 36.4 [CH, $^4J(^{13}C,^{19}F) = 1.0$ Hz, C-6], 32.5 (CH_2, C-3,13), 30.9 [CH, $^3J(^{13}C,^{19}F) = 10.1$ Hz, C-9], 24.9 (CH, C-4); ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): $\delta = -141.86$; IR (KBr): $\nu = 2922$, 2884, 2849, 1459, 1440, 1385, 1341, 1096, 1017, 921, 861, 756, 534 cm^{-1}; HR-MS: $m/z = 206.1462$, calcd. for $C_{14}H_{19}F$: 206.1471; anal. calcd. for $C_{14}H_{19}F$ (206.30): C 81.51, H 9.28; found: C 81.48, H 9.48.

4-Fluorodiamantane (10a)

Using AgF: **10b** (100 mg, 0.37 mmol) was refluxed with AgF (200 mg, 1.58 mmol) in dry cyclohexane (6 mL) for 2 h. Purification by column chromatography on silica gel (CH_2Cl_2, R_f: 0.70 and pentane:CH_2Cl_2 6:4, R_f: 0.53) afforded pure **10a**; yield: 70 mg (91%).

Using DAST: **10c** (100 mg, 0.49 mmol) was stirred with DAST (0.1 mL, 0.76 mmol) for 1.5 h in dry CH_2Cl_2 (20 mL) at 0–5 °C. Purification by column chromatography on silica gel (diethyl ether:pentane 1:1, R_f: 0.64 and CH_2Cl_2:pentane 1:1, R_f: 0.58) gave pure **10a**; yield: 87.1 mg (86%); mp 223–226 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 2.02$ (br s, 3H, H-2,6,12), 1.89–1.84 (m, 6H, H-3,5,13), 1.80 (br s, 1H, H-9), 1.77–1.72 (m, 9H, H-1,7,8,10,11,14); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 92.5$ [C, $^1J(^{13}C,^{19}F) = 182.1$ Hz, C-4], 42.9 [CH_2, $^2J(^{13}C,^{19}F) = 17.1$ Hz, C-3,5,13], 40.4 [CH, $^3J(^{13}C,^{19}F) = 11.1$ Hz, C-2,6,12], 36.9 [CH_2, $^5J(^{13}C,^{19}F) = 2.0$ Hz, C-8,10,14], 36.2 [CH, $^4J(^{13}C,^{19}F) = 2.0$ Hz, C-1,7,11], 25.5 (CH, C-9); ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): $\delta = -139.49$; IR (KBr): $\nu = 2924$, 2908, 2849, 1459, 1437, 1342, 1329, 1248, 1089, 1020, 911, 611 cm^{-1}; HR-MS: $m/z = 206.1463$, calcd. for $C_{14}H_{19}F$: 206.1471; anal. calcd. for $C_{14}H_{19}F$ (206.30): C 81.51, H 9.28; found: C 81.28, H 9.44.

1,6-Difluorodiamantane (11a)

Using AgF: **11b** (100 mg, 0.29 mmol) was refluxed for 2 h with AgF (250 mg, 1.97 mmol) in dry cyclohexane (6 mL). Purification by column chromatography on silica gel (CH_2Cl_2, R_f: 0.69) resulted in pure **11a**; yield: 55.3 mg (85%).

Using DAST: **11c** (100 mg, 0.45 mmol) was stirred for 1 h with DAST (0.2 mL, 1.52 mmol) in dry CH_2Cl_2 (20 mL) at 0–5 °C. Purification by column chromatography on silica flash gel (pentane:CH_2Cl_2 8:2, R_f: 0.26) afforded pure **11a**; yield: 96.1 mg (94%); mp 280–283 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 2.17$ (br s, 2H, H-4,9), 2.14–2.03 (m, 8H, H-2,3,7,8,10,11,12,13), 1.85–1.80 (m, 4H, H-5,14), 1.50–1.41 (m, 4H, H-3,8,10,13); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 93.6$ [C, $^1J(^{13}C,^{19}F) = 188.2$ Hz, C-1,6], 43.9 (CH, higher spin system, C-2,7,11,12), 42.5 (CH_2, higher spin system, C-5,14), 31.4 (CH_2, C-3,8,10,13), 29.8 [CH, $^3J(^{13}C,^{19}F) = 10.1$ Hz, C-4,9]; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): $\delta = -149.49$; IR (KBr): $\nu = 2945$, 2935, 2925, 2915, 1467, 1439, 1388, 1341, 1102, 1011, 965, 887, 595 cm^{-1}; HR-MS: $m/z = 224.1378$, calcd. for $C_{14}H_{18}F_2$: 224.1377; anal. calcd. for $C_{14}H_{18}F_2$ (224.29): C 74.97, H 8.09; found: C 74.68, H 8.09.

4,9-Difluorodiamantane (12a)

Using AgF: **12b** (100 mg, 0.29 mmol) was refluxed with AgF (250 mg, 1.97 mmol) for 2 h in dry cyclohexane (6 mL). Purification by column chromatography on silica gel (CH_2Cl_2, R_f: 0.58) afforded pure **12a**; yield: 60.8 mg (94%).

Using DAST: **11c** (100 mg, 0.45 mmol) was stirred with DAST (0.2 mL, 1.52 mmol) for 1 h at 0–5 °C in dry CH_2Cl_2 (20 mL). Purification by column chromatography on flash silica gel (pentane:CH_2Cl_2 8:2, R_f: 0.16) resulted in pure **12a**; yield: 96.1 mg (94%); mp 288–292 °C (sublimes); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 2.05$ (br s, 6H, H-1,2,6,7,11,12), 1.96–1.90 (m, 12H, H-3,5,8,10,13,14); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 91.5$ [C, $^1J(^{13}C,^{19}F) = 184.1$ Hz, C-4,9], 41.6 (CH_2, higher spin system, C-3,5,8,10,13,14), 39.1 (CH, higher spin system, C-1,2,6,7,11,12); ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): $\delta = -141.07$; IR (KBr): $\nu = 2939$, 2922, 2888, 2864, 1443, 1340, 1251, 1084, 1011, 950, 539 cm^{-1}; HR-MS: $m/z = 224.1381$, calcd. for $C_{14}H_{18}F_2$: 224.1377; anal. calcd. for $C_{14}H_{18}F_2$ (224.29): C 74.97, H 8.09; found: C 74.93, H 8.24.

1,4,9-Trifluorodiamantane (13a)

13b (100 mg, 0.24 mmol) was refluxed with AgF (140 mg, 1.10 mmol) for 3 h in dry cyclohexane (6 mL). Purification by column chromatography on silica gel (CH_2Cl_2, R_f: 0.61) gave pure **13a**; yield: 48.9 mg (86%); mp 266 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.37–2.28 (m, 2H, H-3,13), 2.23 (br s, 2H, H-7,11), 2.17 (br s, 2H, H-2,12), 2.13–2.08 (m, 2H, H-14), 1.98–1.86 (m, 7H, H-5,6,8,10), 1.79–1.71 (m, 2H, H-3,13); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 92.8 [C, $^1J(^{13}C,^{19}F)$ = 192.3 Hz, $^3J(^{13}C,^{19}F)$ = 13.5 Hz, $^4J(^{13}C,^{19}F)$ = 2.0 Hz, C-1], 92.5 [C, $^1J(^{13}C,^{19}F)$ = 187.4 Hz, $^3J(^{13}C,^{19}F)$ = 12.8 Hz, C-9], 90.3 [C, $^1J(^{13}C,^{19}F)$ = 184.1 Hz, C-4], 46.8 [CH_2, $^2J(^{13}C,^{19}F)$ = 19.5 Hz, $^5J(^{13}C,^{19}F)$ = 2.2 Hz, C-14], 43.7 (CH, higher spin system, C-2,12), 41.1 [CH_2, $^2J(^{13}C,^{19}F)$ = 18.8 Hz, $^5J(^{13}C,^{19}F)$ = 1.8 Hz, C-5], 40.7 (CH_2, higher spin system, C-8,10), 39.5 (CH, higher spin system, C-7,11), 37.9 [CH, $^3J(^{13}C,^{19}F)$ = 10.8 Hz, C-6], 36.5 [CH_2, $^2J(^{13}C,^{19}F)$ = 19.6 Hz, C-3,13]; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ = −143.69 [$^7J(^{19}F,^{19}F)$ = 2.7 Hz, F-4], −143.10 [$^4J(^{19}F,^{19}F)$ = 12.3 Hz, F-1], −139.90 [$^4J(^{19}F,^{19}F)$ = 12.3 Hz, $^7J(^{19}F,^{19}F)$ = 2.7 Hz, F-9]; IR (KBr): ν = 2950, 2896, 2873, 1454, 1349, 1164, 1121, 1090, 1021, 987, 932, 540 cm^{-1}; HR-MS: m/z = 242.1290, calcd. for $C_{14}H_{17}F_3$: 242.1282; anal. calcd. for $C_{14}H_{17}F_3$ (242.28): C 69.40, H 7.07; found: C 69.41, H 7.11.

1,4,6,9-Tetrafluorodiamantane (14a)

14b (140 mg, 0.28 mmol) was refluxed with AgF (300 mg, 2.36 mmol) for 5.5 h in dry cyclohexane (6 mL). Purification by column chromatography on silica gel (CH_2Cl_2, R_f: 0.60) afforded pure **14a**; yield: 69.5 mg (96%); mp 268 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.37–2.28 (m, 4H, H-3,8,10,13), 2.27–2.20 (m, 4H, H-2,7,11,12), 2.19–2.11 (m, 4H, H-5,14), 1.79–1.70 (m, 4H, H-3,8,10,13); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 91.6 [C, $^1J(^{13}C,^{19}F)$ = 194.1 Hz, $^3J(^{13}C,^{19}F)$ = 13.7 Hz, $^4J(^{13}C,^{19}F)$ = 2.1 Hz, C-1,6], 91.3 [C, $^1J(^{13}C,^{19}F)$ = 188.3 Hz, $^3J(^{13}C,^{19}F)$ = 12.7 Hz, C-4,9], 46.3 [CH_2, $^2J(^{13}C,^{19}F)$ = 20.3 Hz, C-5,14], 43.0 (CH, higher spin system, C-2,7,11,12), 35.8 [CH_2, $^2J(^{13}C,^{19}F)$ = 21.1 Hz, C-3,8,10,13]; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ = −150.12 [$^4J(^{19}F,^{19}F)$ = 11.3 Hz, F-1,6], −142.03 [$^4J(^{19}F,^{19}F)$ = 11.3 Hz, F-4,9]; IR (KBr): ν = 2965, 2950, 2878, 1448, 1390, 1344, 1286, 1164, 1117, 1028, 1008, 982, 896, 624, 540 cm^{-1}; HR-MS: m/z = 260.1185, calcd. for $C_{14}H_{16}F_4$: 260.1188; anal. calcd. for $C_{14}H_{16}F_4$ (260.27): C 64.61, H 6.20; found: C 64.36, H 6.08.

2-Fluorotriamantane (15a)

15b (100 mg, 0.31 mmol) was refluxed for 2 h with AgF (65 mg, 0.51 mmol) in dry cyclohexane (6 mL). Purification by column chromatography on silica gel (pentane:CH_2Cl_2 95:5, R_f: 0.44) resulted in pure **15a**; yield: 53.5 mg (66%); mp 240–247 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 2.17–2.11 (m, 2H, H-8,18), 1.99–1.94 (m, 2H, H-4,6), 1.85–1.50 (m, 17H, H-3,5,7,9,10,11,12,13,14,15,16,17), 1.49–1.44 (m, 2H, H-8,18), 1.07–1.02 (m, 2H, H-16,17); ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C): δ = 97.5 [C, $^1J(^{13}C,^{19}F)$ = 190.2 Hz, C-2], 50.4 [CH, $^3J(^{13}C,^{19}F)$ = 6.0 Hz, C-12], 42.2 [CH, $^2J(^{13}C,^{19}F)$ = 18.1 Hz, C-3,7], 40.3 [CH, $^3J(^{13}C,^{19}F)$ = 7.6 Hz, C-4,6], 39.4 (CH_2, C-16,17), 37.63 (CH_2, C-10,14), 37.56 (CH_2, C-5), 37.52 (CH, C-11,13), 37.4 [C, $^2J(^{13}C,^{19}F)$ = 18.1 Hz, C-1], 32.4 (CH_2, C-8,18), 27.0 (CH, C-9,15); ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ = −158.33; IR (KBr): ν = 2913, 2882, 2848, 1458, 1442, 1339, 1310, 1049, 1038, 1021, 915, 770, 536 cm^{-1}; HR-MS: m/z = 258.1772, calcd. for $C_{18}H_{23}F$: 258.1784; anal. calcd. for $C_{18}H_{23}F$ (258.37): C 83.67, H 8.97; found: C 83.69, H 9.06.

9,15-Difluorotriamantane (16a)

16b (85 mg, 0.31 mmol) was stirred for 1.5 h with DAST (0.2 mL, 1.52 mmol) in dry CH_2Cl_2 (20 mL) at 0–5 °C. Purification by column chromatography on silica gel (CH_2Cl_2, R_f: 0.63) and washing with 4 mL of pentane afforded pure **16a**; yield: 69.4 mg (81%); mp 254–255 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.09–2.00 (m, 4H, H-3,7,11,13), 1.95–1.79 (m, 8H, H-8,10,14,18), 1.77–1.73 (m, 2H, H-5), 1.70–1.65 (m, 2H, H-4,6), 1.62–1.57 (m, 4H, H-16,17), 1.45 (br s, 2H, H-2,12); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ = 92.0 [C, higher spin system, $^1J(^{13}C,^{19}F)$ = 184.1 Hz, $^5J(^{13}C,^{19}F)$ = 1.6 Hz, C-9,15], 49.0 [CH_2, $^2J(^{13}C,^{19}F)$ = 17.1 Hz, C-16,17], 44.2 [CH, $^4J(^{13}C,^{19}F)$ = 1.0 Hz, C-2,12], 42.5 [CH_2, $^2J(^{13}C,^{19}F)$ = 18.1 Hz, C-8,10,14,18], 40.4 [C, $^3J(^{13}C,^{19}F)$ = 11.1 Hz, C-1], 39.9 (CH, higher spin system, C-3,7,11,13), 35.9 [CH_2, $^5J(^{13}C,^{19}F)$ = 2.0 Hz, C-5], 33.4 (CH, C-4,6); ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ = −139.45; IR (KBr): ν = 2935, 2910, 2884, 2863, 1445, 1338, 1331, 1153, 1071, 1014, 986, 883, 629 cm^{-1}; HR-MS: m/z = 276.1683, calcd. for $C_{18}H_{22}F_2$: 276.1690; A sample was sublimed for analysis: calcd. for $C_{18}H_{22}F_2$ (276.36): C 78.23, H 8.02; found: C 78.27, H 8.03.

3-Fluorotriamantane (17a)

17b (90 mg, 0.35 mmol) was stirred 1 h with DAST (0.15 mL, 1.14 mmol) in dry CH_2Cl_2 (20 mL) at 0–5 °C. Purification by column chromatography on silica flash gel (pentane, R_f: 0.19) resulted pure, colourless **17a**; yield: 85.7 mg (95%); mp 232–233 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 2.18–2.08 (m, 3H, H-5,7,15), 1.94–1.89 (m, 1H, H-13), 1.88–1.78 (m, 4H, H-4,9,18), 1.78–1.70 (m, 2H, H-8,10), 1.69–1.54 (m, 7H, H-2,6,8,10,12,14), 1.45–1.39 (m, 3H, H-5,11,17), 1.35–1.30 (m, 1H, H-17), 1.28–1.19 (m, 2H, H-16); ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C) δ = 95.3 [C, $^1J(^{13}C,^{19}F)$ = 185.6 Hz, C-3], 50.5 [CH, $^2J(^{13}C,^{19}F)$ = 16.6 Hz, C-2], 45.8 (CH, C-11), 44.2 [CH_2, $^4J(^{13}C,^{19}F)$ = 2.2 Hz, C-16], 44.1 [CH_2, $^4J(^{13}C,^{19}F)$ = 2.2 Hz, C-17], 43.1 [CH_2, $^2J(^{13}C,^{19}F)$ = 18.1 Hz, C-18], 40.4 [CH, $^3J(^{13}C,^{19}F)$ = 7.6 Hz, C-13], 39.6 [CH, $^2J(^{13}C,^{19}F)$ = 18.1 Hz, C-4], 37.6 (CH_2, C-10), 37.16 (CH, C-12, from APT), 37.15 (CH_2, C-8, from APT), 37.07 [C, $^3J(^{13}C,^{19}F)$ = 7.6 Hz, C-1], 36.9 (CH_2, C-14), 34.3 (CH, C-6), 32.8 (CH_2, C-5), 32.0 (CH, C-7), 31.2 [CH, $^3J(^{13}C,^{19}F)$ = 9.1 Hz, C-15], 27.3 (CH, C-9); ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ = −145.60; IR (KBr): ν = 2908, 2875, 1458, 1440, 1344, 1334, 1156, 1107, 1038, 1007, 981, 537 cm^{-1}; HR-MS: m/z = 258.1770, calcd. for $C_{18}H_{23}F$: 258.1784; anal. calcd. for $C_{18}H_{23}F$ (258.37): C 83.67, H 8.97; found: C 83.70, H 9.02.

9-Fluorotriamantane (18a)

18b (116 mg, 0.45 mmol) was stirred for 1 h with DAST (0.2 mL, 1.52 mmol) in dry CH_2Cl_2 (20 mL) at 0–5 °C. Purification by column chromatography on silica flash gel (pentane, R_f: 0.15) and on HPLC (MeOH:*tert*-butylmethylether 9:1) resulted in pure, colourless **18a**; yield: 83.2 mg (71%);

mp 201 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 1.99–1.94 (m, 2H, H-7,11), 1.92–1.78 (m, 5H, H-8,10,15), 1.77–1.71 (m, 4H, H-3,13,14,18), 1.70–1.62 (m, 6H, H-4,5,14,16,18), 1.50–1.46 (m, 2H, H-17), 1.43 (br s, 2H, H-2,12), 1.39–1.37 (m, 2H, H-16); ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C): δ = 92.6 [C, $^1J(^{13}C,^{19}F)$ = 182.6 Hz, C-9], 49.7 [CH_2, $^2J(^{13}C,^{19}F)$ = 15.1 Hz, C-17], 45.5 (CH, C-2,12), 44.8 (CH_2, C-16), 42.8 [CH_2, $^2J(^{13}C,^{19}F)$ = 16.6 Hz, H-8,10], 41.0 [CH, $^3J(^{13}C,^{19}F)$ = 10.6 Hz, C-7,11], 37.8 (CH_2, C-14,18), 37.2 [CH_2, $^5J(^{13}C,^{19}F)$ = 1.5 Hz, C-5], 37.1 (CH, C-3,13), 36.7 [C, $^3J(^{13}C,^{19}F)$ = 10.6 Hz, C-1], 34.7 (CH, C-4), 33.9 (CH, C-6), 26.8 (CH, C-15); ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ = −135.48; IR (KBr): ν = 2931, 2910, 2876, 1458, 1442, 1336, 1330, 1155, 1065, 1034, 1007, 898, 619 cm^{-1}; HR-MS: m/z = 258.1761, calcd. for $C_{18}H_{23}F$: 258.1784; anal. calcd. for $C_{18}H_{23}F$ (258.37): C 83.67, H 8.97; found: C 83.84, H 8.99.

6-Fluoro[121]tetramantane (19a)

19b (100 mg, 0.32 mmol) was stirred for 1 h with DAST (0.1 mL, 0.76 mmol) in dry CH_2Cl_2 (20 mL) at 0–5 °C. Purification by column chromatography on silica gel (pentane:CH_2Cl_2 8:2, R_f: 0.37) and on HPLC (MeOH:*tert*-butyl methyl ether 9:1) resulted in pure, colourless **19a**; yield: 75.2 mg (75%); mp 206–208 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 1.99–1.94 (m, 2H, H-4,18), 1.90–1.80 (m, 5H, H-5,13,22), 1.74–1.65 (m, 8H, H-10,11,12,14,15,19), 1.53–1.50 (m, 2H, H-7), 1.49–1.46 (m, 2H, H-2,16), 1.38–1.34 (m, 4H, H-3,9,17), 1.32–1.30 (m, 2H, H-21), 1.29–1.27 (m, 2H, H-20); ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C): δ = 92.8 [C, $^1J(^{13}C,^{19}F)$ = 182.6 Hz, C-6], 48.8 [CH_2, $^2J(^{13}C,^{19}F)$ = 16.6 Hz, C-7], 46.4 (CH, C-2,16), 46.0 [CH, $^4J(^{13}C,^{19}F)$ = 1.5 Hz, C-3,17], 45.2 (CH_2, C-9), 44.5 [CH_2, $^5J(^{13}C,^{19}F)$ = 1.5 Hz, C-20], 44.1 (CH_2, C-21), 42.6 [CH_2, $^2J(^{13}C,^{19}F)$ = 16.6 Hz, C-5,22], 41.0 [CH, $^3J(^{13}C,^{19}F)$ = 9.1 Hz, C-4,18], 38.0 (CH, C-10), 37.7 (CH_2, C-12,14), 36.1 (CH, C-11,15), 35.6 [CH, $^4J(^{13}C,^{19}F)$ = 1.5 Hz, C-19], 34.7 [C, $^3J(^{13}C,^{19}F)$ = 10.6 Hz, C-8], 31.1 (C, C-1), 27.8 (CH, C-13); ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ = −135.76; IR (KBr): ν = 2873, 2848, 1473, 1461, 1357, 1343, 1322, 1294, 1157, 1007, 886, 699, 529 cm^{-1}; HR-MS: m/z = 310.2082, calcd. for $C_{22}H_{27}F$: 310.2097; anal. calcd. for $C_{22}H_{27}F$ (310.45): C 85.11, H 8.77; found: C 84.95, H 8.71.

6,13-Difluoro[121]tetramantane (20a)

20b (85 mg, 0.26 mmol) was stirred for 1.5 h with DAST (0.2 mL, 1.52 mmol) in dry CH_2Cl_2 (20 mL) at 0–5 °C. Purification by column chromatography on silica gel (pentane:CH_2Cl_2 1:1, R_f: 0.41) and filtration over a short silica gel column (CH_2Cl_2:pentane 1:2) afforded pure **20a**; yield: 82.5 mg (96%); mp 285 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.97 (br s, 4H, H-4,11,15,18), 1.94–1.79 (m, 8H, H-5,12,14,22), 1.71 (br s, 2H, H-10,19), 1.56–1.51 (m, 4H, H-7,21), 1.46, (br s, 4H, H-2,3,16,17), 1.43–1.39 (m, 4H, H-9,20); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 92.4 [C, $^1J(^{13}C,^{19}F)$ = 183.1 Hz, C-6,13], 48.5 [CH_2, $^2J(^{13}C,^{19}F)$ = 17.1 Hz, C-7,21], 45.0 (CH, higher spin system, C-2,3,16,17), 43.8 [CH_2, $^4J(^{13}C,^{19}F)$ = 2.0 Hz, C-9,20], 42.4 [CH_2, $^2J(^{13}C,^{19}F)$ = 18.1 Hz, C-5,12,14,22], 40.7 [CH, $^3J(^{13}C,^{19}F)$ = 10.1 Hz, C-4,11,15,18], 34.7 (CH, C-10,19), 34.4 [C, $^3J(^{13}C,^{19}F)$ = 10.1 Hz, C-1,8]; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C) δ = −136.45 ppm; IR (KBr): ν = 2938, 2900, 2885, 2872, 2856, 1452, 1343, 1151, 1068, 994, 864, 761, 508, 463 cm^{-1}; HR-MS: m/z = 328.2010, calcd. for $C_{22}H_{26}F_2$: 328.2003; A sample was sublimed for analysis: calcd. for $C_{22}H_{26}F_2$ (328.44): C 80.45, H 7.98; found: C 80.53, H 8.03.

7-Fluoro[1(2,3)4]pentamantane (21a)

21b (45 mg, 0.12 mmol) was stirred for 1 h with DAST (0.1 mL, 0.76 mmol) in dry CH_2Cl_2 (20 mL) at 0–5 °C. Purification by column chromatography on silica flash gel (pentane, R_f: 0.13) and on HPLC (MeOH:*tert*-butyl methyl ether, 9:1) resulted in pure, colourless **21a**; yield: 29.3 mg (65%); mp > 360 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 1.93–1.87 (m, 3H, H-11,15,19), 1.50–1.47 (m, 6H, H-6,8,26), 1.43–1.40 (m, 6H, H-10,22,23), 1.35–1.27 (m, 12H, H-12,14,16,18,20,21), 0.96 (br s, 1H, H-24), 0.90 (br s, 3H, H-2,4,25); ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C): δ = 92.0 [C, $^1J(^{13}C,^{19}F)$ = 182.6 Hz, C-7], 53.2 (CH, C-24), 52.3 [CH, $^4J(^{13}C,^{19}F)$ = 1.5 Hz, C-2,4,25], 49.3 [CH_2, $^2J(^{13}C,^{19}F)$ = 16.6 Hz, C-6,8,26], 44.6 (CH_2, C-12,14,16,18,20,21), 44.3 (CH_2, C-10,22,23), 37.3 [C, $^3J(^{13}C,^{19}F)$ = 9.1 Hz, C-3,5,9], 33.2 (C, C-1,13,17), 28.3 (CH, C-11,15,19); ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ = −132.82; IR (KBr): ν = 2898, 2840, 1456, 1436, 1329, 1138, 1017, 991, 971, 940, 637 cm^{-1}; HR-MS: m/z = 362.2420, calcd. for $C_{26}H_{31}F$: 362.2410; anal. calcd. for $C_{26}H_{31}F$ (362.52): C 86.14, H 8.62; found: C 86.12, H 8.61.

4-Bromo-9-(2,2,2-trifluoroethoxy)-diamantane (23)

22 (200 mg, 0.66 mmol) was dissolved in dichloromethane (20 mL) and pyridine (65 μL, 0.80 mmol) was added. The solution was stirred in an ice bath and $SOBr_2$ (1 mL, 12.9 mmol) was added within 5 min. The yellow, clear solution was stirred for 30 min in the ice bath and then 1.5 h at room temperature. After the addition of 50 mL distilled water and the separation of the phases the aqueous phase was extracted with dichloromethane (2 × 30 mL). The combined organic phases were washed with 10% HCl solution (30 mL), distilled water (50 mL), and dried over anhydrous Na_2SO_4. The received crude product was purified by column chromatography on silica gel (CH_2Cl_2, R_f: 0.67). Thereby pure, colorless **23** was obtained; yield: 233.4 mg (97%); mp 139–140 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 3.78 (q, J = 8.4 Hz, CH_2-CF_3), 2.40–2.33 (m, 6H, H-3,5,13), 2.06 (br s, 3H, H-1,7,11), 1.89 (br s, 3H, H-2,6,12), 1.80–1.72 (m, 6H, H-8,10,14); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 124.3 [C, $^1J(^{13}C,^{19}F)$ = 277.7 Hz, CF_3], 72.8 (C, C-9), 63.6 (C, C-4), 59.3 [CH_2, $^2J(^{13}C,^{19}F)$ = 34.2 Hz, CH_2-CF_3], 48.4 (CH_2, C-3,5,13), 40.3 (CH_2, C-8,10,14, from APT), 40.3 (CH, C-2,6,12, from APT), 37.8 (CH, C-1,7,11); ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): δ = −74.56; IR (KBr): ν = 2934, 2905, 2858, 1463, 1442, 1290, 1277, 1177, 1117, 1067, 967, 908, 812, 635 cm^{-1}; HR-MS: m/z = 363.0555 ($M-H^+$), calcd. for $C_{16}H_{20}BrF_3O$: 363.0572; anal. calcd. for $C_{16}H_{20}BrF_3O$ (365.23): C 52.62, H 5.52; found: C 52.54, H 5.63.

4-Fluoro-9-(2,2,2-trifluoroethoxy)-diamantane (24)

23 (421 mg, 1.15 mmol) was refluxed with AgF (390 mg, 3.07 mmol) in dry cyclohexane (6 mL) for 2 h. After the removal of the solvent the crude product was purified by column chromatography on silica gel (CH_2Cl_2:pentane 1:1, R_f: 0.40). Thereby the pure, colourless **24** could be isolated; yield: 300 mg (86%); mp 106 °C; ^{1}H NMR (400 MHz,

$CDCl_3$, 25 °C): $\delta = 3.79$ (q, $J = 8.8$ Hz, CH_2-CF_3), 2.08–1.98 (m, 6H, H-1,2,6,7,11,12), 1.97–1.89 (m, 6H, H-3,5,13), 1.84–1.75 (m, 6H, H-8,10,14); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 124.3$ [C, $^1J(^{13}C,^{19}F) = 277.7$ Hz, CF_3], 91.6 [C, $^1J(^{13}C,^{19}F) = 183.1$ Hz, C-4], 73.0 (C, C-9), 59.4 [CH_2, $^2J(^{13}C,^{19}F) = 34.2$ Hz, CH_2-CF_3], 41.8 [CH_2, $^2J(^{13}C,^{19}F) = 18.1$ Hz, C-3,5,13], 40.1 [CH_2, $^5J(^{13}C,^{19}F) = 2.0$ Hz, C-8,10,14], 39.4 [CH, $^3J(^{13}C,^{19}F) = 11.1$ Hz, C-2,6,12], 38.2 [CH, $^4J(^{13}C,^{19}F) = 2.0$ Hz, C-1,7,11]; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): $\delta = -140.92$ (C–F), -74.57 (CF_3); IR (KBr): $\nu =$ 2932, 2862, 1444, 1345, 1297, 1281, 1251, 1171, 1153, 1114, 1096, 1086, 1009, 946, 666 cm^{-1}; HR-MS: $m/z = 304.1464$, calcd. for $C_{16}H_{20}F_4O$: 304.1450; anal. calcd. for $C_{16}H_{20}F_4O$ (304.32): C 63.15, H 6.62; found: C 63.14, H 6.61.

4,9-Bis(trifluoroacetoxy)-diamantane (25)

24 (60 mg, 0.20 mmol) was refluxed for 2 h in CF_3COOH (2 mL). After the removal of the trifluoroacetic acid by distillation the crude product was purified by column chromatography on silica flash gel (CH_2Cl_2, R_f: 0.70) and the colorless product **25** was obtained; yield: 77.8 mg (96%); mp 196–198 °C; ^1H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 2.23$ (br s, 12H, H-3,5,8,10,13,14), 2.14 (br s, 6H, H-1,2,6,7,11,12); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 156.0$ [C, $^2J(^{13}C,^{19}F) = 41.3$ Hz, C=O], 114.3 [C, $^1J(^{13}C,^{19}F) = 287.8$ Hz, CF_3], 84.8 (C, C-4,9), 39.8 (CH_2, C-3,5,8,10,13,14), 38.4 (CH, C-1,2,6,7,11,12); ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): $\delta = -75.74$; IR (KBr): $\nu = 2956$, 2921, 2874, 1771, 1478, 1449, 1375, 1225, 1161, 1071, 909, 861, 777, 748 cm^{-1}; anal. calcd. for $C_{18}H_{18}F_6O_4$ (412.32): C 52.43, H 4.40; found: C 52.44, H 4.24.

4-Acetoxy-9-(2,2,2-trifluoroethoxy)-diamantane (27)

22 (400 mg, 1.32 mmol) was dissolved in dichloromethane (40 mL). To this solution pyridine (0.16 mL, 2 mmol) and acetyl chloride (0.14 mL, 2 mmol) were added. After stirring at room temperature for 1.5 h pyridine (0.60 mL, 7.41 mmol) and acetyl chloride (0.54 mL, 7.59 mmol) were added again and the solution was stirred for another 2 h at the same temperature. Then the solvents were distilled off, leaving a yellow crude product behind. After filtration through silica gel with dichloromethane (150 mL) pure, colorless **27** was obtained; yield: 428.1 mg (94%); mp 126 °C; ^1H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 3.79$ (q, $J = 8.8$ Hz, CH_2-CF_3), 2.15–2.11 (m, 6H, H-3,5,13), 2.03 (br s, 3H, H-1,7,11), 1.99–1.92 (m, 6H, H-2,6,12 + CH_3), 1.79–1.75 (m, 6H, H-8,10,14); ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C): $\delta = 170.4$ (C, C=O), 124.3 [C, $^1J(^{13}C,^{19}F) = 277.7$ Hz, CF_3], 78.7 (C, C-4), 73.1 (C, C-9), 59.3 [CH_2, $^2J(^{13}C,^{19}F) = 34.7$ Hz, CH_2-CF_3], 40.4 (CH_2, C-3,5,13), 40.3 (CH_2, C-8,10,14), 38.7 (CH, C-2,6,12), 38.4 (CH, C-1,7,11), 22.7 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): $\delta = -74.57$; IR (KBr): $\nu = 2928$, 2887, 2865, 1727, 1468, 1444, 1349, 1282, 1237, 1173, 1115, 1079, 1025, 978, 846, 692 cm^{-1}; HR-MS: $m/z = 344.1620$, calcd. for $C_{18}H_{23}F_3O_3$: 344.1599; anal. calcd. for $C_{18}H_{23}F_3O_3$ (344.37): C 62.78, H 6.73; found: C 62.47, H 6.69.

4-Acetoxy-9-bromodiamantane (28)

27 (50 mg, 0.15 mmol) was dissolved in dichloromethane (10 mL) and cooled to −5 °C in an ice-salt-bath. To this solution 0.30 mL of a one molar BBr_3 solution (in CH_2Cl_2) were added and stirred for 50 min at the same temperature. Then distilled water (15 mL) and saturated $NaHCO_3$ solution (5 mL) were added. The phases were separated after adding $CHCl_3$ (20 mL) and the aqueous layer was further extracted with $CHCl_3$ (2 × 20 mL). The combined organic layers were washed with distilled water (50 mL) and dried over anhydrous Na_2SO_4. The obtained crude product was purified by column chromatography on silica gel (CH_2Cl_2, R_f: 0.50) and colourless **28** was obtained; yield: 29.5 mg (63%); mp 178–180 °C; ^1H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 2.37$–2.33 (m, 6H, H-8,10,14), 2.11–2.07 (m, 6H, H-3,5,13), 2.04 (br s, 3H, H-2,6,12), 1.98–1.92 (m, 6H, H-1,7,11 + CH_3); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 170.4$ (C, C=O), 78.5 (C, C-4), 63.9 (C, C-9), 48.5 (CH_2, C-8,10,14), 40.5 (CH_2, C-3,5,13), 40.3 (CH, C-1,7,11), 38.0 (CH, C-2,6,12), 22.6 (CH_3); IR (KBr): $\nu = 2924$, 2883, 2865, 1733, 1468, 1439, 1367, 1260, 1232, 1080, 1068, 1025, 934, 867 cm^{-1}; anal. calcd. for $C_{16}H_{21}BrO_2$ (325.24): C 59.09, H 6.51; found: C 58.99, H 6.45.

As a side product 15.6 mg (31%, R_f: 0.71) of **12b** could be isolated.

4-Acetoxy-9-fluorodiamantane (29)

28 (140 mg, 0.43 mmol) was refluxed for 2 h with AgF (100 mg, 0.79 mmol) in 6 mL dry cyclohexane. After removal of the solvent the crude product was purified by filtration through silica gel with dichloromethane (100 mL). Thereby pure, colourless **29** was obtained; yield: 100 mg (88%); mp 136–137 °C; ^1H NMR (600 MHz, $CDCl_3$, 25 °C): $\delta = 2.15$–2.12 (m, 6H, H-3,5,13), 2.07 (br s, 3H, H-1,7,11), 2.00–1.96 (m, 6H, H-2,6,12 + CH_3), 1.92–1.89 (m, 6H, H-8,10,14); ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C): $\delta = 170.4$ (C, C=O), 91.7 [C, $^1J(^{13}C,^{19}F) = 182.6$ Hz, C-9], 78.7 (C, C-4), 41.8 [CH_2, $^2J(^{13}C,^{19}F) = 16.6$ Hz, C-8,10,14], 40.3 [CH_2, $^5J(^{13}C,^{19}F) = 3.0$ Hz, C3,5,13], 39.3 [CH, $^3J(^{13}C,^{19}F) = 10.6$ Hz, C-1,7,11], 38.5 [CH, $^4J(^{13}C,^{19}F) = 3.0$ Hz, C-2,6,12], 22.6 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): $\delta = -140.60$; IR (KBr): $\nu = 2946$, 2900, 2886, 1726, 1448, 1367, 1346, 1259, 1236, 1103, 1081, 1026, 953 cm^{-1}; HR-MS: $m/z = 264.1537$, calcd. for $C_{16}H_{21}FO_2$: 264.1526; anal. calcd. for $C_{16}H_{21}FO_2$ (264.34): C 72.70, H 8.01; found: C 72.47, H 8.03.

9-Fluorodiamantan-4-ol (30)

29 (22 mg, 0.08 mmol) was dissolved in CH_2Cl_2 (8 mL) and a solution of NaOH (100 mg, 2.50 mmol) in MeOH (2 mL) was added. After stirring 16 h at room temperature acetic acid (0.5 mL) was added and the solvent was removed. The crude product was purified by column chromatography on silica flash gel (diethylether:CH_2Cl_2 1:1, R_f: 0.32) to afford pure, colourless **30**; yield: 17 mg (92%); mp 230–233 °C; ^1H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 2.05$–1.89 (m, 12H, H-1,2,6,7,8,10,11,12,14), 1.78–1.73 (m, 6H, H-3,5,13), 1.30 (br s, 1H, OH); ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C) $\delta = 91.8$ [C, $^1J(^{13}C,^{19}F) = 182.6$ Hz, C-9], 67.0 (C, C-4), 44.4 [CH_2, $^5J(^{13}C,^{19}F) = 3.0$ Hz, C-3,5,13], 41.9 [CH_2, $^2J(^{13}C,^{19}F) = 18.1$ Hz, C-8,10,14], 39.3 [CH, $^3J(^{13}C,^{19}F) = 9.1$ Hz, C-1,7,11], 38.6 [CH, $^4J(^{13}C,^{19}F) = 3.0$ Hz, C-2,6,12]; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): $\delta = -140.51$; IR (KBr): $\nu = 3565$, 3464, 2926, 2884, 1443, 1347, 1248, 1115, 1095, 1017, 958, 803, 549 cm^{-1}; HR-MS: $m/z = 222.1417$, calcd. for $C_{14}H_{19}FO$: 222.1420. A

sample was sublimed for analysis: calcd. for $C_{14}H_{19}FO$ (222.30): C 75.64, H 8.61; found: C 75.49, H 8.67.

4-Amino-9-bromodiamantane (32)

31 (150 mg, 0.68 mmol) was dissolved in dichloromethane (5 mL) and stirred in an ice-bath. Then $SOBr_2$ (1 mL, 12.9 mmol) and triethylamine (0.10 mL, 0.72 mmol) were added which resulted in the formation of a yellow suspension. This suspension was stirred for 45 min at room temperature and then poured on ice (50 g). The mixture was diluted with saturated $NaHCO_3$ (100 mL) and 10% NaOH (3 mL) solution. After the extraction with $CHCl_3$ (3× 50 mL) the combined organic layers were washed with distilled water (50 mL) and dried over anhydrous Na_2SO_4. The obtained oily crude product was sublimed to afford pure **32**; yield: 112.4 mg (58%); mp 184–187 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 2.40$–2.34 (m, 6H, H-8,10,14), 1.94 (br s, 3H, H-2,6,12), 1.85 (br s, 3H, H-1,7,11), 1.60–1.54 (m, 6H, H-3,5,13), 1.13 (br s, 2H, NH_2); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 64.8$ (C, C-9), 48.8 (CH_2, C-8,10,14), 45.6 (CH_2, C-3,5,13), 45.5 (C, C-4), 40.4 (CH, C-1,7,11), 37.4 (CH, C-2,6,12); IR (KBr): $\nu = 3458$, 2889, 2854, 1610, 1464, 1440, 1345, 1321, 1245, 1138, 1069, 1047, 982, 920, 812 cm^{-1}; HR-MS: $m/z = 281.0770$, calcd. for $C_{14}H_{20}BrN$: 281.0779; anal. calcd. for $C_{14}H_{20}BrN$ (282.22): C 59.58, H 7.14, N 4.96; found: C 59.53, H 7.15, N 4.61.

4-Bromo-9-nitrodiamantane (35)

34 (100 mg, 0.40 mmol) was dissolved in dichloromethane (15 mL) and pyridine (48 μL, 0.60 mmol) was added. The solution was stirred in an ice bath and $SOBr_2$ (0.75 mL, 9.68 mmol) was added within 5 min. The yellow, clear solution was stirred for 30 min in the ice bath and then 1.5 h at room temperature. After the addition of 50 mL distilled water and the separation of the phases the aqueous phase was extracted with dichloromethane (2×30 mL). The combined organic phases were washed with 10% HCl solution (30 mL), distilled water (50 mL) and dried over anhydrous Na_2SO_4. The thus obtained crude product was purified by column chromatography on silica gel (CH_2Cl_2, R_f: 0.62). Thereby pure, colourless **35** was obtained; yield: 103.4 mg (83%); mp 283–285 °C (decomposition); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 2.41$–2.35 (m, 6H, H-3,5,13), 2.24–2.19 (m, 6H, H-8,10,14), 2.14 (br s, 3H, H-1,7,11), 1.97 (br s, 3H, H-2,6,12); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta =$ 83.0 (C, C-9), 62.0 (C, C-4), 48.1 (CH_2, C-3,5,13), 40.3 (CH_2, C-8,10,14), 39.6 (CH, C-2,6,12), 37.0 (CH, C-1,7,11); IR (KBr): $\nu = 2929$, 2895, 1530, 1470, 1439, 1361, 1244, 1069, 979, 816, 801, 713 cm^{-1}. A sample was sublimed for analysis: calcd. for $C_{14}H_{18}BrNO_2$ (312.20): C 53.86, H 5.81, N 4.49; found: C 53.81, H 5.79, N 4.31.

4-Fluoro-9-nitrodiamantane (36)

Using AgF: **35** (50 mg, 0.16 mmol) was refluxed for 1.5 h with AgF (43 mg, 0.34 mmol) in dry cyclohexane (5 mL). After removal of the solvent the crude product was purified by column chromatography on silica flash gel (CH_2Cl_2:pentane 1:1, R_f: 0.23) to obtain pure, colourless **36**; yield: 34.4 mg (86%).

Using DAST: **34** (100 mg, 0.40 mmol) was dissolved in dry dichloromethane (20 mL) and DAST (0.1 mL, 0.76 mmol) was added while stirring in an ice-bath. After 1 h at the same temperature saturated $NaHCO_3$ solution (40 mL) and dichloromethane (20 mL) were added. After separation of the layers the aqueous phase was extracted with dichloromethane (2×40 mL). The combined organic phases were washed with distilled water (50 mL) and dried over anhydrous Na_2SO_4. The obtained crude product was purified on silica flash gel (pentane:CH_2Cl_2 7:3, R_f: 0.15) to afford pure, colourless **36**; yield: 87.6 mg (87%); mp 209–211 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): $\delta = 2.28$–2.24 (m, 6H, H-8,10,14), 2.09 (br s, 6H, H-1,2,6,7,11,12), 1.97–1.93 (m, 6H, H-3,5,13); ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C): $\delta = 91.0$ [C, $^1J(^{13}C,^{19}F) = 184.1$ Hz, C-4], 83.1 (C, C-9), 41.6 [CH_2, $^2J(^{13}C,^{19}F) = 18.1$ Hz, C-3,5,13], 40.1 [CH_2, $^5J(^{13}C,^{19}F) =$ 1.5 Hz, C-8,10,14], 38.8 [CH, $^3J(^{13}C,^{19}F) = 12.1$ Hz, C-2,6,12], 37.4 (CH, C-1,7,11); ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): $\delta =$ −141.83; IR (KBr): $\nu = 2942$, 2895, 2865, 1537, 1474, 1448, 1364, 1250, 1094, 1023, 931, 866, 804, 461 cm^{-1}; anal. calcd. for $C_{14}H_{18}FNO_2$ (251.30): C 66.91, H 7.22, N 5.57; found: C 66.71, H 7.15, N 5.71.

4-Amino-9-fluorodiamantane (33)

Using Zn/HCl: **36** (60 mg, 0.24 mmol) and zinc powder (500 mg, 7.65 mmol) were mixed and 16% HCl solution (6 mL) was added. The reaction mixture was stirred at 40 °C. Further additions of zinc [after 1 h (100 mg, 1.53 mmol) and after 1.5 h (50 mg, 0.76 mmol)] were made and after 2 h the solution was diluted with distilled water (30 mL) and 10% NaOH solution (20 mL). The solution was extracted with $CHCl_3$ (4×40 mL) and the combined organic phases were washed with distilled water (50 mL) and dried over anhydrous Na_2SO_4. The obtained crude product was purified *via* its hydrochloride (dissolved in dry diethyl ether) to afford colourless **33**; yield: 38.7 mg (73%).

Hydrolysis of chloroacetamide: **40** (100 mg, 0.34 mmol) was refluxed for 5 h with thiourea (38 mg, 0.5 mmol), ethanol (5 mL) and acetic acid (3 mL). The clear solution was then diluted with distilled water (50 mL) and 20% NaOH solution (10 mL) which resulted in a white precipitate. The mixture was extracted with $CHCl_3$ (3×50 mL) and the combined organic solvents were washed with distilled water (50 mL) and dried over anhydrous Na_2SO_4. The obtained crude product was purified *via* its hydrochloride (dissolved in dry diethyl ether) to afford pure, colourless **33**; yield: 53.7 mg (72%); mp 204–207 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 1.97$ (br s, 3H, H-1,7,11), 1.94–1.86 (m, 9H, H-2,6,8,10,12,14), 1.65–1.59 (m, 6H, H-3,5,13), 1.22 (br s, 2H, NH_2); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): $\delta = 92.0$ [C, $^1J(^{13}C,^{19}F) = 183.1$ Hz, C-9], 45.7 (C, C-4), 45.5 [CH_2, $^5J(^{13}C,^{19}F) = 2.0$ Hz, C-3,5,13], 42.1 [CH_2, $^2J(^{13}C,^{19}F) = 17.1$ Hz, C-8,10,14], 39.4 [CH, $^3J(^{13}C,^{19}F) = 10.1$ Hz, C-1,7,11], 37.8 [CH, $^4J(^{13}C,^{19}F) = 2.0$ Hz, C-2,6,12]; ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): $\delta = -140.10$; IR (KBr): $\nu = 3343$, 3261, 2916, 2886, 1594, 1440, 1353, 1253, 1096, 1019, 960, 887, 800, 551 cm^{-1}; HR-MS: $m/z = 221.1580$, calcd. for $C_{14}H_{20}FN$: 221.1580; anal. calcd. for $C_{14}H_{20}FN$ (221.31): C 75.98, H 9.11, N 6.33; found: C 76.22, H 9.10, N 6.12.

2-Chloro-*N*-[9-(bromo)diamantan-4-yl]acetamide (38)

*From **37***: Compound **37** (100 mg, 0.26 mmol) was dissolved in dichloromethane (7 mL) and 0.60 mL of an one molar BBr_3 solution in dichloromethane were added . The clear solution was stirred at room temperature for 30 min and was then diluted with distilled water (50 mL). After extraction with $CHCl_3$ (3×40 mL) the combined organic phases were washed with distilled water (60 mL) and dried over anhydrous Na_2SO_4. After filtration of the drying agent and removal of the solvent pure, colourless **38** was obtained; yield: 92.4 mg (97%).

*From **39**:* Compound **39** (240 mg, 0.61 mmol) was dissolved in dichloromethane (10 mL) and 2.50 mL of an one molar BBr_3 solution in dichloromethane were added. The clear solution was stirred at room tempertaure for 1.5 h and was then diluted with distilled water (20 mL) and saturated $NaHCO_3$ solution (40 mL). After the separation of the layers the aqueous phase was extracted with dichloromethane (3×30 mL). The combined organic phases were washed with distilled water (50 mL) and dried over anhydrous Na_2SO_4. The obtained crude product was purified by column chromatography on silica flash gel (diethyl ether, R_f: 0.45) to afford pure, colourless **38**; yield: 204.2 mg (93%); mp 210–214 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta=6.23$ (br s, 1H, NH), 3.93 (s, 2H, CH_2Cl), 2.38–2.34 (m, 6H, H-8,10,14), 2.05–1.98 (m, 9H, H-2,3,5,6,12,13), 1.95 (br s, 3H, H-1,7,11); ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C) $\delta=164.9$ (C, C=O), 63.9 (C, C-9), 50.6 (C, C-4), 48.7 (CH_2, C-8,10,14), 42.9 (CH_2, CH_2Cl), 40.6 (CH_2, C-3,5,13), 40.3 (CH, C-1,7,11), 36.8 (CH, C-2,6,12); IR (KBr): $\nu=3301$, 3084, 2924, 2894, 2857, 1674, 1559, 1467, 1442, 1344, 1245, 1232, 1070, 808, 651 cm^{-1}; HR-MS: $m/z=357.0520$, calcd. for $C_{16}H_{21}BrClNO$: 357.0495; anal. calcd. for $C_{16}H_{21}BrClNO$ (358.70): C 53.57, H 5.90, N 3.90; found: C 53.17, H 5.77, N 3.89.

2-Chloro-*N*-[9-(fluoro)diamantan-4-yl]acetamide (40)

38 (62 mg, 0.17 mmol) was refluxed for 2 h with AgF (50 mg, 0.39 mmol) in dry cyclohexane (6 mL). After removal of the solvent the crude product was purified by column chromatography on silica gel (diethyl ether, R_f: 0.54) to afford pure, colourless **40**; yield: 46.4 mg (90%); mp 169–171 °C; ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): $\delta=6.24$ (br s, 1H, NH), 3.94 (s, 2H, CH_2Cl), 2.10–2.05 (m, 9H, H-1,3,5,7,11,13), 1.95 (br s, 3H, H-2,6,12), 1.93–1.90 (m, 6H, H-8,10,14); ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C): $\delta=164.9$ (C, C=O), 91.7 [C, $^1J(^{13}C,^{19}F)=182.6$ Hz, C-9], 50.8 (C, C-4), 42.9 (CH_2, CH_2Cl), 42.0 [CH_2, $^2J(^{13}C,^{19}F)=18.1$ Hz, C-8,10,14], 40.4 [CH_2, $^5J(^{13}C,^{19}F)=3.0$ Hz, C-3,5,13], 39.3 [CH, $^3J(^{13}C,^{19}F)=10.6$ Hz, C-1,7,11], 37.2 (CH, C-2,6,12); ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C): $\delta=-140.57$; IR (KBr): $\nu=3410$, 2946, 2899, 2884, 1676, 1525, 1473, 1446, 1354, 1346, 1239, 1101, 1025, 883, 754, 647, 504 cm^{-1}; HR-MS: $m/z=297.1290$, calcd. for $C_{16}H_{21}ClFNO$: 297.1296; A sample was sublimed for analysis: calcd. for $C_{16}H_{21}ClFNO$ (297.80): C 64.53, H 7.11, N 4.70; found: C 64.21, H 7.21, N 4.74.

Acknowledgements

*This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We are grateful to MolecularDiamond Technologies for providing compounds **2–5** and to N. A. Fokina and B. A. Tkachenko for the synthesis of triamantane (**3**) and [121]tetramantane (**4**) alcohols.*

References

[1] Functionalized Nanodiamonds. Part 18. For part 17, see: W. A. Clay, Z. Liu, W. Yang, J. D. Fabbri, J. E. P. Dahl, R. M. K. Carlson, Y. Sun, P. R. Schreiner, A. A. Fokin, B. A. Tkachenko, N. A. Fokina, P. A. Pianetta, N. Melosh, Z.-X. Shen, *Nano Lett.* **2009**, *9*, 57–61.

[2] H. Schwertfeger, A. A. Fokin, P. R. Schreiner, *Angew. Chem.* **2008**, *120*, 1038–1053; *Angew. Chem. Int. Ed.* **2008**, *47*, 1022–1036.

[3] S. Landa, V. Machacek, *Collect. Czech. Chem. Commun.* **1933**, *5*, 1–5.

[4] S. Hála, S. Landa, V. Hanus, *Angew. Chem.* **1966**, *78*, 1060–1061; *Angew. Chem. Int. Ed. Engl.* **1966**, *5*, 1045–1046.

[5] a) W. Burns, T. R. B. Mitchell, M. A. McKervey, J. J. Rooney, G. Ferguson, P. Roberts, *J. Chem. Soc. Chem. Commun.* **1976**, 893–895; b) W. Burns, M. A. McKervey, T. R. B. Mitchell, J. J. Rooney, *J. Am. Chem. Soc.* **1978**, *100*, 906–911.

[6] J. E. Dahl, S. G. Liu, R. M. K. Carlson, *Science* **2003**, *299*, 96–99.

[7] J. E. P. Dahl, J. M. Moldowan, T. M. Peakman, J. C. Clardy, E. Lobkovsky, M. M. Olmstead, P. W. May, T. J. Davis, J. W. Steeds, K. E. Peters, A. Pepper, A. Ekuan, R. M. K. Carlson, *Angew. Chem.* **2003**, *115*, 2086–2090; *Angew. Chem. Int. Ed.* **2003**, *42*, 2040–2044.

[8] A. A. Fokin, B. A. Tkachenko, P. A. Gunchenko, D. V. Gusev, P. R. Schreiner, *Chem. Eur. J.* **2005**, *11*, 7091–7101.

[9] P. R. Schreiner, N. A. Fokina, B. A. Tkachenko, H. Hausmann, M. Serafin, J. E. Dahl, S. Liu, R. M. K. Carlson, A. A. Fokin, *J. Org. Chem.* **2006**, *71*, 6709–6720.

[10] a) B. A. Tkachenko, N. A. Fokina, L. V. Chernish, J. E. P. Dahl, S. Liu, R. M. K. Carlson, A. A. Fokin, P. R. Schreiner, *Org. Lett.* **2006**, *8*, 1767–1770; b) A. A. Fokin, E. D. Butova, L. V. Chernish, N. A. Fokina, J. E. P. Dahl, R. M. K. Carlson, P. R. Schreiner, *Org. Lett.* **2007**, *9*, 2541–2544; c) A. A. Fokin, B. A. Tkachenko, N. A. Fokina, H. Hausmann, M. Serafin, J. E. P. Dahl, R. M. K. Carlson, P. R. Schreiner, *Chem. Eur. J.* **2009**, *15*, 3851–3862; d) A. A. Fokin, A. Merz, N. A. Fokina, H. Schwertfeger, S. Liu, J. E. P. Dahl, R. M. K. Carlson, P. R. Schreiner, *Synthesis* **2009**, 909-912.

[11] A. A. Fokin, P. R. Schreiner, N. A. Fokina, B. A. Tkachenko, H. Hausmann, M. Serafin, J. E. P. Dahl, S. Liu, R. M. K. Carlson, *J. Org. Chem.* **2006**, *71*, 8532–8540.

[12] N. A. Fokina, B. A. Tkachenko, A. Merz, M. Serafin, J. E. P. Dahl, R. M. K. Carlson, A. A. Fokin, P. R. Schreiner, *Eur. J. Org. Chem.* **2007**, 4738–4745.

[13] W. L. Yang, J. D. Fabbri, T. M. Willey, J. R. I. Lee, J. E. Dahl, R. M. K. Carlson, P. R. Schreiner, A. A. Fokin, B. A. Tkachenko, N. A. Fokina, W. Meevasana, N. Mannella, K. Tanaka, X. J. Zhou, T. van Buuren, M. A. Kelly, Z. Hussain, N. A. Melosh, Z.-X. Shen, *Science* **2007**, *316*, 1460–1462.
[14] H. Richter, H. Schwertfeger, P. R. Schreiner, R. Fröhlich, F. Glorius, *Synlett* **2009**, 193–197.
[15] H. Schwertfeger, C. Würtele, M. Serafin, H. Hausmann, R. M. K. Carlson, J. E. P. Dahl, P. R. Schreiner, *J. Org. Chem.* **2008**, *73*, 7789–7792.
[16] a) W. K. Hagmann, *J. Med. Chem.* **2008**, *51*, 4359–4369; b) J. T. Welch, *Tetrahedron* **1987**, *43*, 3123–3197.
[17] a) S. Samnick, S. Ametamey, K. L. Leenders, P. Vontobel, G. Quack, C. G. Parsons, H. Neu, P. A. Schubiger, *Nucl. Med. Biol.* **1998**, *25*, 323–330; b) A. Kolocouris, C. Zikos, R. W. Broadhurst, *Bioorg. Med. Chem. Lett.* **2007**, *17*, 3947–3952; c) A. Kolocouris, R. K. Hansen, R. W. Broadhurst, *J. Med. Chem.* **2004**, *47*, 4975–4978; d) S. Samnick, S. Ametamey, M. R. Gold, P. A. Schubiger, *J. Labelled Compd. Radiopharm.* **1997**, *39*, 241–250.
[18] V. J. Jasys, F. Lombardo, T. A. Appleton, J. Bordner, M. Ziliox, R. A. Volkmann, *J. Am. Chem. Soc.* **2000**, *122*, 466–473.
[19] a) J. L. Adcock, H. Luo, *J. Org. Chem.* **1992**, *57*, 2162–2163; b) H.-C. Wei, S. Corbelin, R. J. Lagow, *J. Org. Chem.* **1996**, *61*, 1643–1644.
[20] J. N. Hart, P. W. May, N. L. Allan, J. E. P. Dahl, S. Liu, R. M. K. Carlson, J. L. Adcock, *Chem. Phys. Lett.* **2008**, *460*, 237–240.
[21] a) G. A. Olah, J. G. Shih, B. P. Singh, B. G. B. Gupta, *Synthesis* **1983**, 713–715; b) G. A. Olah, J. G. Shih, V. V. Krishnamurthy, B. P. Singh, *J. Am. Chem. Soc.* **1984**, *106*, 4492–4500; c) V. V. Krishnamurthy, J. G. Shih, G. A. Olah, *J. Org. Chem.* **1985**, *50*, 1161–1164; d) G. A. Olah, J. G. Shih, B. P. Singh, B. G. B. Gupta, *J. Org. Chem.* **1983**, *48*, 3356–3358.
[22] V. V. Krishnamurthy, J. G. Shih, B. P. Singh, G. A. Olah, *J. Org. Chem.* **1986**, *51*, 1354–1357.
[23] D. H. R. Barton, R. H. Hesse, R. E. Markwell, M. M. Pechet, H. T. Toh, *J. Am. Chem. Soc.* **1976**, *98*, 3034–3035.
[24] a) S. Rozen, C. Gal, *J. Org. Chem.* **1988**, *53*, 2803–2807; b) C. Gal, S. Rozen, *Tetrahedron Lett.* **1985**, *26*, 2793–2796.
[25] R. D. Chambers, A. M. Kenwright, M. Parsons, G. Sandford, J. S. Moilliet, *J. Chem. Soc. Perkin Trans. 1* **2002**, 2190–2197.
[26] S. Stavber, M. Zupan, *Tetrahedron* **1989**, *45*, 2737–2742.
[27] B. Zajc, M. Zupan, *Bull. Chem. Soc. Jpn.* **1986**, *59*, 1659–1661.
[28] K. R. Brower, *J. Org. Chem.* **1987**, *52*, 798–802.
[29] M. Aoyama, T. Fukuhara, S. Hara, *J. Org. Chem.* **2008**, *73*, 4186–4189.
[30] S. Hara, M. Aoyama, *Synthesis* **2008**, 2510–2512.
[31] G. Bolte, A. Haas, *Chem. Ber.* **1984**, *117*, 1982–1986.
[32] a) K. S. Bhandari, R. E. Pincock, *Synthesis* **1974**, 655–656; b) R. C. Fort, P. v. R. Schleyer, *J. Org. Chem.* **1965**, *30*, 789–796.
[33] R. P. Singh, J. M. Shreeve, *Synthesis* **2002**, 2561–2578.
[34] T. M. Gund, P. v. R. Schleyer, G. D. Unruh, G. J. Gleicher, *J. Org. Chem.* **1974**, *39*, 2995–3003.
[35] G. P. Sollott, E. E. Gilbert, US Patent 4,535,193, **1985**.
[36] S. I. Kozhushkov, D. S. Yufit, R. Boese, D. Bläser, P. R. Schreiner, A. de Meijere, *Eur. J. Org. Chem.* **2005**, 1409–1415.
[37] J. Jankü, J. Burkhard, L. Vodička, *Z. Chem.* **1981**, *21*, 325–326.
[38] G. A. Olah, B. G. B. Gupta, S. C. Narang, *Synthesis* **1979**, 274–276.
[39] M. R. Peterson, G. H. Wahl, *Chem. Commun. (London)* **1968**, 1552–1553.
[40] A. Jirgensons, V. Kauss, I. Kalvinsh, M. R. Gold, *Synthesis* **2000**, 1709–1712.
[41] W. L. F. Armarego, C. L. L. Chai, *Purification of Laboratory Chemicals*, 5th edn., Butterworth-Heinemann, London, **2003**.
[42] L. Vodička, J. Jankü, J. Burkhard, *Collect. Czech. Chem. Commun.* **1983**, *48*, 1162–1172.

