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Cyclopropanation of [2,2′]biadamantylidene with $Me_3Al–CH_2I_2$ reagent

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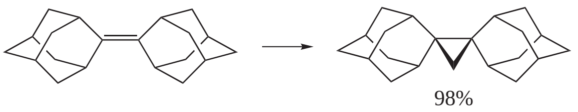
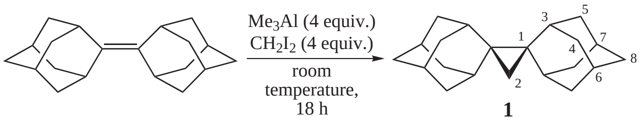
Reagent system $Me_3Al–CH_2I_2$ was found optimal for cyclopropanation of [2,2′]biadamantylidene.



The Simmons–Smith reaction[1,2] is widely used in the synthesis of cyclopropane compounds.[3,4] Zinc carbenoid ICH_2ZnEt turned out to be extremely useful reagent for the cyclopropanation of the double bond. Later, the new reagents were developed based on zinc carbenoids [the Furukawa–Kawabata ($Et_2Zn–CH_2I_2$),[5,6] Wittig ($ZnI_2–CH_2N_2$),[7] Sawada ($EtZnI–CH_2I_2$),[8] Denmark ($Et_2Zn–CH_2Cl_2$),[9] Shi ($Et_2Zn–CH_2I_2–CF_3CO_2H$)[10,11] and Charette ($Et_2Zn–CH_2I_2$–2,4,6-$Cl_3C_6H_2OH$)[12] reagents]. The use of these reagents allowed one to overcome some shortcomings of the original protocol by Simmons and Smith, as poor reproducibility, low reactivity towards allylamines and non-functionalized alkenes.[13,14] However, the relatively bulky zinc carbenoid impedes the cyclopropanation of sterically hindered olefins, *e.g.*, bicyclopropylidenes, bicyclobutylidenes and vinylidenecyclopropane.[15–17] Cyclopropanation of bicyclopropylidene gave [3]triangulane in 80% yield under Doering conditions,[18] but furnished a complex mixture of products with $CH_2N_2/Pd(OAc)_2$ reagent.[19] We have previously demonstrated that aluminum carbenoids perform more easily the cyclopropanation of alkyl- and phenyl-substituted allenes with the steric demand compared to the zinc carbenoids.[20] Unlike the zinc carbenoids used,[21,22] aluminum carbenoids give substituted spiropentanes from both alkyl- and phenyl-substituted allenes and penta-3,4-dien-1-ol.[23] Palladium-promoted reaction of phenylallene with CH_2N_2 affords only benzylidenecyclopropane in ~50% yields.[24] Cyclopropanation of 1,2-cyclononadiene with CH_2N_2 in the presence of a palladium catalyst involved only one double bond to produce bicyclo[7.1.0]dec-1-ene in 70% yield.[24,25] Its repeated treatment with CH_2N_2–[Pd(acac)$_2$] afforded tricyclic compound in the yield of 15%. At the same time, the product of the twofold cyclopropanation of 1,2-cyclononadiene was prepared in 95% yield in one step with the use of $Et_3Al–CH_2I_2$ reagent.[20] We can assume that aluminum carbenoids are active enough to react with intermediate cyclopropylidene derivatives and may be useful for cyclopropanation of sterically hindered olefins. Despite the fact that Maruoka and Yamamoto successfully used $R_3Al–CH_2I_2$ reagent for cyclopropanation of ordinary olefins,[26] its use for sterically hindered olefins was not reported. In this work, we first investigated the reaction of [2,2′]biadamantylidene with aluminum carbenoids *in situ* generated from trialkylaluminums and CH_2I_2. A comparison of the reactivity of various cyclopropanating agents toward to [2,2′]biadamantylidene was performed.

The double bond in [2,2′]biadamantylidene should possess high nucleophilicity due to the presence of four carbon substituents with a positive inductive effect. However, the reactivity of [2,2′]biadamantylidene is low due to the poor accessibility of the double bond. In particular, to the best of our knowledge only one example is reported for its cyclopropanation using dichlorocarbene to give dichlorocyclopropyl derivative in 11% yield.[27] We have found that the reaction of [2,2′]biadamantylidene with 4 equiv. of Me_3Al and CH_2I_2 for 18 h at room temperature affords the cyclopropanation product **1** in quantitative yield (Scheme 1).† After recrystallization from hexane, the isolated yield of dispiro[adamantane-2,1′-cyclopropane-2′,2″-adamantane] **1** was 89%. The conversion of [2,2′]biadamantylidene was 84% (GC) on using 2 equiv. of Me_3Al and CH_2I_2 under the same conditions. The



Scheme 1

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† *Dispiro[adamantane-2,1′-cyclopropane-2′,2″-adamantane]* **1**. Trimethylaluminum (0.8 ml, 8.3 mmol) was added to a solution of [2,2′]biadamantylidene (0.536 g, 2 mmol) and CH_2I_2 (0.64 ml, 8 mmol) in CH_2Cl_2 (8 ml) at 0 °C under argon. (*Caution:* Neat trimethylaluminum is highly pyrophoric and can ignite on contact with air, water or any oxidizer. In contrast to Et_3Al, the self-ignition of neat Me_3Al, used in this procedure, on contact with air proceeds with probability of 100% without the special precautions. This reagent is extremely dangerous. In contrast to this, the commercially available 20% solution in hexanes is much less dangerous.) The mixture was stirred at room temperature for 18 h. Then, the reaction mixture was diluted with 5 ml of CH_2Cl_2 and 3 ml of water was added dropwise while cooling the reactor flask in an ice bath. The precipitate was filtered off on a filter paper. The aqueous layer was extracted with diethyl ether (3×5 ml). The combined organic layers were washed with brine (10 ml), dried over anhydrous $CaCl_2$ and concentrated to give crude product which was recrystallized from hexane to afford **1** (0.50 g, 89%) as white crystals. Mp 124–126 °C. ^1H NMR, δ: 0.03 (s, 2H, 2-Me), 1.49 (br. s, 4H, C^3H), 1.73 (d, 4H, C^4H_a, J 12 Hz), 1.78 (br. s, 4H, C^8H_2), 1.81 (d, 4H, C^5H_a, J 12 Hz), 1.86 (d, 4H, C^4H_b, J 12 Hz), 1.92 (s, 2H, C^6H_2), 1.96 (s, 2H, C^7H_2), 2.03 (d, 4H, C^5H_b, J 12 Hz). ^{13}C NMR, δ: 25.90 (C^2), 27.96 (2C, C^7), 28.30 (2C, C^6), 32.26 (4C, C^3), 37.15 (4C, C^4), 37.58 (4C, C^5), 37.92 (2C, C^8). MS, m/z (%): 282 (100) $[M]^+$, 267 (<1), 239 (6), 225 (4), 187 (2), 161 (8), 135 (23), 119 (12), 91 (28), 79 (29), 67 (14), 41 (10). Found (%): C, 89.14; H, 10.65. Calc. for $C_{21}H_{30}$ (%): C, 89.29; H, 10.71.

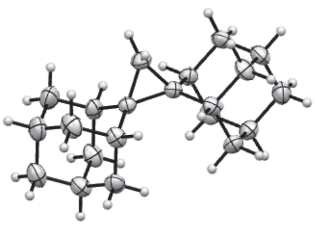

Figure 1 The model of crystal structure of compound **1**.

reaction of [2,2′]biadamantylidene with 4 equiv. of Et_3Al and CH_2I_2 for 18 h at room temperature afforded compound **1** in only 30% GC yield due to incomplete conversion of the starting olefin. We suppose that the lower reactivity of the $Et_3Al–CH_2I_2$ reagent compared to $Me_3Al–CH_2I_2$ system is caused by more pronounced steric interactions in the reaction intermediates.

The structure of compound **1** was elucidated using advanced spectroscopic methods (1D and 2D NMR spectroscopy, mass spectrometry)† and X-ray diffraction analysis (Figure 1).‡ Due to C_{2v} symmetry of the molecule of **1**, seven signals with relative intensities of 1 : 2 : 2 : 2 : 4 : 4 : 4 appear in the ^{13}C NMR spectrum. Signals of two quaternary carbon atoms C(1) were not observed in the ^{13}C NMR spectrum because of their low intensity. Our assignments of ^{1}H and ^{13}C NMR signals are in good agreement with NMR shielding tensor calculations on the level PBE0/6-311+G(2d,p)(giao,scrf)//B3LYP/6-31+G(d,p) (gas phase) using the SMD implicit solvation model.[28] The signals of the hydrogen atoms at C^4 and C^5 are observed in the ^{1}H NMR spectrum as broad doublets ($w_{1/2}$ = 7–9 Hz) with J 12 Hz. The signal of the hydrogen atom at C^3 has singlet character ($w_{1/2}$ = 10 Hz). Although tertiary hydrogen atoms at C^6 and C^7 are in a vicinal position with respect to the six hydrogen atoms, their signals appear as distorted singlets with $w_{1/2}$ = 12 Hz. Singlet character of the signals may be due to small values of the vicinal constants $^3J_{HH}$. According to quantum chemical calculation of the spin–spin coupling constants in **1** by the B3LYP/6-31G(d,p)//B3LYP/6-31G(d) method,[29] the vicinal constants $^3J_{HH}$ amount to 3.0–3.2 Hz. At the same time, the calculated values of the constants for the interaction of geminal hydrogen atoms at C^4 and C^5 are equal to 12 Hz, which agree well with experimental data.

It was interesting to make a comparison of the reactivity of various cyclopropanating agents towards [2,2′]biadamantylidene. Despite the fact that the Shi reagent is one of the active cyclopropanating agents based on zinc carbenoids, the reaction of [2,2′]biadamantylidene with 4 equiv. of Et_2Zn, CH_2I_2 and CF_3COOH in CH_2Cl_2 at room temperature for 18 h gave compound **1** in only 42% GC yield with incomplete conversion of the olefin (Table 1). The use of Furukawa–Kawabata reagent under the same conditions led to compound **1** in 22% GC yield. However, our attempts to carry out the cyclopropanation of [2,2′]biadamantylidene using $CH_2N_2–Pd(acac)_2$ were unsuccessful.[4,30] [2,2′]Biadamantylidene did not react with 350-fold excess of CH_2N_2 and CuCl in the presence of 2.2 equiv. of $Cu(OTf)_2$. Earlier this procedure was successfully used for the preparation of linear [15]triangulane.[31]

Table 1 The cyclopropanation of [2,2′]biadamantylidene using various carbenoid agents.[a]

Reagent system	Reagents ratio (equiv.)	t/h	GC yield of **1** (%)
$Me_3Al–CH_2I_2$	4 : 4	18	98
$Me_3Al–CH_2I_2$	2 : 2	18	84
$Et_3Al–CH_2I_2$	4 : 4	18	30
$Et_2Zn–CH_2I_2–CF_3COOH$	4 : 4 : 4	18	42
$Et_2Zn–CH_2I_2$	4 : 4	18	22
$CH_2N_2–Pd(acac)_2$	~7 : 0.02	1	n.d.[b]
$CH_2N_2–CuCl–Cu(OTf)_2$	~350 : 314 : 2.2	3	n.d.[b]

[a] For detailed procedures, see Online Supplementary Materials. [b] Not determined.

In conclusion, the reagent $Me_3Al–CH_2I_2$ showed the highest activity among the tested cyclopropanating agents, which can be caused by a lower activation energy of the reaction of the olefin with aluminum carbenoid compared to zinc carbenoid.[32] According to B3LYP/6-311G(d,p) calculations, the activation energy of the reaction of ethylene with Me_2AlCH_2I is 12.8 kcal mol^{-1} and with $IZnCH_2I$, 21.2 kcal mol^{-1}.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2016.09.024.

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‡ *X-ray diffraction data for* **1**. A suitable crystal was selected and mounted on an Xcalibur EOS diffractometer and kept at 293(2) K during data collection. The structure was solved using Olex2,[33] with the ShelXS structure solution program[10,34] using direct methods and refined with the ShelXL refinement package using least-squares minimization. Crystal data: $C_{21}H_{30}$, M = 282.45, monoclinic, space group $P2_1/c$ (no. 14), a = 12.0687(6), b = = 10.5212(6) and c = 12.5930(7) Å, β = 90.598(5), V = 1598.94(16) Å^3, Z = 4, μ(MoKα) = 0.065, 6948 reflections measured, 4299 unique (R_{int} = = 0.0204) which were used in all calculations. The final wR_2 was 0.1708 (all data) and R_1 was 0.0533 [$I > 2\sigma(I)$].

CCDC 1034952 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.

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