DOI: 10.1002/chem.201000680

Synthesis of Unusual Oxime Ethers by Reaction of Tetranitromethane with *B*-Alkylcatecholboranes

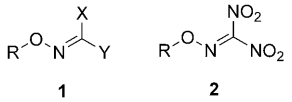
Monique Lüthy,[a] Kurt Schenk,[b] and Philippe Renaud*[a]

Abstract: The reaction of tetranitromethane with *B*-alkylcatecholboranes leads to the formation of unusual dinitrooxime ethers. A tentative mechanism is provided, which suggests the involvement of extremely fast addition of alkyl radicals to tetranitromethane. The substitution of one of the nitro groups in the oxime ethers by nucleophiles (such as secondary amines, halogens and styrene) and by radicals generated from *B*-alkylcatecholboranes is reported.

Keywords: boranes · nitroalkanes · oxime ethers · radical reactions · radical traps

Introduction

Oxime ethers are important sub-structures of biologically active compounds used extensively by the pharmaceutical and agrochemical industries.[1] They are useful motifs with which to introduce diversity and create large libraries of compounds (for example, in parallel combinatorial chemistry,[2] in dynamic combinatorial chemistry with mixed libraries,[3] in libraries that use chemical-domain shuffling[4] and in combinatorial chemistry in the agrosciences).[5] In organic synthesis, oxime ethers are also interesting building blocks because of the electrophilic oxime moiety and for the potential to undergo rearrangement.[6] The chemistry of oxime ethers of the general structure **1** is widely known when R, X and Y are alkyl or aryl substituents.[7] Compounds with the structure **1** that have two heteroatoms bonded to the oxime function (X,Y = heteroatoms) are, in contrast, much less documented in the literature. Sulfur-substituted oxime ethers **1** (X,Y = S) were reported by Kim and Yoon and used in a free-radical acylation reaction.[8] Amino-substituted **1** (X,Y = N,N or N,S) can be easily derived from guanidine or thiourea precursors.[9] *N*-Alkoxyimidoyl halides are also described in the literature but oxime ethers **1** substituted with two halides (X,Y = F, Cl or Br) are extremely rare.[10] The formation of nitrolate ethers **1** (X = NO_2, Y = C) was achieved by self-condensation of 1,1-dinitroalkanes,[11] alkylation of nitrolate salts[12] and methylation of nitrolic acids with diazomethane.[13] To the best of our knowledge, dinitro-substituted oxime ethers of type **2** have not been reported in the literature. Over the last decade, we have demonstrated that *B*-alkylcatecholboranes (RBCat), easily available by hydroboration of alkenes, are remarkable precursors for primary, secondary and tertiary alkyl radicals.[14] During our study on the reactivity of *B*-alkylcatecholboranes, we discovered that they react spontaneously with tetranitromethane to afford dinitrooxime ethers **2**. Herein, we report a detailed study of this unexpected reaction as well as some further transformations of dinitrooxime ethers **2**.



1 **2**

Results and Discussion

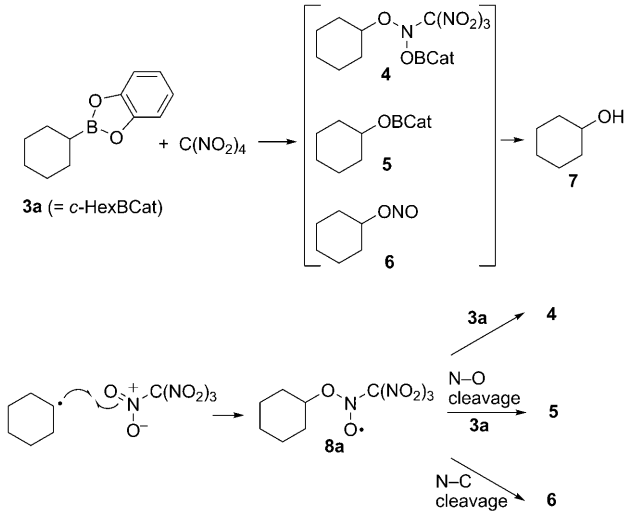
The reaction of tetranitromethane with *B*-cyclohexylcatecholborane (**3a**), prepared in situ from cyclohexene and catecholborane (CatBH), was investigated first. It was anticipated that this reaction should afford cyclohexanol **7** after hydrolysis of one or more of the intermediates **4–6**. Indeed, addition of a radical to the oxygen atom of a nitro group (additions that involve tin,[15] silyl[16] and alkyl[17] radicals are well documented in the literature) should afford the inter-

[a] M. Lüthy, Prof. P. Renaud
Department of Chemistry and Biochemistry, University of Bern
Freiestrasse 3, 3012 Bern (Switzerland)
Fax: (+41) 31-631-3426
E-mail: philippe.renaud@ioc.unibe.ch

[b] Dr. K. Schenk
École Polytechnique Fédérale de Lausanne
Laboratoire de Cristallographie
Le Cubotron, Dorigny, 1015 Lausanne (Switzerland)

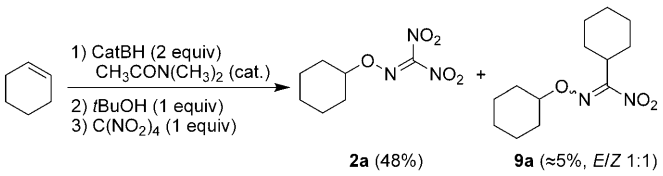
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201000680.

mediate radical **8a**, which was expected to give either **4**, **5** or **6** (or a mixture thereof) after fragmentation. Aqueous workup should produce cyclohexanol **7** in all three cases (Scheme 1).



Scheme 1. Expected reactions between *B*-cyclohexylcatecholborane and tetranitromethane.

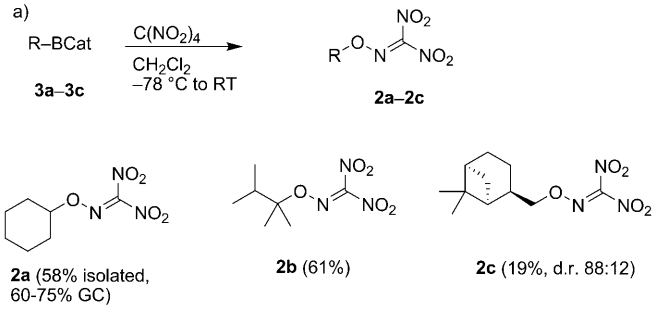
To test our hypothesis, cyclohexene was hydroborated with catecholborane (2 equiv) and catalytic *N,N*-dimethylacetamide in dichloromethane at reflux temperature.[18] The excess of catecholborane was solvolysed with *tert*-butanol and the solution of organoborane **3a** was cooled to −78 °C before a dilute solution of tetranitromethane was slowly added. Without addition of any radical initiator, a spontaneous, highly exothermic reaction took place. The solution was stirred at room temperature before aqueous workup. Analysis of the crude product by GC did not show the presence of cyclohexanol, instead the oxime ether **2a** was isolated in 48% yield by column chromatography (Scheme 2). The

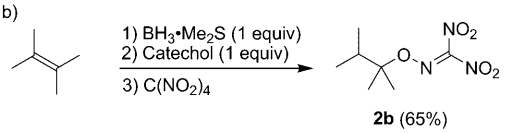


Scheme 2. Reaction of tetranitromethane with *B*-cyclohexylcatecholborane generated in situ from cyclohexene.

structure of **2a** was determined by multinuclear NMR spectroscopy. The ^{14}N NMR spectra revealed the three nitrogen atoms as two strong singlets ($\delta = -32.9$ and -40.9 ppm relative to CH_3NO_2) for the nitro groups and a broad flat peak ($\delta = -18.8$ ppm). According to this data, rotation around the C=N double bond is prevented. Furthermore, $^{1}H/^{15}N$ HMBC analysis suggested a C–O–N connectivity of the alkyl group and excluded a direct C–N connection because only one coupling interaction was observed. A small amount of a side product, unambiguously identified as the mononitrooxime ether **9a** (5%), was also isolated. Attempts to optimize the reaction conditions by the use of an excess of tetranitromethane were unsuccessful and led to lower yield and several unidentified side reactions. The use of an excess of **3a** resulted in enhanced formation of the side-product **9a** (see below).

The scope of the reaction was examined (Scheme 3a). To avoid problems associated with the in situ formation of the boronate, pure boronates **3a–c** were prepared and distilled



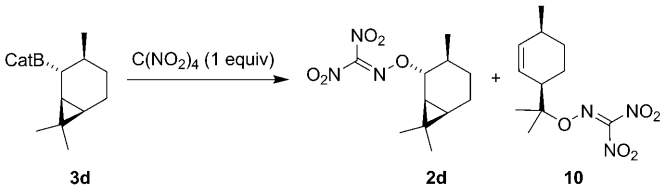


Scheme 3. Reaction of *B*-alkylcatecholboranes **3** with tetranitromethane.

under inert atmosphere prior to use.[19] The reaction of pure **3a** with tetranitromethane (1 equiv) gave **2a** in 60–75% yield (GC). Due to product contamination by traces of **9a**, the dinitrooxime ether **2a** must be chromatographed twice, which results in a decreased isolated yield (58%). We next studied the reaction with boronates **3b** and **3c**, which have a tertiary and primary alkyl group, respectively. Whereas the tertiary alkylcatecholborane **3b** was as efficient as **3a** (**2b**, 61%), the primary alkylboronate **3c** afforded **2c** only in low yield (19%). With this latter substrate, side products are formed but none of them could be clearly identified. For instance, a double-addition product similar to **9a** was not observed. Similar results were obtained with *B*-*n*-propyl- and *B*-*n*-octylcatecholboranes. Nevertheless, the preparation of secondary and tertiary *O*-alkyl dinitro methanone oximes is possible and a one-pot procedure from hindered tri- or tetra-substituted olefins can be envisaged. For example, when **3b** was generated in situ by hydroboration of 2,4-dimethyl-2-butene with borane dimethyl sulfide complex[20] followed by subsequent esterification with catechol, the reaction with tetranitromethane afforded **2b** in 65% isolated yield from the alkene (Scheme 3b).

From our past experience of *B*-alkylcatecholborane-mediated reactions, it was expected that alkyl radicals were in-

volved in the process. To substantiate this assumption, the boronate **3d**, generated from (+)-carene, was used as a radical probe (Scheme 4 and Figure 1). The boronate **3d** was



Scheme 4. Radical probe experiment with *B*-alkylcatecholborane **3d**, derived from (+)-carene.

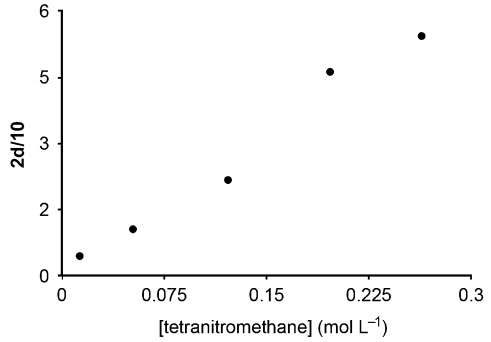
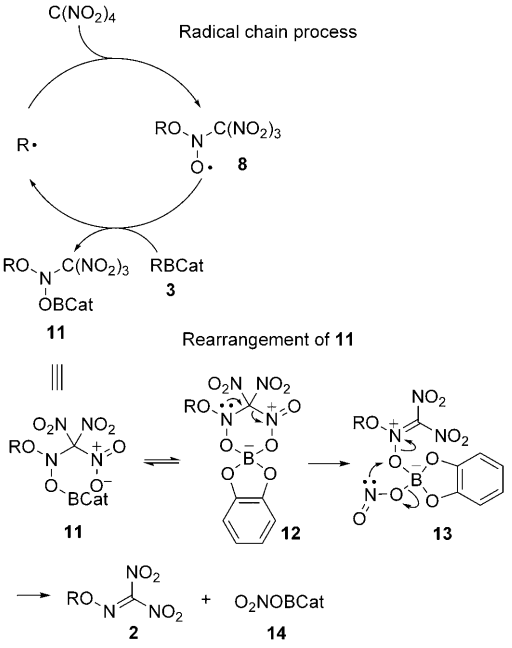


Figure 1. Influence of the concentration of tetranitromethane on the reaction of **3d** depicted in Scheme 4.

previously used as a successful probe to demonstrate the presence of radical intermediates in reactions that involve *B*-alkylcatecholboranes.[21] Reaction of **3d** with tetranitromethane gives a mixture of the bicyclic compound **2d** and monocyclic compound **10**. The ratio of **2d**/**10** was determined by GC analysis. The GC yields were only moderate (cumulative yields of **2d** and **10** ranged between 26 and 34%), however, this was sufficient to identify a clear trend in the results. It was found that the ratio **2d**/**10** varies substantially upon changes of tetranitromethane concentration (Figure 1). Under the standard conditions used in Scheme 3 ($[C(NO_2)_4]=0.19$ M), the major product was the non-rearranged **2d**. At lower concentration ($[C(NO_2)_4]\leqq 0.02$ M), the product **10**, a result of cyclopropane ring opening, becomes the major product. This behaviour suggests that a very fast reaction takes place between the alkyl radical and tetranitromethane. The modest yield of the process did not allow for a precise kinetic study, but it is evident that tetranitromethane is one of the fastest radical traps described to date. This is in accordance with the work of Steenken et al. who reported that addition of the methoxymethyl radical to tetranitromethane occurs with a rate constant of 6×10^9 $M^{-1}s^{-1}$.[17a]

On the basis of these results, a tentative mechanism is proposed in Scheme 5. This mechanism involves an efficient radical-chain process followed by a rearrangement to the



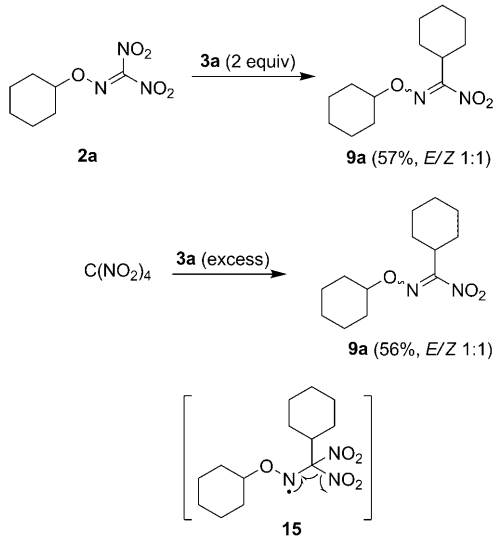
Scheme 5. Tentative mechanism for the reaction of *B*-alkylcatecholboranes **3** with tetranitromethane.

product. The radical process involves fast addition of the alkyl radical to tetranitromethane to afford the aminoxyl radical **8**.[17] This type of radical are known to decompose slowly when R = methoxymethyl to afford the methoxymethyl cation, NO_2 and the nitroform anion $(NO_2)_3C^-$ ($k=1.1\times 10^4$ s^{-1} at 2 °C).[17a] When a *B*-alkylcatecholborane **3** is present, fast reaction with **8** should overcome the radical-fragmentation process and lead to the borate ester **11**, accompanied by regeneration of the starting alkyl radical. This step is closely related to the fast reaction observed between nitroxides, such as 2,2,6,6-tetramethylpiperidine *N*-oxide (TEMPO), and *B*-alkylcatecholboranes.[21,22] The radical process may be initiated by traces of oxygen or by a single-electron-transfer process between tetranitromethane and the *B*-alkylcatecholborane, which leads to an alkyl radical, a boron nitronate of nitroform and nitrogen dioxide.[23] The relative inefficiency of the reaction observed with primary *B*-alkylcatecholboranes may be explained by the fact that the reaction between **8** and organoborane **3**, a two-step process that involves the reversible formation of a complex followed by an irreversible fragmentation process, is not taking place efficiently. This increases the lifetime of **8**, which finally decomposes, probably by β-fragmentation of the trinitromethyl radical, and leads to a range of unidentified side products. The second part of the mechanism represents a rearrangement of the borate **11**. Borate **11** is probably in equilibrium with the ate complex **12**, which may decompose to give **13** and, after a final rearrangement, lead to the dinitrooxime ether **2** and the nitrate boronate **14**.

The following two observations are in accordance with the proposed mechanism. Firstly, reaction of tricyclohexylborane[24] with tetranitromethane requires initiation with air

and only affords traces of the oxime **2a**. It is to be expected that the radical steps, in particular the reaction of the aminoxyl radical **8** with tricyclohexylborane, will be less efficient because trialkylboranes are far less reactive in radical-chain processes than *B*-alkylcatecholboranes. Secondly, an attempt was made to use 1,1-dinitrocyclohexane[25] instead of tetranitromethane. Under the standard conditions, no oxime formation was observed; under initiation with air, partial decomposition of **3a** was observed and 1,1-dinitrocyclohexane was partly recovered. This could be explained by the lower reactivity of 1,1-dinitrocyclohexane relative to tetranitromethane as a radical trap, by the absence of an efficient initiation mechanism based on a single-electron-transfer process or by the inefficiency of the rearrangement depicted in Scheme 5 (**11**→**2**) when the *gem*-dinitro groups are replaced by alkyl residues.

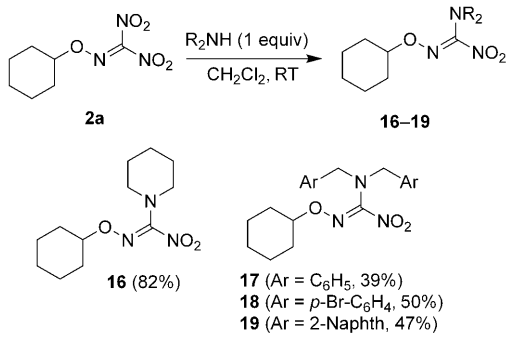
The reaction of the dinitrooxime ether **2a** with *B*-alkylcatecholborane **3a** was examined to determine the origin of the side-product **9a**. The reaction affords **9a** as a 1:1 *E*/*Z* mixture in 56% yield (GC). A similar yield of **9a** was obtained from the reaction of tetranitromethane with an excess of boronate **3a** (Scheme 6). Interestingly, the analo-



Scheme 6. The reaction of **2a** with *B*-alkylcatecholborane **3a**.

gous side reaction of tetranitromethane with **2b** was not observed, presumably due to increased steric hindrance. We assume that the formation of **9a** involves addition of the cyclohexyl radical to the oxime moiety to afford the radical adduct **15**, followed by β-fragmentation of nitrogen dioxide. The radical mechanism of this process was further supported by the fact that no reaction takes place between **2a** and cyclohexylpinacolborane under similar reaction conditions. Indeed, it is well established that alkylpinacolboranes are very poor radical precursors.

The reactivity of the unusual oxime ether **2a** was also investigated. It was found that one of the nitro groups could be easily displaced by weakly nucleophilic species. Analogous to the derivatisation of nitrolate methyl ethers presented by Walser and Fryer,[13] a variety of amines displaced one of the nitro groups in **2a** (Scheme 7). The reaction of **2a**



Scheme 7. Reaction of dinitrooxime ether **2a** with secondary amines.

with piperidine in dichloromethane at room temperature afforded **16** in 82% yield as a single stereoisomer. When an excess of piperidine is used only one nitro group is substituted.[26] Similar results were obtained with dibenzylamine, bis(4-bromobenzyl)amine and bis(naphth-2-ylmethyl)amine; compounds **17**–**19** were obtained in 39–50% unoptimised yield. Compound **19** afforded single crystals suitable for X-ray analysis, which confirmed the *E* geometry of the oxime moiety (see Figure 2 and the Supporting Information).[27] It is very likely that **16**–**18** also possess the *E* geometry. Indirectly, the X-ray crystal structure of **19** confirmed the postulated structure of the dinitrooxime ether **2a**.

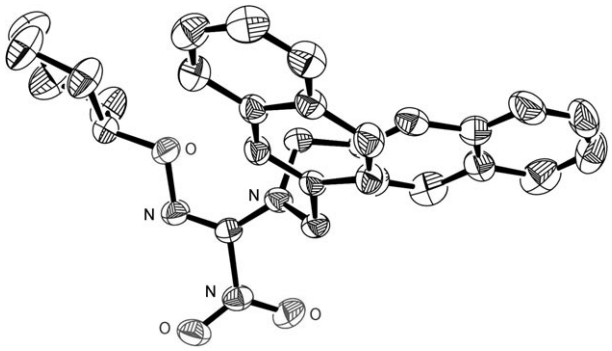
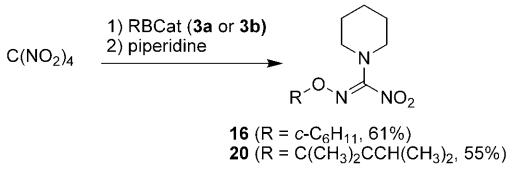


Figure 2. X-ray crystal structure of **19**.

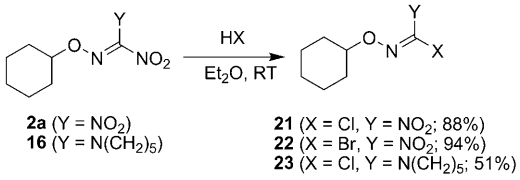
The substitution of one nitro group by piperidine could also be performed in a sequential manner. Reaction of *B*-alkylcatecholboranes **3a** and **3b** with tetranitromethane, followed by treatment with piperidine directly afforded the mono-nitro derivatives **16** and **20** in 61 and 55% yield, respectively (Scheme 8).

The displacement of the nitro group in nitrolate ethers by a solution of hydrogen chloride in alcohol was observed in 1955.[11b] An identical derivatisation of **2a** with chloride or bromide was achieved upon treatment with aqueous HCl or



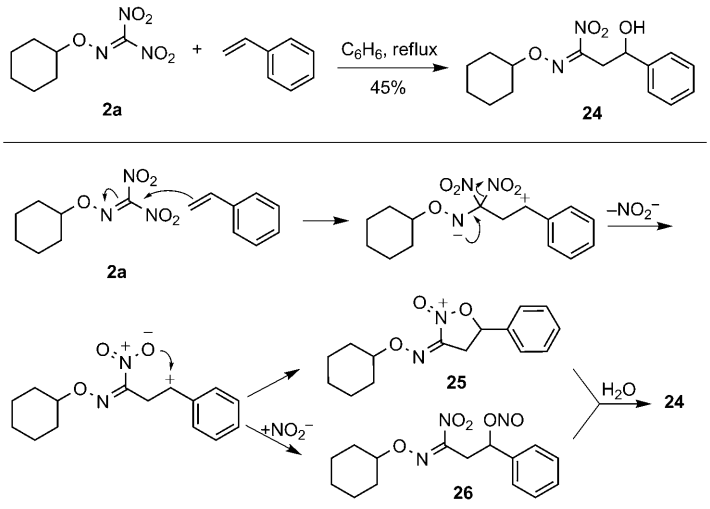
Scheme 8. Sequential one-pot reaction of tetranitromethane with *B*-alkylcatecholboranes **3** and piperidine.

HBr, respectively. The acid-catalysed reaction in ether at room temperature afforded the chloro and bromo derivatives **21** and **22** in good yields as single isomers (Scheme 9). The two remaining nitrogen atoms were visualised by ^{14}N NMR and $^{1}H/^{15}N$ HMBC spectroscopic analysis. The relative configurations of **21** and **22** were not determined. Under similar conditions, ether **23** was generated from **16** in moderate yield. The single isomer **23** showed a slow isomerisation upon standing for several months to give a mixture of *E* and *Z* isomers.



Scheme 9. Reaction of **2a** and **16** with HX (X = Cl, Br).

The reaction of **2a** with different olefins was examined. With most alkenes, including tetramethylethylene, 3,3-dimethylbut-1-ene and methyl acrylate, no reaction was observed. With allylsilane the disappearance of **2a** was observed but no product could be identified. Interestingly, it was found that styrene added to the oxime moiety and substituted a nitro group to give product **24** (Scheme 10). The reaction is slow at ambient temperature (several days) but **24** was isolated in 45% yield after reaction in hot benzene for 15 h. A plausible mechanism involves electrophilic addition of **2a** to styrene, nitrite elimination and formation of the cyclic intermediate **25** or the nitrite ester **26**, both of which can undergo hydrolysis to give **24** (Scheme 10).



Scheme 10. Reaction of **2a** with styrene.

Conclusion

The reaction of tetranitromethane with *B*-alkylcatecholboranes leads to the formation of unusual dinitrooxime ethers. A radical mechanism that involves extremely fast addition of alkyl radicals to tetranitromethane is proposed. Furthermore, we have demonstrated that substitution of one of the nitro groups by nucleophiles or alkyl radicals generated from *B*-alkylcatecholboranes is possible.

Experimental Section

Preparation of reagents

Tetranitromethane: Prepared according to the literature procedure.[28] The isolated tetranitromethane (9.36 g, 38%), a colourless crystalline solid, was stored at 4°C. M.p. 14°C; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 118.6$ ppm (nonet, $J(C,N) = 9.4$ Hz). Spectral data are in accordance with the literature.[29] ***Caution!*** Tetranitromethane is a weak but highly sensitive explosive. Conditions contributing to instability: heat, sparks and open flames. In the presence of impurities tetranitromethane may be highly explosive. Mild shocks can ignite combustible organic matter that is wet with tetranitromethane.

*2-Cyclohexylbenzo[d][1,3,2]dioxaborole (**3a**)*: A mixture of cyclohexene (5.1 mL, 50 mmol) and catecholborane (6.4 mL, 60 mmol) was stirred at 100°C for 16 h. The disappearance of the olefinic protons was followed by ^{1}H NMR spectroscopy in degassed C_6D_6 under nitrogen atmosphere. The mixture was transferred by cannula to a distillation apparatus and the excess of catecholborane was removed ($p = 25$ mbar, $T = 45$°C). The crude product was distilled under vacuum ($p = 10^{-1}$ mbar, $T = 90$°C) to afford **3a** as a colourless liquid. ^{1}H NMR (300 MHz, C_6D_6): $\delta = 7.07$–7.01 (m, 2H), 6.83–6.77 (m, 2H), 1.90–1.80 (m, 2H), 1.65–1.47 (m, 5H), 1.39–1.23 ppm (m, 4H); ^{13}C NMR (75 MHz, C_6D_6): $\delta = 148.9$, 122.7, 112.6, 28.2, 27.3, 27.0, 22.0 ppm (br; C–B); ^{11}B NMR (160 MHz, C_6D_6): $\delta = 35.8$ ppm.

*2-(2,3-Dimethylbutan-2-yl)benzo[d][1,3,2]dioxaborole (**3b**)*: A mixture of 2,3-dimethyl-2-butene (1.2 mL, 10 mmol) and borane dimethyl sulfide (90% in SMe_2, 1.1 mL, 10 mmol) was stirred at 0°C for 2.5 h. CH_2Cl_2 (8 mL) was added and the mixture was transferred by cannula to a suspension of catechol (1.1 g, 10 mmol) in CH_2Cl_2 (5 mL) at 0°C. Hydrogen evolution was observed. The mixture was stirred at 0°C for 3 h and then at RT for 1 h. The solvents and dimethyl sulfide were removed in vacuo. The crude product was filtered under inert atmosphere (glove box) to afford **3b** as a colourless liquid. ^{1}H NMR (300 MHz, C_6D_6): $\delta = 7.08$–7.01 (m, 2H), 6.81–6.76 (m, 2H), 1.77 (sept, $J = 6.9$ Hz, 1H), 1.14 (s, 6H), 0.90 ppm (d, $J = 6.9$ Hz, 6H); ^{13}C NMR (75 MHz, C_6D_6): $\delta = 148.8$, 122.8, 112.7, 35.9, 22.1, 19.0 ppm.

Radical addition to tetranitromethane

Method a: *Synthesis of dinitromethanone O-alkyl oximes from B-alkylcatecholboranes (**2a**)*: A solution of tetranitromethane (4 mmol) in CH_2Cl_2 (6 mL) was cautiously added to a solution of *B*-alkylcatecholborane **3a** (808 mg, 4 mmol) in CH_2Cl_2 (12 mL) over a period of 10 min at −78°C. After complete addition, more CH_2Cl_2 (2 mL) was added. During the addition the solution turned yellow and finally into a dark-brown mixture. The mixture was stirred overnight and allowed to warm up slowly from

−78 °C to RT. Filtration of the crude reaction mixture over a pad of silica gel then short flash chromatography on silica gel (100:0, 98:2, 90:10 pentane/Et_2O) gave crude **2a** contaminated by side-product **9a** (4%) (GC evaluation). Purification by a second flash chromatography (pentane/0–1% Et_2O) afforded **2a** (511 mg, 58%) as a pale-yellow liquid.

Method b: *One-pot procedure from cyclohexene (1–8 mmol scale)*: Catecholborane (1.7 mL, 16 mmol) was added to a solution of cyclohexene (0.81 mL, 8 mmol) and *N,N*-dimethylacetamide (0.11 mL, 1.2 mmol) in CH_2Cl_2 (16 mL). The mixture was stirred at 40 °C for 5 h. After cooling to 0 °C, *tert*-butanol (0.75 mL, 8 mmol) was added to solvolyse the excess of catecholborane. Hydrogen evolution was observed. The solution was stirred at RT for 30 min and then further diluted with CH_2Cl_2 (9 mL). The reaction mixture was cooled to −78 °C and a solution of tetranitromethane (1.57 g, 8 mmol) in CH_2Cl_2 (10 mL) was cautiously added through a dropping funnel over a period of 25 min. A yellow colouration of the reaction mixture was observed after addition of the first few drops. With further addition the reaction mixture turned a dark-brown colour and some brown vapour was observed. After complete addition, more CH_2Cl_2 (3 mL) was added and the reaction was stirred at −78 °C for 5 min. The cooling bath was removed and the mixture allowed to warm to RT. The reaction mixture turned black immediately and was stirred overnight at RT. The mixture was purified by flash chromatography on silica gel (99:1, 95:5, 90:10 cyclohexane/*tert*-butyl methyl ether) afforded **2a** (839 mg, 48%) as a pale yellow liquid (contaminated by traces of side-product **9a**). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 4.56$–4.48 (m, 1H), 2.04–1.97 (m, 2H), 1.81–1.71 (m, 2H), 1.68–1.51 (m, 3H), 1.45–1.26 ppm (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 146.6$ (br), 89.8, 30.9, 25.0, 23.3 ppm; ^{14}N NMR (36 MHz, $CDCl_3$): $\delta = -18.8$ (br, 1N; oxime N, exact value taken from the ^{15}N-trace of the ^{1}H/^{15}N-HMBC spectra), −32.9 (s, 1N; NO_2), −40.9 ppm (s, 1N; NO_2); IR (film): $\tilde{\nu} = 2942$, 2863, 1557, 1451, 1322, 1050, 1004 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 171 [$M^+ - NO_2$] (2), 98 (10), 83 (99), 67 (30), 55 (100); elemental analysis calcd (%) for $C_7H_{11}N_3O_5$: C 38.71, H 5.10, N 19.35; found: C 38.85, H 5.04, N 19.47.

Cyclohexyl(nitro)methanone *O*-cyclohexyl oxime (9a): Compound **3a** (96 mg, 0.475 mmol) was added to a solution of **2a** (87 mg, 0.4 mmol) in CH_2Cl_2 (1 mL) at 0 °C. The solution turned yellow, then brown and finally black. The reaction mixture was stirred at 0 °C for 3 h and then at RT for 4 h. The black mixture was purified by flash chromatography on silica gel (100:0, 98:2 pentane/Et_2O). Residual starting material was removed by a second flash chromatography (pentane/0–1% Et_2O) to afford **9a** (30 mg, 30%, $E/Z \approx 1{:}1$) as a yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 4.24$–4.15 (m, 1H), 4.12–4.03 (m, 1H), 3.21–3.11 (m, 1H), 2.64–2.54 (m, 1H), 1.99–1.64 (m, 20H), 1.57–1.20 ppm (m, 20H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 164.7$, 156.1, 84.2, 82.8, 38.7, 37.0, 31.3, 31.1, 29.3, 27.7, 26.1, 25.63, 25.61, 25.60, 25.55, 25.4, 23.6, 23.5 ppm; IR (film): $\tilde{\nu} =$ 2933, 2856, 1539, 1450, 1046, 983 cm^{-1}; MS (EI, GC-MS, 70 eV): *m*/*z* (%): first isomer: 208 [$M^+ - NO_2$] (3), 126 (100), 98 (8), 93 (18), 83 (43), 67 (27), 55 (52), 41 (38); second isomer: 208 [$M^+ - NO_2$] (2), 126 (32), 98 (4), 93 (8), 83 (100), 67 (14), 55 (54), 41 (29).

*GC determination of yield from **2a***: At 0 °C, a solution of **3a** (206 mg, 1.02 mmol) in CH_2Cl_2 (1 mL) was added to a solution of **2a** (111 mg, 0.51 mmol) in CH_2Cl_2 (1 mL). The mixture was stirred at RT for 19 h. Undecane (100 μL, 0.473 mmol) was added to the black reaction mixture as a standard for yield determination by GC (GC: HP-5890; column: HP Ultra 2, length: 10 m; pressure: 0.80 bar; starting temperature: 40 °C, hold: 1 min, rate: 6 °C min^{-1}). Yield of **9a** = 57%, *E*/*Z* or *Z*/*E* = 1:1.03; retention time (t_R) = 23.2 and 23.7 min.

GC determination of yield from tetranitromethane: At −78 °C, a solution of tetranitromethane (100 mg, 0.5 mmol) in CH_2Cl_2 (0.75 mL) was added cautiously to a solution of **3a** (410 mg, 2 mmol) in CH_2Cl_2 (1.7 mL) over a period of 10 min. More CH_2Cl_2 (0.3 mL) was added after complete addition. The dry-ice bath was removed and the black mixture was stirred at RT for 15 h. Undecane (100 μL, 0.473 mmol) was added to the reaction mixture as a standard for yield determination by GC. Yield of **9a** = 56%, *E*/*Z* or *Z*/*E* = 1:1.07.

Nitro(piperidin-1-yl)methanone *O*-cyclohexyl oxime (16)

Method a: *Synthesis from **2a***: Piperidine (70 μL, 0.71 mmol) was added to a solution of **2a** (62 mg, 0.28 mmol) in CH_2Cl_2 (1 mL) at 0 °C. The solution immediately turned a dark-yellow colour. The reaction mixture was stirred at 0 °C for 1 h and then at RT for 3.5 h. The mixture was extracted with Et_2O. The combined organic layers were washed with water and brine then dried over anhydrous Na_2SO_4, filtered and the solvents were removed under reduced pressure. Purification by flash chromatography (98:2 pentane/Et_2O) afforded **16** (59 mg, 82%) as a dark-yellow liquid.

Method b: *One-pot synthesis from **3a***: A solution of tetranitromethane (1 mmol) in CH_2Cl_2 (1.5 mL) was added cautiously to a solution of **3a** (213 mg, 1.05 mmol) in CH_2Cl_2 (3.2 mL) at −78 °C over a period of 10 min. After complete addition, more CH_2Cl_2 (0.5 mL) was added. The reaction mixture was stirred overnight and allowed to warm up slowly from −78 °C to RT. At 0 °C, piperidine (4 mmol) was slowly added. Some brown vapour was observed. The mixture was stirred at 0 °C for 1 h and then at RT for 4 h. The dark mixture was purified by flash chromatography on silica gel (98:2, 96:4 pentane/Et_2O) to afford **16** (162 mg, 61%) as a dark-yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 4.08$–4.02 (m, 1H), 3.17–3.15 (m, 4H), 1.96–1.92 (m, 2H), 1.73–1.61 (m, 8H), 1.55–1.44 (m, 3H), 1.40–1.25 ppm (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 82.8$, 48.6, 31.3, 25.7, 25.6, 23.9, 23.6 ppm; IR (film): $\tilde{\nu} = 2933$, 2856, 1656, 1543, 1450, 1200, 993 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 255 [M]$^+$ (3), 209 (20), 127 (35), 111 (77), 99 (9), 81 (41), 69 (34), 55 (100), 41 (58); elemental analysis calcd (%) for $C_{12}H_{21}N_3O_3$: C 56.45, H 8.29, N 16.46; found: C 56.48, H 8.37, N 16.44.

Acknowledgements

This work was supported by the Swiss National Science Foundation (grant numbers 21-67106.01 and 7SUPJ062348). We thank BASF Corporation for a donation of chemicals and Dr. Kandhasamy Sarkunam for running preliminary experiments that triggered our study.

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Received: March 17, 2010
Revised: May 14, 2010
Published online: July 19, 2010

