Stable organic azides based on rigid tetrahedral methane and adamantane structures as high energetic materials†

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A four-folded azidation of tetrakis(4-iodophenyl)methane and -adamantane leads to stable organic azides, but yet energetic materials, measured by differential scanning calorimetry (DSC). The rigid and symmetrical structures can be useful for new polymer and nanomaterial developments in material sciences as well as bioconjugations, after 1,3-dipolar cycloaddition reactions with terminal alkynes to 1,2,3-triazoles.

The research of highly energetic materials, especially polyazides, has attracted the attention of chemists in the last few years. Inorganic azides of the type $M(N_3)_n$ were investigated[1,2] as well as numerous organic compounds.[3] Banert *et al.*[4] reported a remarkable example of explosive polyazides, the tetraazidomethane. A nitrogen-rich compound as an intermediate stage in a one-pot synthesis, based on the tetraphenylmethane structure, was recently reported by Chen *et al.*[5]

Nowadays, aryl azides are increasingly used in organic synthesis,[6] due to the versatile transformations of the azide functional group. Anilines and nitrenes[7] can be generated and azides are useful for the preparation of different heterocycles.[8,9] Polyazido organic compounds have high relative heats of formation measurable by differential scanning calorimetry. One azido group typically adds about 364 kJ mol^{-1} of endothermicity to the organic frame.[2,10]

Furthermore, the significant Huisgen-variant of the 1,3-dipolar cycloaddition reaction, a metal catalyzed azide/alkyne 'click' reaction,[11,12] leads to 1,4- or 1,5-substituted heterocycles.

Tetrafunctionalized molecules with a rigid structure, like the newly developed symmetrical polyazides are promising compounds for polymerization processes, material and macromolecular sciences,[13] as well as for the investigation of novel nanomaterials. The 1,4-disubstituted 1,2,3-triazoles, easily accessible from polyazides, found applications prevalently in drug discovery and bioconjugations.[7]

However, structures like the tetrasubstituted polyazides of tetraphenylmethane **3d** and its analogue, the 1,3,5,7-tetraphenyladamantane **4d**, have not yet been synthesized.‡ Herein, we report stable aryl azides that, unlike alkyl azides,[2,14] combine high energetic properties with non-explosive ones under ambient conditions (25 °C, 1 atm).

The synthesis of the polyazides is based on iodoarylated compounds in both cases: the tetrakis(4-iodophenyl)-methane **1**[15] was obtained in two steps from tritylchloride.[16,17] Its analogue, 1,3,5,7-tetrakis(4-iodophenyl)adamantane **2**,[18,19] was synthesized from 1,3,5,7-tetraphenyladamantane in one step.[20]

The aryl azides **3d**, **4a–d** were prepared *via* Ullmann-type coupling reactions,[21] using CuI as catalyst[22] to activate the aryl halides for the nucleophilic substitution. The reaction rate is influenced by factors like ligands, for example L-proline or diamines, and solvent systems.[8]

The first attempts to obtain 1,3,5,7-tetrakis(4-azidophenyl)-adamantane **4d** using L-proline as catalyst gave lower substituted homologues **4a–c** as side products (Scheme 1, entries 1–3) in DMSO–H_2O (5 : 1) as solvent. Different ligands and solvents were tested. Optimized conditions delivered tetraazide **4d** with yields up to 34%. *N*,*N'*-Dimethylethylenediamine (1.2 equiv.) as ligand, NaN_3 (16 equiv.), sodium ascorbate (0.4 equiv.) and CuI (0.8 equiv.) in DMSO–H_2O (10 : 1) were added to a solution of tetraiodoaryl **2** in DMSO. The similarity of the molecular structures, the thermal resistance of the adamantane core and the well known insolubility of high symmetrical compounds made the purification and characterization of all derivatives very difficult. All samples were purified by flash chromatography (cyclohexane–CH_2Cl_2, 5 : 1) and characterized by ^1H and ^{13}C NMR analysis.

1 X = C (methane core) **3d** $R^{1-4} = N_3$

2 X = 1,3,5,7-adamantyl (adamantane core) **4a** $R^1 = N_3$; $R^{2-4} = I$; **4b** $R^{1,2} = N_3$; $R^{3,4} = I$; **4c** $R^{1-3} = N_3$; $R^4 = I$; **4d** $R^{1-4} = N_3$

Entry	Core X	Product	Ligand [mol%]	DMSO/H_2O	Yield[c] [%]
1	**2**	**4a-d** (mixture)	60[a]	5:1	3 (**4a**)
2	**2**		60[a]	5:1	9 (**4b**)
3	**2**		60[a]	5:1	12 (**4c**)
4	**2**		60[a]	5:1	7 (**4d**)
5	**2**	**4d**	120[b]	10:1	34 (**4d**)
6	**1**	**3d**	120[b]	20:1	41

[a] see Supporting Information: Variant B with *L*-proline; [b] Variant A with *N,N'*-dimethylethylenediamine;
[c] isolated yield

Scheme 1 Ullmann-type coupling with iodoaryl **1** and **2**.

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We found that tetrasubstituted compounds **3d** and **4d** can best be prepared using a solvent ratio of DMSO–H_2O 5 : 1 and 20 : 1 respectively (Scheme 1). All other tested solvents like EtOH, THF, *t*-BuOH and other common solvent mixtures suffered from solubility problems.

Thus, tetraiodoaryl **1** yielded 1,3,5,7-tetrakis(4-azidophenyl)-methane **3d** under the conditions optimized for the preparation of **4d** (100 °C in DMSO–H_2O 20 : 1). Polyazide **3d** was isolated after 24 h by flash chromatography (cyclohexane–CH_2Cl_2, 5 : 1) in 41% yield (Scheme 1, entry 6).

Furthermore, all isolated azides containing the adamantane core **4a–d** as well as the methane tetraazide **3d** were analyzed by differential scanning calorimetry and thermal gravimetric measurements were performed.

Obviously, the tetrasubstituted azides **3d** (Fig. 1, Table 1) and **4d** showed the highest exothermicity. A thermal energy of 700 kJ mol^{-1} (1445 kJ kg^{-1}) for polyazide **3d** and 741 kJ mol^{-1} (1225 kJ kg^{-1}) for compound **4d** were measured while heating.

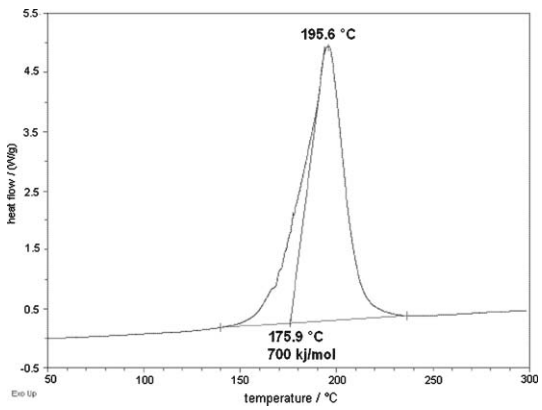


Fig. 1 DSC analysis of tetrakis(4-azidophenyl)methane **3d**.

Depending on the molecule structure, different N_2-eliminations were detected, visible in several $T_{Decomp.}$, T_{max} and ΔH (Table 1). The data for all polyazides are listed in Table 1. Increasing the number of azide functions in a molecule, *e.g.* mono- **4a**, di- **4b**, tri- **4c** and tetrasubstituted **4d** aryl azide derivatives of the adamantane core, goes along with an enhancement of the exothermicity (Table 1). Hence, the expected drift for the exothermic effect could be shown.

Table 1 Data of DSC analysis for all polyazides

Azide	$T_{Decomp.}$ [a] °C	T_{max} [b] °C	Σ ΔH kJ mol^{-1}
3d	175.9	195.6	700
4a	181.8	204.7	73
4b	166.3	198.4	430
	311.6	331.4	
4c	167.9	199.2	435
	344.0	355.1	
4d	174.1	193.9	741

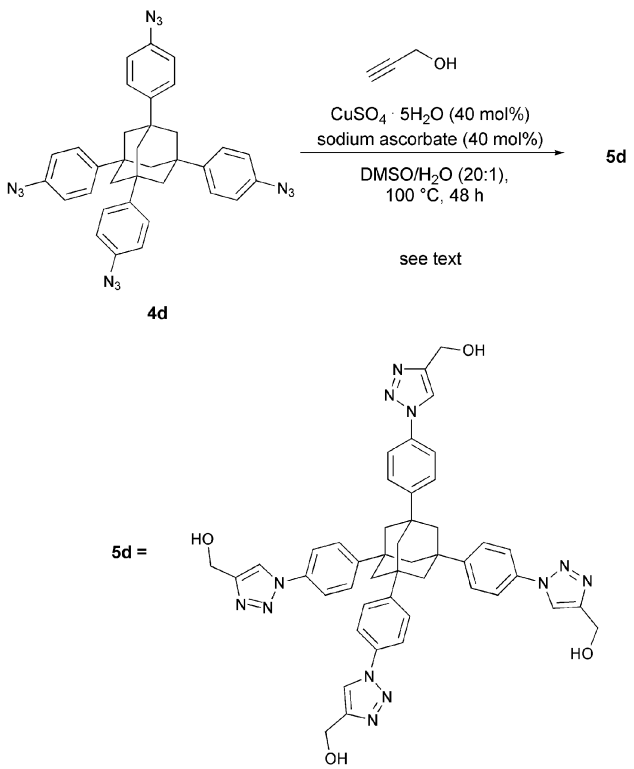
[a] Thermal decomposition starts. [b] Temperature with a maximum energy. [c] Endothermicity was detected more often during the measurement, depending on the structure.

Tetrakis(4-azidophenyl)methane **3d** gave a higher reported heat than polyazide **4d**. The reason may be due to a lower molecular weight and consequently a lower C–N ratio in the core structure. Despite its high energetic potential, we never had problems in isolating this product,[6] compared to an analogue, the unstable azidobenzene (344 kJ mol^{-1} in liquid phase).[23] The decomposition of this azide was measured by Waddell *et al.* and led to molecular explosions upon irradiation in diluted solutions of azidobenzene.[24]

The samples of the polyazides were heated (5.0 K min^{-1}) in an aluminium pan under a N_2-atmosphere. Here, an empty pan acted as a reference.

Thermal gravimetric measurements were performed as further evidence for the molecular structure. Analysis of compound **4d** showed a stepwise mass loss of 19%, 20% and 11% relative to its molecular mass of 604.3 g mol^{-1} caused by the fragmentation of the molecule. Derivative **4a** could also be identified by mass spectrometry (FAB-MS) probably due to the relatively small exothermic effect during thermal decomposition caused by its sole azide functional group. The high thermal energy of all other compounds leads to a complete fragmentation of the sample during ionization. Thus, characterization by mass spectrometry was unsuccessful

Furthermore, a Cu(I)-catalyzed 1,3-dipolar cycloaddition reaction, named as 'click' reaction, was performed with compound **4d** and prop-2-yn-1-ol (12 equiv.), as a terminal alkyne, to form 1,3,5,7-tetrakis(4-(4-hydroxymethyl-1,2,3-triazol-1-yl)phenyl)adamantane **5d**‡ in up to 11% yield (Scheme 2) after purification by flash chromatography (CH_2Cl_2–MeOH, 5 : 1).[7,10] Other conditions, like higher temperatures (100 °C) and longer reaction times (48 h), were required for a successful addition despite the mild conditions reported in previous investigations.[7,8]



Scheme 2 'Click' reaction with polyazide **4d**.

Attempts using less equivalents of alkyne for the cycloaddition led to mono- **5a** (up to 22%) and di-adduct **5b** (up to 14%). The compounds were characterized by ^{1}H and ^{13}C NMR after purification.

Conclusions

In summary, we have successfully synthesized polyazides, based on adamantane and methane cores. Despite the high energetic properties of tetrasubstituted azides (for safety issues, please see ref. 5), measured by differential scanning calorimetry, all synthesized azides were stable and could be handled without special precautions.

Further 'click' reactions with tetrasubstituted azides led to rigid tetrahedral 1,2,3-triazoles with a variety of applicable functional groups for bioconjugations or material sciences.

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Notes and references

‡ Some elected spectral data of **3d**, **4d**, **5d**. For experimental procedures and detailed characterizations of all structures see ESI. 1,3,5,7-Tetrakis(4-azidophenyl)methane (**3d**): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.9$ (dd, $^{3}J = 8.8$ Hz, $^{4}J = 4.9$ Hz, 8 H, Ar_o–H), 7.13 (dd, $^{3}J = 8.8$ Hz, $^{4}J = 4.9$ Hz, 8 H, Ar_m–H) ppm. 1,3,5,7-Tetrakis(4-azidophenyl)adamantane (**4d**): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.10$ (s, 12 H, Ad-CH_2), 7.02 (d, $^{3}J = 8.64$, 8 H, Ar_o–H), 7.45 (d, $^{3}J = 8.64$, 8 H, Ar_m–H) ppm. 1,3,5,7-Tetrakis(4-(4-hydroxymethyl-1,2,3-triazol-1-yl)phenyl)adamantane (**5d**): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.15$ (s, 12 H, Ad–CH_2), 4.61 (s, 6 H, –CH_2OH), 7.53 (d, $^{3}J = 8.8$ Hz, 8 H, Ar_o–H), 7.60 (d, $^{3}J = -8.7$ Hz, 8 H, Ar_m–H), 7.98 (s, 4 H, –*H*C=CCH_2OH) ppm.

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