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Tetrahedron Letters
Tetrahedron Letters 48 (2007) 8583–8586

# Dzhemilev reaction for the synthesis of spiro[3.3]heptane and spiro[3.4]octanes

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Received 12 September 2007; revised 1 October 2007; accepted 12 October 2007
Available online 14 October 2007

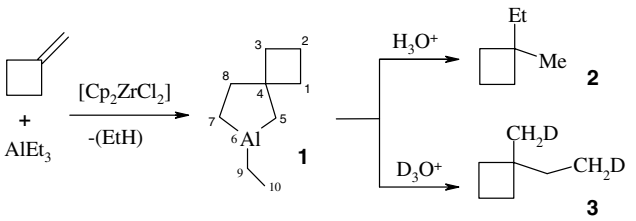
**Abstract**—For the first time cycloalumination of methylenecyclobutane with the aid of $Et_3Al$ in the presence of $Cp_2ZrCl_2$ leading to 6-ethyl-6-aluminaspiro[3.4]octane has been realized. The latter, without isolation, was converted into spiro[3.3]heptane, 6-thiaspiro[3.4]octane and also spiro[3.4]octan-6-ol and 6-spiro[3.4]octyl formate with high yields and selectivity.


Methods for the synthesis of strained hydrocarbons such as spiro[3.3]heptanes and spiro[3.4]octanes are complex and multistage. These approaches are frequently based on the transformations of difficult to prepare reagents, including spiro[3.3]heptane or spiro[3.4]octane fragments.[1] The above mentioned compounds are of great interest both from the synthetic point of view and as monomers, which can find use as liquid-crystal systems[2,3] as well as for obtaining natural compounds and high-energy components for rocket propellants.[4]

Herein, we propose a new approach to obtain spiro compounds, which is based on the reaction of methylenecyclobutane with $Et_3Al$ in the presence of $Cp_2ZrCl_2$, that is, the catalytic cycloalumination of unsaturated compounds (*Dzhemilev reaction*).[5–8] This reaction has been widely studied using as examples, α-olefins,[9–17] 1,2-dienes,[18,19] norbornenes,[20] [60]fullerene[21,22] and acetylenes[23–28] leading to aluminacyclopentanes, aluminacyclopentenes and aluminacyclopentadienes under mild conditions. Efforts to utilize compounds containing a 1,1-disubstituted double bond failed. We envisaged that strained cyclic compounds with an activated methylene bond, for example, methylenecyclobutane, in contrast to acyclic hydrocarbons with less active 1,1-disubstituted double bonds could be implicated in the catalytic reaction with $Et_3Al$. Furthermore, we assumed that such a reaction, if successful, may afford aluminacyclopentanes containing a spirane fragment, which can potentially be used in the synthesis of spiro hetero(carbo)cycles, and strained hydrocarbons with a cyclobutane fragment as well.

We conducted investigations and established that the reaction of methylenecyclobutane and $Et_3Al$ (excess) under previously[9] optimized conditions (5 mol % $Cp_2ZrCl_2$, 4 h, pentane) led to organoaluminium compound (OAC) **1**. Hydrolysis or deuterolysis converted **1** into 1-ethyl-1-methylcyclobutane **2** or 1-(2-deuterioethyl)-1-(deuteriomethyl)cyclobutane **3** in 92% yields[29] (Scheme 1).

The structure of compound **1** was established by $^{13}C$ NMR and mass spectrometry. The structures of **2** and




**Scheme 1.**

*Keywords*: Catalysis; Organoaluminium compounds; Methylencyclobutane; Cycloalumination; Spiro[3.3]heptane; 6-Thiaspiro[3.4]octane; Spiro[3.4]octane-6-ol.
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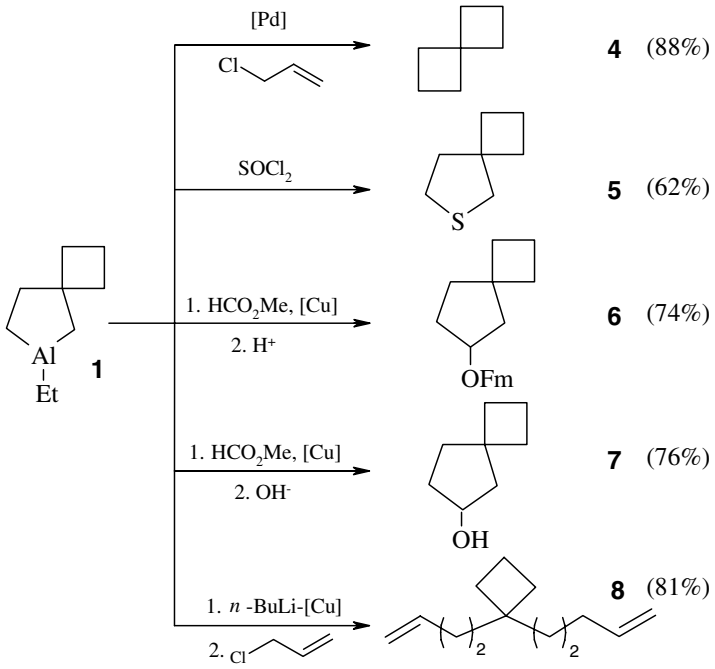
doi:10.1016/j.tetlet.2007.10.065




**Scheme 2.**

**3** were identified from $^{1}H$ and $^{13}C$ NMR spectra. The $^{13}C$ NMR spectrum of OAC **1** contained nine signals, with three signals of low intensity at 1.07 C(9), 6.61 C(5) and 17.58 C(7) ppm, for the carbons connected to Al. The signals were broadened due to the quadrupole relaxation on the Al ($I = 5/2$) nuclei.[27] The signals at 14.88, 34.55 and 34.32 ppm were due to the C(1)–C(3) carbons in the cyclobutane fragment. The signal at 44.22 ppm was due to the central carbon atom of the spirane fragment. The remaining two signals at 8.27 and 38.91 ppm were due to the terminal C(10) carbon atom of the ethyl fragment and to C(8) of the alumina-cyclopentane fragment.

The $^{13}C$ NMR spectra of compounds **2** and **3** were characterized by the presence of six high-field signals. In the spectrum of deuterated compound **3**, up-field α-isotopic shifts were observed for C(6) and C(7) ($\Delta\delta = 0.25$ and 0.31, respectively) with triplet splitting ($J_{CD} = 19.1$ and $J_{CD} = 19.05$ Hz for C(6) and C(7), respectively). The results obtained indicate the formation of a 1,4-dideuterated hydrocarbon, so it is reasonable to assume the presence of two Al–C bonds in starting OAC **1**.

The mass spectra showed the presence of the molecular ions MS 98 (27%) and 100 (21%) for compounds **2** and **3**, respectively. The data obtained for OAC **1** were in full agreement with the proposed structure of 6-ethyl-6-aluminaspiro[3.4]octane.

For additional confirmation of the structure of OAC **1**, and also to demonstrate the potential of the developed procedure in the synthesis of spiro[3.3]heptane and spiro[3.4]octanes as well as hydrocarbons containing a cyclobutane fragment, we have realized the transformations of **1** into spiro[3.3]heptane **4**,[30] 6-thiaspiro[3.4]-octane **5**,[31] 6-spiro[3.4]octyl formate **6**,[32] spiro[3.4]-octan-6-ol **7**[33] and 5-[1-(3-butenyl)cyclobutyl]pent-1-ene **8**[34] according to Scheme 2.

In conclusion, we have shown that methylenecyclobutane undergoes a catalytic cycloalumination reaction with the aid of $Et_3Al$ in the presence of $Cp_2ZrCl_2$ to afford 6-ethyl-6-aluminaspiro[3.4]octane in a yield of more than 90%. The latter, without isolation, was converted into spiro hetero(carbo)cyclic compounds and hydrocarbons containing a cyclobutane fragment. Presently we are conducting investigations on the catalytic cycloaluminations of more complex hydrocarbons for application of this procedure to a wide range of compounds containing an active methylene bond.

## Acknowledgements

The work was financially supported by the Russian Foundation for Basic Research (Grant No. 05-03-32367) and by Grants of the RF President (MC-1039.2007.3 and Sci.Sh.-7470.2006.3).

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29. *Synthesis of compounds* **1**–**3**: A 50 mL glass reactor was charged with $Cp_2ZrCl_2$ (0.5 mmol) in dry pentane (3 mL), methylenecyclobutane (10 mmol) and $AlEt_3$ (12 mmol) under a dried argon atmosphere at 0 °C. The resulting solution was raised to ambient temperature and stirred for 4 h. The reaction was quenched with an 8–10% aqueous solution of HCl **2** (or DCl, 10–12% solution in $D_2O$, **3**). The crude products **2** or **3**, respectively, were extracted with $Et_2O$ or pentane, quenched with an 8–10% (aq) solution of HCl or DCl. The layers were separated and the aqueous phase was extracted with $Et_2O$ or hexane. The combined organic extracts were washed with water, saturated aqueous $NaHCO_3$, dried ($CaCl_2$), filtered and distilled. 6-Ethyl-6-aluminaspiro[3.4]octane (**1**). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 1.07, 6.61, 8.27, 14.88, 17.58, 34.32, 34.55, 38.91, 44.22. 1-Ethyl-1-methylcyclobutane (**2**). Bp 88–89 °C. $^1H$ NMR (100 MHz, $CDCl_3$): $\delta$ 0.81 (t, $J = 6.0$ Hz, 3H, $CH_3$), 1.04 (s, 3H, $CH_3$), 1.48 (m, 2H, $CH_2$), 1.71 (m, 6H, $CH_2$ ring); $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 8.49, 14.84, 25.68, 32.84, 34.8, 39.1. MS (*m*/*z*, %): 98 (27, $M^+$), 70 (66), 69 (37), 56 (26), 55 (76), 42 (25), 41 (100). Anal. Calcd for $C_7H_{14}$: C, 85.63; H, 14.37. Found: C, 85.42; H, 14.29. Yield 92%. 1-(2-Deuterioethyl)-1-(deuteriomethyl)cyclobutane (**3**). $^1H$ NMR (100 MHz, $CDCl_3$): $\delta$ 0.83 (t, $J = 6.0$ Hz, 2H, $CH_2D$), 1.02 (s, 2H, $CH_2D$), 1.45 (m, 2H, $CH_2$), 1.76 (m, 6H, $CH_2$ ring); $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 8.24 (t, $J_{CD} = 19.1$ Hz), 14.81, 25.37 (t, $J_{CD} = 19.05$ Hz), 32.81, 34.76, 39.15. MS (*m*/*z*, %): 100 (21, $M^+$), 72 (28), 71 (41), 70 (34), 57 (30), 56 (48), 55 (20), 44 (69), 43 (27), 42 (63), 41 (64), 40 (100). Anal. Calcd for $C_7H_{12}D_2$: C, 83.92; H, 12.07; D, 4.01. Found: C, 83.79; H + D, 15.93. Yield 92%.
30. *Synthesis of spiro[3.3]heptane* (**4**): To crude **1** at 0 °C were added $Et_2O$ (5 ml), $Ph_3P$ (0.5 mmol), $Pd(acac)_2$ (0.5 mmol) and allyl chloride (30 mmol) dropwise. The reaction mixture was allowed to warm to ~20 °C and stirred for 8 h. The reaction was quenched with an 8–10% (aq) solution of HCl. The layers were separated and the aqueous phase was extracted with $Et_2O$ or pentane. The combined organic extracts were washed with water, saturated aqueous $NaHCO_3$, dried ($CaCl_2$), filtered and distilled. Bp 96–97 °C. $^1H$ NMR (100 MHz, $CDCl_3$): $\delta$ 0.92–2.54 (m, 12H, $CH_2$ ring); $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 16.34, 35.19, 44.21. MS, *m*/*z*: 96 ($M^+$). Anal. Calcd for $C_7H_{12}$: C, 87.42; H, 12.58. Found: C, 87.21; H, 12.39. Yield 88%.
31. *Synthesis of 6-thiaspiro[3.4]octane* (**5**): To crude **1** at −40 °C, thionyl chloride (30 mmol) was added dropwise, the reaction stirred for 8 h and then treated with an 8–10% (aq) solution of HCl. The crude was extracted with diethyl ether or hexane and purified by distillation in vacuo. Bp 92–93 °C (20 Torr). $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 1.1–1.23 (m, 2H, $C(1)H_a$, $C(3)H_a$), 1.31–2.15 (m, 7H, $C(1)H_b$, $C(2)H_2$, $C(3)H_b$, $C(5)H_a$, $C(8)H_2$), 2.21–3.24 (m, 3H, $C(5)H_b$, $C(7)H_2$); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ 15.29, 30.60, 32.75, 40.95, 42.19, 42.64. MS (*m*/*z*, %): 128 (56, $M^+$), 100 (74), 99 (54), 85 (100), 79 (13), 72 (14), 67 (22), 65 (10), 54 (11), 53 (12), 45 (18), 41 (15). Anal. Calcd for $C_7H_{12}S$: C, 65.56; H, 9.43; S, 25.01. Found: C, 65.34; H, 9.21; S, 24.89. Yield 62%.
32. *Synthesis of spiro[3.4]oct-6-yl ester formic acid* (**6**): To crude **1** at −15 °C were added CuCl (1 mmol) and methylformate (30 mmol) dropwise. The reaction mixture was allowed to warm to ~20 °C and stirred for 8 h. The reaction was quenched with an 8–10% (aq) solution of HCl. The layers were separated and the aqueous phase was extracted with $Et_2O$ or hexane. The combined organic extracts were washed with water and saturated aqueous $NaHCO_3$, dried ($CaCl_2$), filtered and concentrated in vacuo. The products were isolated by column chromatography on silica gel (40–100 mesh grade) with hexane/EtOAc = 10:1 as eluent. Bp 91–92 °C (10 Torr). $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 1.35–1.71 (m, 5H, $C(1)H_a$, $C(3)H_a$, $C(5)H_a$, $C(7)H_a$, $C(8)H_a$), 1.75–2.13 (m, 7H, $C(1)H_b$, $C(2)H_2$, $C(3)H_b$, $C(5)H_b$, $C(7)H_b$, $C(8)H_b$), 4.37–4.42 (m,

CH–OFm), 6.68 (s, 1H, O—C(=O)*H*); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 16.24, 31.35, 33.82, 33.89, 37.11, 39.55, 45.87, 76.02, 160.84. Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15; O, 20.75. Found: C, 70.02; H, 9.07; O, 20.51.Yield 74%.

33. *Synthesis of spiro[3.4]octan-6-ol* (**7**): To crude **1** at −15 °C were added CuCl (1 mmol) and methylformate (30 mmol) dropwise. The reaction mixture was allowed to warm to ~20 °C and stirred for 8 h. The reaction was quenched with a 15–20% (aq) solution of NaOH. The layers were separated and the aqueous phase was extracted with $Et_2O$ or hexane. The combined organic extracts were washed with water and saturated aqueous $NaHCO_3$, dried ($CaCl_2$), filtered and concentrated in vacuo. The products were isolated by column chromatography on silica gel (40–100 mesh grade) with hexane/EtOAc = 10:1 as eluent. Bp 94–95 °C (10 Torr). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 1.39–1.68 (m, 5H, C(1)$H_a$, C(3)$H_a$, C(5)$H_a$, C(7)$H_a$, C(8)$H_a$), 1.73–2.07 (m, 7H, C(1)$H_b$, C(2)$H_2$, C(3)$H_b$, C(5)$H_b$, C(7)$H_b$, C(8)$H_b$), 4.23–4.30 (m, CH–OH); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 16.74, 34.76, 34.81, 35.06, 37.87, 45.80, 49.56, 73.55. MS (*m*/*z*, %): 126 (2, $M^+$), 125 (3), 111 (6), 108 (3), 98 (26), 97 (28), 83 (81), 80 (54), 79 (42), 70 (100), 69 (92), 67 (24), 57 (20), 56 (83), 55 (50), 54 (15), 53 (21), 43 (30), 42 (14), 41 (52). Anal. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18; O, 12.68. Found: C, 76.01; H, 11.13; O, 12.46.Yield 76%.

34. *Synthesis of 5-[1-(3-butenyl)cyclobutyl]pent-1-ene* (**8**): To crude **1** at −78 °C was added *n*-BuLi (10 mmol) and the reaction mixture was stirred for 15 min then CuCl (1 mmol) and allyl chloride (30 mmol) were added dropwise. The reaction mixture was allowed to warm to ~20 °C and stirred for 6 h. The reaction was quenched with an 8–10% (aq) solution of HCl. The layers were separated and the aqueous phase was extracted with $Et_2O$ or hexane. The combined organic extracts were washed with water and saturated aqueous $NaHCO_3$, dried ($CaCl_2$), filtered and distilled in vacuo.Bp 87–88 °C (8 Torr). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 1.11–1.39 (m, 6H, $CH_2$), 1.41–2.23 (m, 10H, C$H_2$—CH=$CH_2$, $CH_2$ ring), 4.75–5.25 (m, 4H, C$H_2$=CH—), 5.34–6.05 (m, 2H, —C*H*=$CH_2$); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 15.16, 23.34, 28.45, 31.81, 34.47, 37.86, 37.99, 41.41, 113.89, 114.38, 139.12, 139.68. MS, *m*/*z*: 178 ($M^+$). Anal. Calcd for $C_{13}H_{22}$: C, 87.56; H, 12.44. Found: C, 87.36; H, 12.18. Yield 81%.