Synthesis of cyclopropane-containing organoaluminum compounds by the reaction of acetylenes with CH_2I_2 and Et_3Al

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Reactions of disubstituted and terminal acetylenes with CH_2I_2 and Et_3Al in the molar ratio 1 : 4 : 6 lead to the selective formation of organoaluminum compounds containing di-, tri-, or tetrasubstituted cyclopropane fragments depending on the nature of acetylene and reaction conditions.

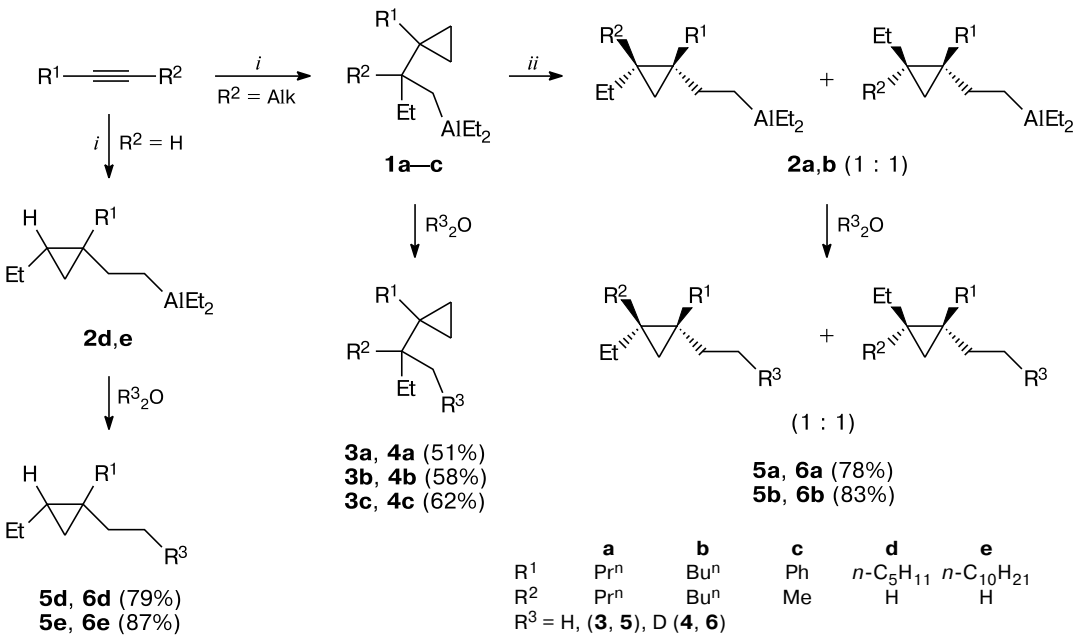
Key words: triethylaluminum, organoaluminum compounds, diiodomethane, cyclopropanes, alkynes.

Earlier,[1,2] we have found that the reaction of mono- and disubstituted acetylenes with CH_2I_2 and Et_3Al taken in excess leads to the selective enough formation of tri- and tetrasubstituted cyclopropanes, respectively, in up to 80% yields.

The purpose of the present work is to evaluate the scope of this reaction, as well as to identify the intermediate organoaluminum compounds (OAC).

It was found that the reaction of dialkyl-substituted acetylenes (oct-4-yne, dec-5-yne) with CH_2I_2 and Et_3Al in the molar ratio of the reactants 1 : 4 : 6 and the reaction time of 1 h leads to the formation of organoaluminum compounds **1a**,**b** in 51 and 58% yields, respectively (Scheme 1). When the reaction time was increased to 8 h, the cyclopropane-containing OAC **1a**,**b** were transformed to **2a**,**b** in 78 and 83% yields, respectively. The best results

Scheme 1



Reagents and conditions: *i.* CH_2I_2 (4 equiv.), Et_3Al (6 equiv.), CH_2Cl_2, 22 °C; *ii.* 22 °C, 7 h.

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 7, pp. 1311—1314, July, 2009.

1066-5285/09/5807-1349

were achieved when the reaction was performed in halogen-containing solvents (dichloromethane, dichloroethane). In hydrocarbon solvents (hexane, benzene), the formation of the cyclopropane occurs at lower rate and in lower yields. For instance, the reaction of oct-4-yne with CH_2I_2 and Et_3Al in hexane for 8 h gives compound **2a** in 41% yield. The use of ether solvents (diethyl ether, THF) inhibits the reaction.

The structures of compounds **1a**,**b** and **2a**,**b** were established based on the analysis of their hydrolysis and deuterolysis products. The presence in the ^{13}C NMR spectrum of compound **4b** of intensive signal for the CH_2 group at 6.05 and 6.15 ppm with the spin-spin coupling constant $^1J_{CH}$ = 155.65 Hz is characteristic of cyclopropane systems and the presence in the ^1H NMR spectrum of a multiplet in the region 0.05—0.40 ppm indicates the presence of the cyclopropane fragment in the molecule of compound **4b**. In addition, in the mass spectrum of compound **4b**, there is no signal of the molecular ion, rather the signal for the fragment $[M - 28]^+$ formed by elimination of ethylene from the molecular ion is present, which is characteristic of 1,1-disubstituted cyclopropanes with α-substituted alkyl substituents.[3] The nonequivalence of the CH_2 protons of the cyclopropane fragment apparently is due to the presence of the diastereotopic carbon atom in the ring. Assignment of the signals in the ^{13}C NMR spectra of compounds **4a**,**b** were made according to the known spectral parameters of analogous cyclopropane compounds[3] and the Lindeman—Adams additive scheme.[4] The structures of tetrasubstituted cyclopropanes **5a**,**b** and equal proportion of *cis*- and *trans*-isomers in them have been established by us earlier[1].

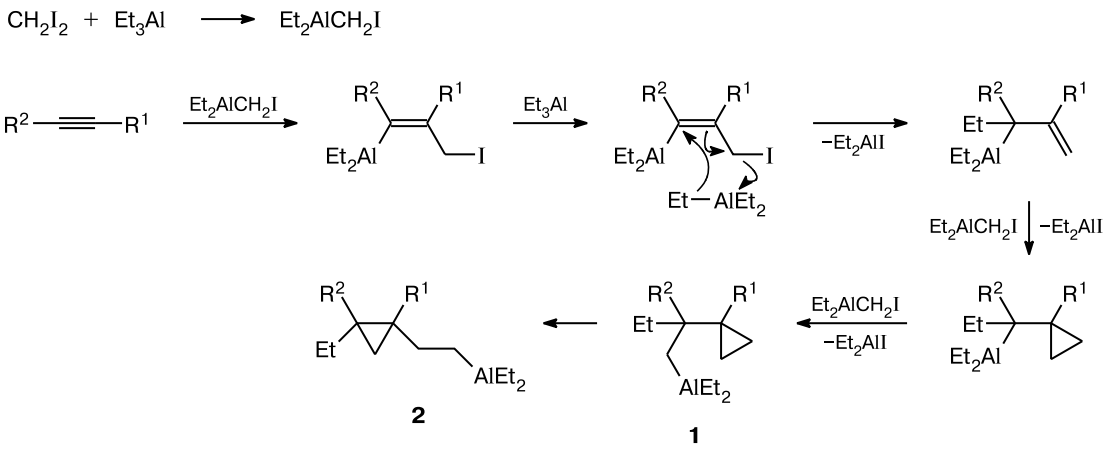
Phenylmethylacetylene under conditions chosen and the reaction time of 8 h is transformed to the only product **1c** in 62% yield. No subsequent rearrangement of disubstituted cyclopropane **1c** to tetrasubstituted cyclopropane **2** under the reaction conditions occurs.

Terminal acetylenes (hept-1-yne, dodec-1-yne) react with CH_2I_2 and Et_3Al (the molar ratio acetylene : CH_2I_2 : Et_3Al = 1 : 4 : 6) to form OAC **2d**,**e** in 79 and 87% yields, respectively. The structures of trisubstituted cyclopropanes **5d**,**e** were established by spectroscopic methods.[1] The ^{13}C NMR spectra of **6d**,**e** exhibit one set of signals, which indicates the formation of one stereoisomer, the configuration of which can not be established by NMR.

Based on the literature data and our experimental results, we suggested the following pathway for the reaction (Scheme 2). The reaction starts from the generation of diethyl(iodoomethyl)aluminum.[5] The latter is capable of carboalumination of acetylene to form iodine-containing alkenylalane,[6] the subsequent reaction of which with Et_3Al leads to the formation of unsaturated OAC. Further cyclopropanation of the double bond[7] and insertion of the CH_2 group at the Al—C bond lead to OAC **1**, which then rearranges to **2**. According to the mechanism suggested, three molecules of CH_2I_2 and four molecules of Et_3Al are involved into formation of one molecule of cyclopropane, which agrees with the optimum molar proportion of reactants found experimentally.

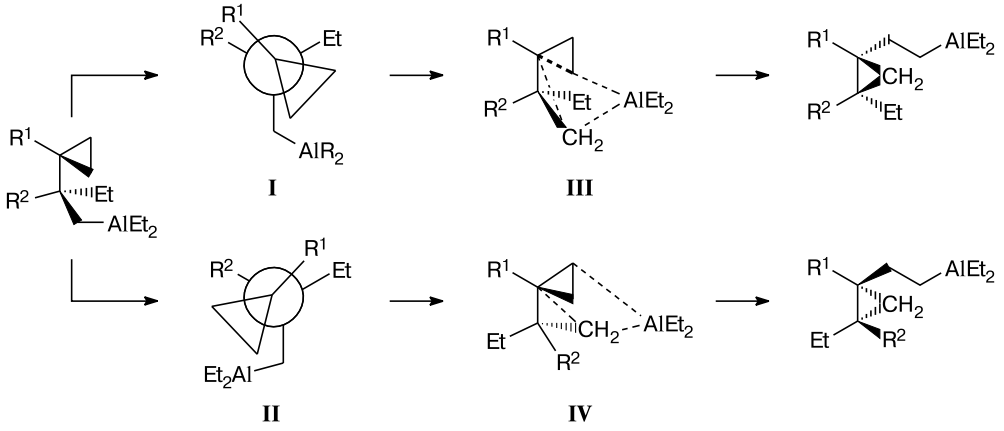
As it has been already noted, terminal acetylenes in the reactions with Et_3Al and CH_2I_2 form only one stereoisomer, whereas the reaction with oct-4-yne gives rise to a mixture of stereoisomers **2a** in the ratio 1 : 1 (see Scheme 1). According to the mechanism suggested (see Scheme 2), the stereoconfiguration of final product **2** is determined in the rearrangement stage of OAC **1** to **2** and in first approximation depends on the relative stability of eclipsed conformations **I** and **II** (Scheme 3). For instance, in the case of oct-4-yne ($R^1 = R^2 = Pr^n$) the difference between potential energy of conformations **I** and **II** will be minimum

Scheme 2



R^1, R^2 = alkyl, alkyl; Ph, H; alkyl, H

Scheme 3



due to the small difference in the bulkiness of ethyl and propyl groups, which leads to the realization of both stereoconfigurations of compound **2a**. In the case of hept-1-yne (R^1 = *n*-C_5H_{11}, R^2 = H), conformation **I** will be energetically more favorable, which provides formation of only one stereoisomer of compound **2** with the *cis*-arranged substituents R^1 and R^2. However, a strict description of the rearrangement process suggests calculation of its activation barrier, which was made using the PM3 semiempirical method (see Ref. 8). The calculated values of the formation enthalpy of transition states **III** and **IV** confirmed conclusions made by qualitative consideration of eclipsed conformers **I** and **II**. For instance, in the case of oct-4-yne, the potential energy difference of transition states **III** and **IV** was only 0.7 kcal mol^{-1}, whereas for hept-1-yne transition state **III** has proved energetically more favorable by 7.1 kcal mol^{-1}. In conclusion, terminal acetylenes R—C≡C—H under the reaction conditions apparently are transformed to trisubstituted cyclopropanes with *cis*-arrangement of substituents R and H.

Experimental

Commercially available reactants were used in this work. Dichloromethane was distilled over P_2O_5 before use. The reaction products were analyzed on a Carlo Erba chromatograph (an Ultra-1 glass capillary column (Hewlett Packard) 25 m × 0.2 mm, a flame ionization detector, thermostate temperature was 50—170 °C, carrier gas was helium). Mass spectra were measured on a Finnigan 4021 instrument with the ionization potential of 70 eV and the temperature of ionizing chamber of 200 °C. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL FX-90Q (22.5 MHz for ^{13}C and 90 MHz for ^{1}H) and Bruker AM-300 (75.46 MHz for ^{13}C and 300 MHz for ^{1}H) spectrometers using $SiMe_4$ (^{1}H) and $CDCl_3$ (^{13}C) as internal standards. ^{13}C NMR spectra were recorded in the modes with the full proton coupling, as well as using the INEPT (Insensitive Nuclei Enhanced by Polarization Transfer) procedure. The atoms numeration is given in Fig. 1.

The product yields were determined by GC of the hydrolysis products of the corresponding OAC using an internal standard.

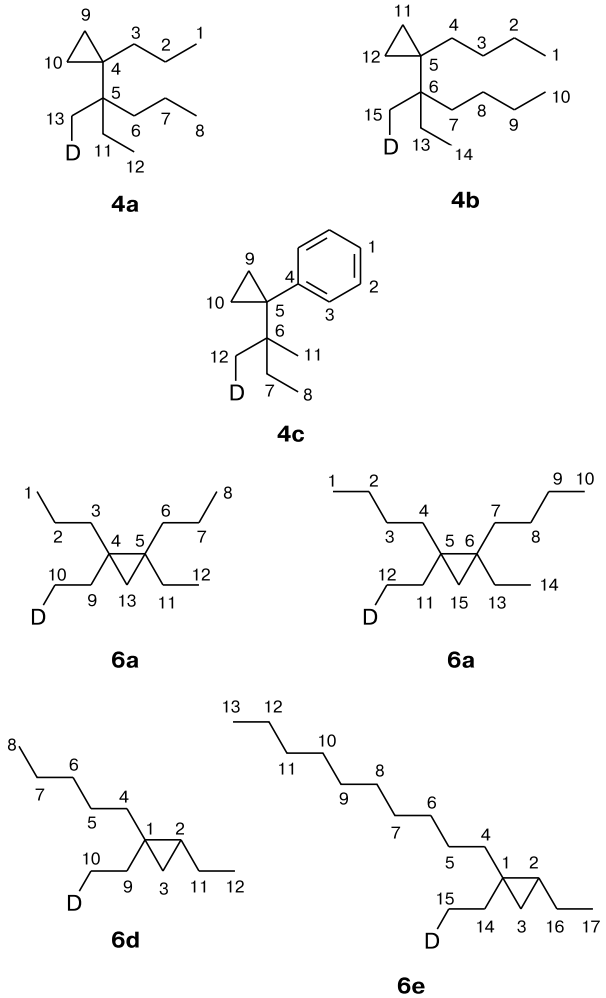


Fig. 1. The carbon atoms numeration in the ^{13}C and ^{1}H NMR spectra of compounds **4a—c**, **6a**,**b**,**d**,**e**.

Quantum chemical calculations were performed with full optimization of geometry by the restricted Hartree—Fock method in the PM3 semiempirical basis using the GAMESS program.[8]

Synthesis of substituted cyclopropanes (general procedure). Dichloromethane (30 mL), alkyne (10 mmol), CH_2I_2 (3.2 mL, 40 mmol), and Et_3Al (60 mmol) were sequentially placed under an inert gas into a 50-mL glass reaction flask equipped with a magnetic stirring bar and cooled with an ice bath, the mixture was stirred for a required time at 20—25 °C. Then the reaction mixture was hydrolyzed with 10% aqueous HCl or 15% DCl in D_2O, the water layer was extracted with diethyl ether. The extract was combined with the organic layer, kept over anhydrous $CaCl_2$, and concentrated *in vacuo*. Individual products were isolated by distillation *in vacuo*.

3-Deuteromethyl-3-(1-propylcyclopropyl)hexane (4a), b.p. 96 °C (15 Torr). Found (%): C, 84.91; (H+D), 15.09. $C_{13}H_{25}D$. Calculated (%): C, 85.16; H, 13.74; D, 1.10. The yield was 51%. ^{13}C NMR, δ: 6.06 (t, C(9)); 6.17 (t, C(10)); 8.95 (q, C(12)); 15.01 (q, C(1)); 15.26 (q, C(8)); 17.79 (t, C(2)); 19.85 (C(13), $^1J_{CD}$ = 19.05 Hz); 20.13 (t, C(7)); 22.71 (s, C(4)); 31.65 (t, C(11)); 35.42 (t, C(6)); 37.36 (s, C(5)); 43.48 (t, C(3)). ^1H NMR, δ: 0.06—0.42 (m, 4 H, $C(9)H_2$, $C(10)H_2$); 0.73 (s, 2 H, $C(13)H_2D$); 0.83—0.88 (m, 9 H, $C(1)H_3$, $C(8)H_3$, $C(12)H_3$); 1.01—1.52 (m, 10 H, $C(2)H_2$, $C(3)H_2$, $C(6)H_2$, $C(7)H_2$, $C(11)H_2$). MS, *m/z*: 155 $[M - C_2H_4]^+$.

3-(1-Butylcyclopropyl)-3-deuteromethylheptane (4b), b.p. 91 °C (3 Torr). Found (%): C, 85.01; (H+D), 14.99. $C_{15}H_{29}D$. Calculated (%): C, 85.22; H, 13.83; D, 0.95. The yield was 58%. ^{13}C NMR, δ: 6.05 (t, C(11)); 6.15 (t, C(12)); 8.82 (q, C(14)); 14.28 (q, C(1), C(10)); 19.87 (C(15), $^1J_{CD}$ = 19.07 Hz); 22.67 (s, C(5)); 23.65 (s, C(9)); 23.91 (t, C(2)); 26.44 (t, C(8)); 28.78 (t, C(3)); 31.38 (t, C(7)); 31.77 (t, C(13)); 37.30 (s, C(6)); 38.73 (t, C(4)). ^1H NMR, δ: 0.05—0.40 (m, 4 H, $C(11)H_2$, $C(12)H_2$); 0.56 (s, 2 H, $C(15)H_2D$); 0.75—0.80 (m, 9 H, $C(1)H_3$, $C(10)H_3$, $C(14)H_3$); 1.00—1.45 (m, 14 H, $C(2)H_2$, $C(2)H_2$, $C(3)H_2$, $C(4)H_2$, $C(7)H_2$, $C(8)H_2$, $C(9)H_2$, $C(11)H_2$). MS, *m/z*: 183 $[M - C_2H_4]^+$.

1-(2-Deuteromethylbut-2-yl)-1-phenylcyclopropane (4c), b.p. 109 °C (10 Torr). Found (%): C, 88.34; (H+D), 11.66. $C_{14}H_{19}D$. Calculated (%): C, 88.82; H, 10.12; D, 1.06. The yield was 62%. ^{13}C NMR, δ: 8.76 (t, C(9), C(10)); 9.09 (q, C(8)); 23.84 (C(12), $^1J_{CD}$ = 19.01 Hz); 24.17 (q, C(11)); 32.88 (t, C(7)); 33.60 (s, C(5)); 34.96 (s, C(6)); 126.00 (d, C(1)); 127.17 (d, C(3)); 132.38 (d, C(2)); 145.77 (s, C(4)). ^1H NMR, δ: 0.50—0.75 (m, 4 H, $C(9)H_2$, $C(10)H_2$); 0.82 (s, 5 H, $C(11)H_3$, $C(12)H_2D$); 0.90 (t, $C(8)H_3$, J = 7.33 Hz); 1.28 (q, J = 6.96 Hz); 7.10—7.35 (m, Ph). MS, *m/z*: 189 $[M]^+$ (10), 161 $[M^+ - C_2H_4]$ (36), 159 $[M^+ - C_2H_4D]$ (45); 145 $[M^+ - C_3H_6D]$ (55); 117 $[M^+ - C_5H_{10}D]$ (69); 72 $[C_5H_{10}D]$ (90).

1-(2-Deuteroethyl)-2-ethyl-1,2-dipropylcyclopropane (6a), b.p. 105 °C (20 Torr). Found (%): C, 84.79; (H+D), 15.21. $C_{13}H_{25}D$. Calculated (%): C, 85.16; H, 13.74; D, 1.10. The yield was 78%. ^{13}C NMR, δ: 11.25 (C(10), $^1J_{CD}$ = 19.05 Hz); 11.29 (q, C(12)); 14.74 (t, C(1,8)); 20.20 (t, C(2,7)); 24.43 (t, C(9), C(11)); 24.43 (t, C(13)); 30.02 (s, C(4)); 33.47, 33.60 (both t, C(3), C(6)). ^1H NMR, δ: 0.73—1.00 (m, 13 H, $C(13)H_2$, $C(1)H_3$, $C(8)H_3$, $C(12)H_3$, $C(10)H_2D$); 1.05—1.48 (m, 12 H, $C(2)H_2$, $C(3)H_2$, $C(6)H_2$, $C(7)H_2$, $C(9)H_2$, $C(11)H_2$). MS, *m/z*: 183 $[M]^+$ (3), 154 $[M^+ - Et]$ (23), 140 $[M^+ - Pr]$ (25).

1,2-Dibutyl-1-(2-deuteroethyl)-2-ethylcyclopropane (6b), b.p. 65 °C (1 Torr). Found (%): C, 84.66; (H+D), 15.34. $C_{15}H_{29}D$. Calculated (%): C, 85.22; H, 13.83; D, 0.95. The yield was 83%. ^{13}C NMR, δ: 11.15 (C(12), $^1J_{CD}$ = 19.03 Hz); 11.18 (q, C(14)); 14.22 (q, C(1,10)); 23.30 (t, C(2), C(9)); 24.27 (t, C(11), C(13)); 24.27 (t, C(15)); 29.24 (t, C(3), C(8)); 30.04 (s, C(5)); 30.72, 30.77 (both t, C(4), C(7)). ^1H NMR, δ: 0.68—1.10 (m, 13 H, $C(15)H_2$, $C(1)H_3$, $C(10)H_3$, $C(14)H_3$, $C(12)H_2D$); 1.17—1.53 (m, 16 H, $C(2)H_2$, $C(3)H_2$, $C(4)H_2$, $C(7)H_2$, $C(8)H_2$, $C(9)H_2$, $C(11)H_2$, $C(13)H_2$). MS, *m/z*: 211 $[M]^+$ (4), 182 $[M^+ - Et]$ (26), 154 $[M^+ - Bu]$ (25).

1-[1-(2-Deuteroethyl)-2-ethylcyclopropyl]pentane (6d), b.p. 87 °C (20 Torr). Found (%): C, 84.42; (H+D), 15.58. $C_{15}H_{29}D$. Calculated (%): C, 85.12; H, 13.69; D, 1.19%. The yield was 79%. ^{13}C NMR, δ: 10.66 (C(10), $^1J_{CD}$ = 19.01 Hz); 14.22 (q, C(8)); 14.67 (q, C(12)); 18.31 (t, C(3)); 22.54 (t, C(7)); 22.87 (t, C(11)); 24.82 (s, C(1)); 26.25 (d, C(2)); 26.64 (t, C(5)); 29.82 (t, C(9)); 30.47 (t, C(4)); 32.55 (t, C(6)). ^1H NMR, δ: 0.18—0.42 (m, 3 H, C(2)H, $C(3)H_2$); 0.85 (t, 6 H, $C(10)H_3$, $C(12)H_3$, $^3J_{CH}$ = 4.9 Hz); 0.97 (t, 3 H, $C(8)H_3$, $^3J_{CH}$ = 6.8 Hz); 1.07—1.50 (m, 12 H, $C(4)H_2$, $C(5)H_2$, $C(6)H_2$, $C(7)H_2$, $C(9)H_2$, $C(11)H_2$). MS, *m/z*: 169 $[M]^+$ (4), 140 $[M^+ - Et]$ (3), 98 $[M^+ - C_5H_{11}]$ (41).

1-[1-(2-Deuteroethyl)-2-ethylcyclopropyl]decane (6e), b.p. 121 °C (3 Torr). Found (%): C, 85.30; (H+D), 14.70. $C_{17}H_{23}D$. Calculated (%): C, 85.27; H, 13.89; D, 0.84%. The yield was 87%. ^{13}C NMR, δ: 10.71 (C(15), $^1J_{CD}$ = 19.07 Hz); 14.28 (q, C(17)); 14.67 (t, C(13)); 18.38 (t, C(3)); 22.61 (t, C(14)); 22.87 (t, C(12)); 24.88 (s, C(1)); 27.03 (s, C(2)); 26.31 (t, C(5)); 29.56 (t, C(10)); 29.95 (t, C(6), C(7), C(8), C(9)); 30.41 (t, C(4)); 30.54 (t, C(16)); 32.10 (t, C(11)). ^1H NMR, δ: 0.15—0.35 (m, 3 H, C(2)H, $C(3)H_2$); 0.65—1.00 (m, 11 H, $C(13)H_3$, $C(17)H_3$, $C(15)H_2D$); 1.05—1.55 (m, 22 H, $C(4)H_2$, $C(5)H_2$, $C(6)H_2$, $C(7)H_2$, $C(8)H_2$, $C(9)H_2$, $C(10)H_2$, $C(11)H_2$, $C(12)H_2$, $C(14)H_2$, $C(16)H_2$). MS, *m/z*: 239 $[M]^+$ (3).

References

1. I. R. Ramazanov, M. P. Luk´yanova, A. Z. Sharipova, A. G. Ibragimov, U. M. Dzhemilev, O. M. Nefedov, *Izv. Akad. Nauk, Ser. Khim.*, 2001, 1338 [*Russ. Chem. Bull., Int. Ed.*, 2001, **50**, 1406].
2. U. M. Dzhemilev, I. R. Ramazanov, A. G. Ibragimov, L. I. Dyachenko, M. P. Lukjyanova, O. M. Nefedov, *J. Organometal. Chem.*, 2001, **636**, 91.
3. U. M. Dzhemilev, A. G. Ibragimov, I. R. Ramazanov, M. P. Luk´yanova, A. Z. Sharipova, L. M. Khalilov, *Izv. Akad. Nauk, Ser. Khim.*, 2000, 1092 [*Russ. Chem. Bull., Int. Ed.*, 2000, **49**, 1086].
4. L. P. Lindeman, J. Q. Adams, *Anal. Chem.*, 1971, **43**, 1245.
5. D. B. Miller, *Tetrahedron Lett.*, 1964, **17**, 989.
6. H. Hoberg, *Lieb. Ann.*, 1962, **656**, 1.
7. K. Maruoka, Y. Fukutani, H. Yamamoto, *J. Org. Chem.*, 1985, **50**, 4412.
8. M. W. Schmidt, K. K. Baldridge, J. A. Boatz, S. T. Elbert, M. S. Gordon, J. J. Jensen, S. Koseki, N. Matsunaga, K. A. Nguyen, S. Su, T. L. Windus, M. Dupuis, J. A. Montgomery, *J. Comput. Chem.*, 1993, **14**, 1347.

Received September 2, 2008;
in revised form March 27, 2009