Communication

2-(4-(Dimethylamino)phenyl)-3,3-difluoro-4,6-diphenyl-3,4-dihydro-1,2,4,5,3-tetrazaborinin-2-ium-3-ide

Ida A. Lupanova, Dzhamiya N. Konshina, Nikita A. Elkov and Valery V. Konshin *

Abstract: Reaction of 1-(4-(dimethylamino)phenyl)-3,5-diphenylformazane with boron trifluoride diethyl etherate (5 equiv) in the presence of triethylamine (3 equiv) in toluene medium gave “boratetrazine”—2-(4-(dimethylamino)phenyl)-3,3-difluoro-4,6-diphenyl-3,4-dihydro-1,2,4,5,3-tetrazaborinin-2-ium-3-ide in a 58% yield.

Keywords: formazane; boron trifluoride; boron chelate

1. Introduction

Various boron chelates are some of the most common fluorophores, finding widespread practical application in bioimaging [1], as molecular reporters and chemodosimeters [2,3], in sensors [4–6], in optoelectronic applications [7–9] and others. The most studied are BODIPY [10–12] and their structural analogs 2 [13], BOPHY 3 [14], boron difluoride 1,3-diketonates 4 [15] and 1,3-ketoiminates 5 [16]. Difluoroboron derivatives of different types of hydrazones 6 [17], such as N-acylhydrazones 7 [18] and azohydrazones (formazanes) 8 [19] (Figure 1), are also of interest and are being extensively studied at the present time.

Figure 1. Examples of various boron chelates.

The pioneering work on the reaction of formazans with boron trifluoride diethyl etherate showed it to afford triphenyltetrazolium tetrafluoroborate [20]. Later, the first representatives of boron formazanate complexes, “boratetrazines” 10, were obtained by the
The reaction of formazans with diboron tetraacetate (in situ synthesized from boric acid, acetic acid and acetic anhydride) (Scheme 1) [21].

![Scheme 1: Examples of preparation “boratetrazines”](image)

The purposeful study of boron formazanates was started in 2007 by Gilroy et al. [22]. Later, efficient synthesis of them was proposed in toluene medium in the presence of triethylamine [23]. Different derivatives based on cyano- [24], nitro- [25] and triarylformazans [19,26-29] have been obtained.

The reaction between boron trifluoride etherate and more complex substrates containing additional groups, which can coordinate to the boron, proceeds nontrivially, as in the case of 11-14 (Figure 2), where coordination is realized through the oxygen atom [30-33].

![Figure 2: Examples of various boron formazanates](image)

To date, only one representative of “boratetrazines” having a donor N,N-dialkylamino group has been described [34]. It was prepared from cyanoformazan containing the 4-(dimethylamino)phenyl fragment in the N1 and N5 positions. The aim of the present work was to study the reaction of triarylformazan containing the N,N-dialkylamino group in the N1 position with boron trifluoride etherate.

2. Results and Discussion

To begin, 1-(4-(dimethylamino)phenyl)-3,5-diphenylformazan 17 was synthesized from phenylhydrazone benzaldehyde 15 [35] and diazotized N,N-dimethyl-p-phenylenediamine in a pyridine medium (Scheme 2). The target formazane 17 was purified by flash chromatography and recrystallization from ethanol. Its physical constants and spectral data are in agreement with the literature data [36].

![Scheme 2: Synthesis of 1-(4-(dimethylamino)phenyl)-3,5-diphenylformazan 17](image)
The reaction of 1-(4-(dimethylamino)phenyl)-3,5-diphenylformazan 17 with fivefold excess boron trifluoride diethyl etherate was performed in the presence of threefold excess triethylamine in toluene medium. Monitoring of the reaction by analytical thin-layer chromatography (TLC) showed that complete conversion was achieved after 5 h of stirring the reaction mixture at 90 °C (Scheme 3).

Scheme 3. Reaction of 1-(4-(dimethylamino)phenyl)-3,5-diphenylformazan 17 with boron trifluoride diethyl etherate.

After flash chromatography and recrystallization from ethanol, the yield of target “boratetrazine” 18 was 58%.

The structure of 2-(4-(dimethylamino)phenyl)-3,3-difluoro-4,6-diphenyl-3,4-dihydro-1,2,4,5,3-tetrazaborinin-2-ium-3-ide 18 was unambiguously confirmed by single-crystal X-ray analysis (Figure 3) and 1H, 13C, 11B, 19F NMR and mass spectrometry.

Figure 3. Crystal structure of compound 18 with labeling schemes and 50% thermal ellipsoids.

In conclusion, it was shown that the reaction of triarylformazane with a donor dimethylamino group 17 with boron trifluoride etherate leads to the formation of “boratetrazine” 18. The notion that the coordination of boron occurs only due to the azohydrazone fragment was confirmed.

3. Materials and Methods

The reactions were monitored by thin-layer chromatography (Sorbfil, Imid Ltd., Krasnodar, Russia). The 1H-NMR, 13C-NMR, 11B-NMR and 19F-NMR spectra were acquired on ECA400 (JEOL) (400 and 100 MHz, respectively) spectrometers in CDCl3 at room temperature. The chemical shifts δ were measured in ppm with reference to the residual solvent resonances (1H: CDCl3, δ = 7.25 ppm; 13C: CDCl3, δ = 77.2 ppm). The splitting patterns are referred to as s, singlet; d, doublet; t, triplet; m, multiplet. Coupling constants (J) are given in hertz. IR spectra were recorded on an IR Prestige (Shimadzu, Kyoto, Japan), using tablets of samples with KBr. High-resolution and accurate mass measurements were carried out using a Bruker MaXis Impact (electrospray ionization/time of flight). The melting points were determined on a Stuart SMP30 apparatus and left uncorrected. The commercial reagents employed in the synthesis were benzaldehyde (for synthesis, ≥99.0%, Aldrich,
St. Louis, MO, USA), Phenylhydrazine (for synthesis, ≥97%, Aldrich, St. Louis, MO, USA) and \textit{N,N-Dimethyl-p-phenylenediamine dihydrochloride} (≥99%, Vekton, Russia), boron trifluoride diethyl etherate (for synthesis, ≥97%, Aldrich, St. Louis, MO, USA). CCDC 1919508 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at http://www.ccdc.cam.ac.uk/or (accessed on 29 November 2021) from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44-1223-336033; E-mail: deposit@ccdc.cam.ac.uk.

3.1. 1-(4-(Dimethylamino)phenyl)-3,5-diphenylformazan (17)

Diazoium salt solution (obtained from 3.52 g (0.0168 mol) \textit{N,N-dimethyl-p-phenylenediamine dihydrochloride}, 1.16 g NaNO\textsubscript{2} and 4 mL conc. HCl in 30 mL water) was added to a solution of 3.5 g (0.0153 mol) of phenylhydrazine benzaldehyde in 100 mL pyridine at −5 °C. Then, a solution of 2.5 g NaOH in 6 mL water was added and stirred at −5 °C for 1 h. Then, the temperature was raised to 15 °C and the reaction mixture was allowed to stand for 6 h. The reaction mixture was poured into 500 mL of cooled 2M HCl; the resulting brown precipitate was filtered off, washed on a filter with water and dried in the desiccator. It was purified by flash chromatography on alumina (neutral) eluting with a hexane–dichloromethane mixture (10:1) and subsequent recrystallization from ethanol. Yield 2.78 g (53%); violet–black microcrystalline solid; mp 184–185 °C.

This compound has the following supplementary crystallographic data:

\textbf{Crystal data for C\textsubscript{21}H\textsubscript{20}BF\textsubscript{2}N\textsubscript{3}}

\[\text{M} = 391.25 \text{ g/mol}\] ~ monoclinic, space group \textit{P2\textsubscript{1}/c}, \(a = 17.9429(15)\ \text{Å}, b = 13.3212(11)\ \text{Å}, c = 8.1555(7)\ \text{Å}, \alpha = 90°, \beta = 93.752(2)°, \gamma = 90°, V = 1945.2(3)\ \text{Å}^3, Z = 4, T = 120 \text{ K}, \mu = 0.95 \text{ cm}^{-1}, Dcalc. = 1.36 \text{ g/cm}^3. \]

In total, 26,190 reflections were measured, 4241 of which were unique and used in all calculations. The final \(R\_1\) was 0.0438, and the \(wR_2\) was 0.1360 (all data) (SI, Tables S1–S5).

3.2. 2-(4-(Dimethylamino)phenyl)-3,3-difluoro-4,6-diphenyl-3,4-dihydro-1,2,4,5,3-tetrazaborinin-2-ium-3-ide (18)

Triethylamine 0.237 mL (1.7 mmol) was added to a solution of 0.2 g (0.58 mmol) of 1-(4-(dimethylamino)phenyl)-3,5-diphenylformazan in 15 mL of dry toluene, stirred for several minutes and 0.358 mL (2.9 mmol) boron trifluoride diethyl etherate was added. The reaction mixture, colored dark blue, was incubated at 90 °C for 5 h. Then, it was transferred to a separating funnel, washed with water, and the toluene layer was dried with Na\textsubscript{2}SO\textsubscript{4}. After separation of the drying agent and concentration under vacuum, the residue was purified by flash chromatography (silica, hexane–dichloromethane eluting with a hexane–dichloromethane mixture (10:1) and subsequent recrystallization from ethanol. Yield 2.78 g (53%); violet–black microcrystalline solid; mp 184–185 °C.

This compound has the following supplementary crystallographic data:

\textbf{Crystal data for C\textsubscript{21}H\textsubscript{20}BF\textsubscript{2}N\textsubscript{3}}

\[\text{M} = 391.25 \text{ g/mol}\] ~ monoclinic, space group \textit{P2\textsubscript{1}/c}, \(a = 17.9429(15)\ \text{Å}, b = 13.3212(11)\ \text{Å}, c = 8.1555(7)\ \text{Å}, \alpha = 90°, \beta = 93.752(2)°, \gamma = 90°, V = 1945.2(3)\ \text{Å}^3, Z = 4, T = 120 \text{ K}, \mu = 0.95 \text{ cm}^{-1}, Dcalc. = 1.36 \text{ g/cm}^3. \]

In total, 26,190 reflections were measured, 4241 of which were unique and used in all calculations. The final \(R\_1\) was 0.0438, and the \(wR_2\) was 0.1360 (all data) (SI, Tables S1–S5).
Supplementary Materials: The following supporting information can be downloaded. Figure S1: IR-spectrum of 17; Figure S2: $^1$H NMR of 17; Figure S3: $^{13}$C NMR of 17; Figure S4: HRMS of 17; Figure S5: IR-spectrum of 18; Figure S6: $^1$H NMR of 18; Figure S7: $^{13}$C NMR of 18; Figure S8: $^{19}$F NMR of 18; Figure S9: $^{11}$B NMR of 18; Figure S10: HRMS of 18; Tables S1–S5: Crystal data of 18.

Author Contributions: Conceptualization, V.V.K; methodology, V.V.K; software, D.N.K.; validation, V.V.K. and D.N.K.; formal analysis, D.N.K.; investigation, I.A.L. and N.A.E.; resources, I.A.L. and N.A.E.; data curation, V.V.K.; writing—original draft preparation, V.V.K. and D.N.K.; writing—review and editing, V.V.K. and D.N.K.; supervision, V.V.K.; project administration, V.V.K.; funding acquisition, V.V.K., D.N.K. and I.A.L. All authors have read and agreed to the published version of the manuscript.

Funding: This work was financially supported by the Ministry of Science and Higher Education of the Russian Federation (project no. FZEN-2020-0022).

Acknowledgments: The X-ray diffraction study was performed using the equipment (Bruker APEX DUO diffractometer) of the Center for Molecular Composition Studies of INEOS RAS, and the HRMS study was accomplished with the use of scientific equipment of the Collective Employment Centre “Ecoanalytical Centre”, Kuban State University (A. Z. Temerdashev).

Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

References
1. Kaur, P.; Singh, K. Recent advances in the application of BODIPY in bioimaging and chemosensing. J. Mater. Chem. C 2019, 7, 11361–11405. [CrossRef]
2. Yang, Y.; Zhao, Q.; Feng, W.; Li, F. Luminescent chemodosimeters for bioimaging. Chem. Rev. 2013, 119, 232–290. [CrossRef] [PubMed]
3. Wang, H.-Y.; Zhang, H.; Chen, S.; Liu, Y. Fluorescein-inspired near-infrared chemodosimeter for luminescence bioimaging. Curr. Med. Chem. 2019, 26, 4029–4041. [CrossRef] [PubMed]
4. McNaughton, D.A.; Fares, M.; Picci, G.; Gale, P.A.; Caltagirone, C. Advances in fluorescent and colorimetric sensors for anionic species. Coord. Chem. Rev. 2021, 427, 213573. [CrossRef]
5. Wang, L.; Ding, H.; Ran, X.; Tang, H.; Cao, D. Recent progress on reaction-based BODIPY probes for anion detection. Dyes Pigm. 2020, 172, 107857. [CrossRef]
6. Mellerup, S.K.; Wang, S. Boron-based stimuli responsive materials. Chem. Soc. Rev. 2019, 48, 3537–3549. [CrossRef]
7. Li, D.; Zhang, H.; Wang, Y. Four-coordinate organoboron compounds for organic light-emitting diodes (OLEDs). Chem. Soc. Rev. 2013, 42, 8416–8433. [CrossRef]
8. Doddar, M.; Misra, R. Recent advances of BODIPY based derivatives for optoelectronic applications. Coord. Chem. Rev. 2020, 421, 213462. [CrossRef]
9. Squeo, B.M.; Ganzer, L.; Virgili, T.; Pasini, M. BODIPY-based molecules, a platform for photonic and solar cells. Molecules 2020, 26, 153. [CrossRef]
10. Loudet, A.; Burgess, K. BODIPY dyes and their derivatives: Syntheses and spectroscopic properties. Chem. Rev. 2007, 107, 4891–4932. [CrossRef]
11. Ulrich, G.; Ziesel, R.; Harriman, A. The chemistry of fluorescent bodipy dyes: Versatility unsurpassed. Angew. Chem. Int. Ed. 2008, 47, 1140–1201. [CrossRef] [PubMed]
12. Boens, N.; Verbelen, B.; Ortiz, M.J.; Jiao, L.; Dehaen, W. Synthesis of BODIPY dyes through postfunctionalization of the boron dipyrromethene core. Coord. Chem. Rev. 2019, 399, 213024. [CrossRef]
13. Shamova, L.I.; Zatsikha, Y.V.; Nemykin, V.N. Synthesis pathways for the preparation of the BODIPY analogues: Aza-BODIPYs, BOPHYs and some other pyrrole-based aromatic chromophores. Dalton Trans. 2021, 50, 1569–1593. [CrossRef] [PubMed]
14. Bismillah, A.N.; Aprahamian, I. Fundamental studies to emerging applications of pyrrole-BF$_2$(BOPHY) fluorophores. Chem. Soc. Rev. 2021, 50, 5631–5649. [CrossRef]
15. Collot, M. Recent advances in dioxygenase-based fluorescent materials for bioimaging applications. Mater. Horiz. 2021, 8, 501–514. [CrossRef]
16. Fedorenko, E.V.; Mirochnik, A.G.; Belolipetsv, A.Y.; Svistunova, I.V.; Tretyakova, G.O. Design, synthesis, and crystallization-induced emission of boron difluorides β-ketoiminates. ChemPivesChem 2018, 83, 117–127. [CrossRef]
17. Cappello, D.; Therien, D.A.B.; Staroverov, V.N.; Lagugn-Mater. Horiz. 2021, 8, 501–514. [CrossRef] [PubMed]
18. Dilman, A.D.; Arkhipov, D.E.; Levin, V.V.; Belyakov, P.A.; Korlyukov, A.A.; Struchkova, M.I.; Tartakovskv, V.A. Trifluoromethylation of N-benzoylhydrazones. J. Org. Chem. 2008, 73, 5643–5646. [CrossRef]
19. Gilroy, J.B.; Otten, E. Formazanate coordination compounds: Synthesis, reactivity, and applications. Chem. Soc. Rev. 2020, 49, 85–113. [CrossRef]
20. Acarbay, M. Über Formazyl-Verbindungen, XI. Über die reaktion von Formazyl-Verbindungen mit Bortrifluorid-ätherat. *Justus Liebigs Ann. Chem.* 1964, 677, 127–128. [CrossRef]

21. Stepanov, B.I.; Avramenko, G.V. Boron—nitrogen compounds I. Reactions of triarylformazans with diboron tetraacetate. Synthesis of boratetrazines. *J. Gen. Chem. (USSR)* 1980, 50, 292–295.

22. Gilroy, J.B.; Ferguson, M.J.; McDonald, R.; Patrick, B.O.; Hicks, R.G. Formazans as β-diketiminate analogues. Structural characterization of boratetrazines and their reduction to boraverdazyl radical anions. *Chem. Commun.* 2007, 2, 126–128. [CrossRef]

23. Barbon, S.M.; Price, J.T.; Reinkeluers, P.A.; Gilroy, J.B. Substituent-dependent optical and electrochemical properties of triarylformazanate boron difluoride complexes. *Inorg. Chem.* 2014, 53, 10585–10593. [CrossRef] [PubMed]

24. Barbon, S.M.; Reinkeluers, P.A.; Price, J.T.; Staroverov, V.N.; Gilroy, J.B. Structurally tunable 3-cyanoformazanate boron difluoride dyes. *Chem. Eur. J.* 2014, 20, 11340–11344. [CrossRef] [PubMed]

25. Kumar, C.; Agrawal, A.R.; Ghosh, N.G.; Karmakar, H.S.; Das, S.; Kumar, N.R.; Banewar, V.W.; Zade, S.S. Boron difluoride formazanates with thiophene and 3,4-ethylenedioxythiophene capping and their electrochemical polymerization. *Dalton Trans.* 2020, 49, 13202–13206. [CrossRef]

26. Maar, R.R.; Katzman, B.D.; Boyle, P.D.; Staroverov, V.N.; Gilroy, J.B. Cationic boron formazanate dyes. *Angew. Chem. Int. Ed.* 2021, 60, 5152–5156. [CrossRef] [PubMed]

27. Van Belois, A.; Maar, R.R.; Workentin, M.S.; Gilroy, J.B. Dialkynylborane complexes of formazanate ligands: Synthesis, electronic properties, and reactivity. *Inorg. Chem.* 2019, 58, 834–843. [CrossRef]

28. Kostryukov, S.G.; Balandina, A.V.; Kozlov, A.S.; Kraynov, E.V.; Pryanichnikova, M.K.; Chernyaeva, O.Y.; Akhmatova, A.A.; Lukschina, Y.I. Synthesis and electrochemical properties of 2-(4-R¹-phenyl)-6-(4-R²-phenyl)-4-phenyl-3,4-dihydropyrazin-1(2H)-yls. *Russ. J. Gen. Chem.* 2020, 90, 341–351. [CrossRef]