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# A CONVENIENT HIGHLY STEREOSELECTIVE SYNTHESIS OF CYCLOPROPYLBORONATES

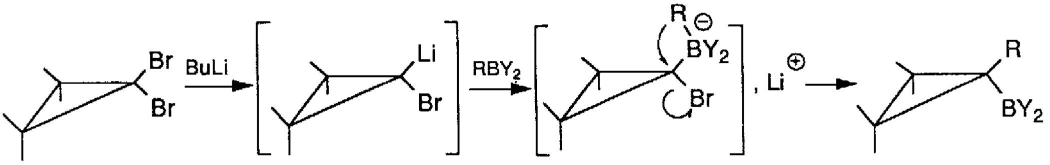
Pierre Fontani, Bertrand Carboni*, Michel Vaultier and Robert Carrié

*Groupe de Recherches de Physicochimie Structurale , U.R.A. C.N.R.S. 704, Université de Rennes I, Campus de Beaulieu, 35042 Rennes Cedex, France.*

**Abstract** : Carbenes generated from diazocompounds in the presence of palladium acetate add to vinylboronates, thus achieving an efficient highly stereoselective synthesis of functionalized cyclopropylboronates.

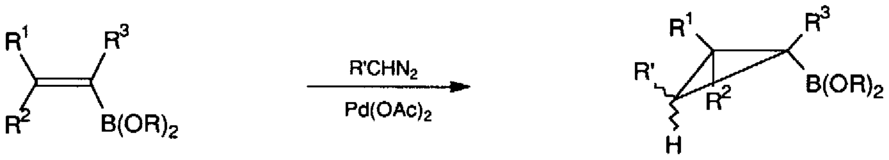
The utility of cyclopropane derivatives in the construction of a variety of cyclic and acyclic organic compounds has been amply demonstrated [1]. Like most of other functional groups, the reactivity of the cyclopropane moiety can be strongly influenced by the neighbouring substituents. For instance the combination of cyclopropyl ring with adjacent heteroatom containing groups such as hydroxy, alkoxy [2], amino [3] or trimethylsilyl [4] has been the source of unexpected and useful reactions.

Similarly,a boron substituent should offer multiple synthetic possibilities owing to the subsequent known transformations of the carbon-boron bond [5] and (or) the expected modification of the reactivity of the ring. Surprisingly, only few examples of such a class of compounds have been reported in the literature. Recently, R.L. Danheiser and A.C. Savoca proposed a two-step stereocontrolled synthesis of cyclopropylboranes [6] (scheme 1). Other previously reported approaches appear to suffer disadvantages such as low yield, limited scope and relative inaccessibility of the starting materials [7].



**Scheme 1**

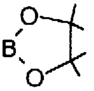
In this note, we report a new simple and efficient method for the preparation of cyclopropylboronic esters **1.** The cyclopropanation of vinylboronates 2 was achieved by the addition of a carbene, generated by diazocompounds decomposition in the presence of palladium acetate (scheme 2 ).(9)



**2** **1**

**Scheme 2**

This sequence was first explored with diazomethane and a typical procedure is as follows : vinylboronates **2** (2 mmoles) and palladium acetate (10 mg) were mixed in ether (5 ml). Then, was added dropwise an etheral solution of diazomethane (10) (30 ml, 14 mmoles) with continuous stirring (10 minutes). After removal of the catalyst by filtration, the solution was concentrated under reduced pressure and the residue purified by Kugelrohr distillation. The results are summarized in the table.

**Table** - Synthesis of cyclopropylboronates **1** ( R' = H ; $B(OR)_2$ =  )(11)

| Entry | 1 | $R^1$ | $R^2$ | $R^3$ | Yield (%) | B.p. (°C/mm Hg)[a] |
|---|---|---|---|---|---|---|
| 1 | **1a** | H | H | H | 92 | 40-45/15 |
| 2 | **1b** | $n\text{-}C_4H_9$ | H | H | 75 | 50-55/0,01 |
| 3 | **1c** | H | $n\text{-}C_4H_9$ | H | 67 | 50-555/0,01 |
| 4 | **1d** | $Cl\text{-}(CH_2)_3$ | H | H | 90 | 75-80/0,01 |
| 5 | **1e** | H | H | $CH_3$ | 72 | 55-60/0,01 |
| 6 | **1f** | $CH_3OCO$ | H | H | 63 | 50-55/0,01 |
| 7 | **1g** | $PhSCH_2$ | H | H | 62 | 110-115/0,001 |
| 8 | **1h** | $(CH_3)_3Si$ | H | H | 83 | 50-55/0,01 |
| 9 | **1j** | $CH_3$ | $CH_3$ | H | 0 (b) | - |
| 10 | **1k** | $CH_3$ | H | $CH_3$ | (c) | - |
| 11 | **1l** | PhS | H | H | 0(d) | - |

a) Kugelrohr distillation, oven temperature given. b) Starting material is recovered unchanged. c) A 40/60 mixture of **1k** and **2k** was obtained. d) This reaction gave a mixture of unidentified products which contained neither **1l** nor **2l**.

Several points are worthy of note:

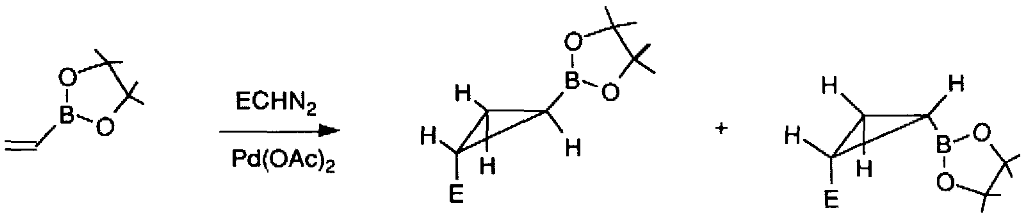
- The starting vinylboronates **2** are easily accessible with a wide range of substitution patterns [12]. They are stable, especially as pinacolic esters [13] and may also be obtained as pure geometric isomers E [14] or Z [13]. Furthermore , unlike others more electrophilic boranes, boronates only slowly decompose diazo compounds[15], thus allowing their use as carbenes precursors .In addition, cyclopropanation can evidently be achieved in other different ways from a wide variety of precursors [1].

- Yields are good ,except for trisubstituted olefins which did not react or gave only minute amounts of cyclopropane.

- The methylene transfert occurs with conservation of the stereochemistry of the starting olefin( entry 2 and 3 )[16]

- As expected, chemoselective cyclopropanation can be achieved on functionnalized olefins (entry 4, 6, 7 and 8).

This route to **1** is not limited to the use of methylene carbene itself. For example, the addition of the methoxycarbonylcarbene, generated from methyldiazoacetate as described previously, to vinylboronate **2a** *give a 60/40 mixture of cis and trans cyclopropanes* **1f** *and* **1m** *in* 65 % yield.(scheme 3)[17]. Under the same conditions , this reaction was not observed with the disubstituted olefin **2b**.



**2a** **1f** **1m**

E = $CO_2Me$

**1f** / **1m** =60/40

**Scheme 3**

In conclusion, cyclopropanation of vinylboronates (and more generally vinylboranes) should offer a convenient new route to α-boronsubstituted cyclopropane. The development of the chemistry of this potentially valuable building blocks is in progress in our laboratory as well as investigations for other synthesis of **1**.

## References and notes

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7 a) Rearrangement of the dihydroboration product of propargyl halide : P. Binger and R. Köster, Angew. Chem., 1962, 74, 652. H.C. Brown and S.P. Rhodes, J. Am. Chem. Soc., 1969, 91, 4306.

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c) Addition of diborontetrahalides to cyclopropenes and vinylcyclopropenes : A. Rosen and M. Zeldin, J. Organomet. Chem., 1971, 31, 319.

d) Reaction of triallylboranes with cyclopropene : B.M. Mikhailow and Y.N. Bubnov in "Organoboron compounds in Organic synthesis" ; Harwood, London, 1984, p. 402-406.

e) Cyclization in basic medium of the radical addition product of bromomalonitrile or bromomalonate to vinylboronate : D.S. Matteson and G.D. Schaumberg, J. Org. Chem., 1966, 31, 726.

8 Vinylboronates were prepared according to reported procedures : **2a**, **2e**, **2j**, **2k** : J. Braun and H. Normant, Bull. Soc. Chim. Fr., 1966, p. 2557. **2b**, **2d** : ref. 13 **2c** : ref. 14 ; **2f**, **2g**, **2h**, **2l** : P.M. Fresneda and M. Vaultier, Tetrahedron Letters, in press.

9 G. Maas, Topics in Current Chemistry, 1987, 137, 75 and references cited.

10 T.J. De Boer and H.J. Backer, Organic Synthesis, John Wiley and sons, New York, 1967, Collective volume IV, p. 250.

11 All the new compounds gave satisfactory elemental analysis and/or mass spectra and spectroscopic data in agreement with given structure.For instance:

$^1$H NMR (300 MHz, $CDCl_3$, δ) : **1b**, : -0,43 (dt, J = 9.4 and 5.7, 1H) ; 0.37 (ddd, J = 9.4, 3.3 and 5,5, 1H) ; 0.65 (ddd, J = 3.3, 5.7 and 7.6, 1H) ; 0.85 - 0.96 (m, 4H) ; 1.11 - 1.50 (m, 6H) ; 1.20 (s, 12H). **1c** : -0,23 (dt, J = 6.7 and 9.2, 1H) ; 0.38 (ddd, J = 5.7, 3.4 and 6.7, 1H) ; 0.76 (ddd, J = 9.2, 7.7 and 3.4, 1H) ; 0.86 - 0.92 (m, 3H) ; 0.99 - 1.06 (m, 1H) ; 1.21 (s, 6H) ; 1.23 (s, 6H) ; 1.21 - 1.46 (m, 6H).

$^{13}$C N.M.R. (75 MHz ,$CDCl_3$, δ) : **1b** : 11.4 (t) ; 14.1 (q) ; 18.3 (d) ; 22.5 (t) ; 24.9 (q) ; 31.8 (t) ; 34.9 (t) ; 82.7 (m). **1c** : 10.9 (t) ; 14.1 (q) ; 18.4 (d) ; 22.6 (t) ; 24,6 (q) ; 25.1 (q) ; 30.8 (t) ; 32.5 (t) ; 82.8 (m).

12 See for instance E. Negishi in "Comprehensive organometallic Chemistry, vol. 7, G. Wilkinson, F.G.A. Stone, E.W. Abel, Eds, Pergamon Press, 1982, p. 303. D.S. Matteson in "The Chemistry of the Metal-Carbon bond", vol. 4, Edited by F.R. Hartley, John Wiley and Sons, Chichester, 1987.

13 H.C. Brown, N.G. Bhat and V. Somayaji, Organometallics, 1983, 2, 1311.

14 H.C. Brown and T. Imai, Organometallics, 1984, 3, 1392.

15 Reference 13 in H.C. Brown and T.Imai, J. Org. Chem., 1984, 49, 892.

16 Stereoisomeric purity was better than 95/5 and was established by examination of the $^{13}$C N.M.R.spectra of the reaction product of **2** with methylene carbene.

17 The ration **1f**/**1m** was deduced from the relative intensities of the two signals at 3,21 (**1f**) and 3,24 (**1m**) in $^1$H NMR (3OO MHz, $C_6D_6$). The trans isomer **1f** was obtained pure by reaction of **2f** with $CH_2N_2$ in the presence of $Pd(OAc)_2$.

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