Regioselective splitting of 3-alkyl-1-ethylaluminacyclopentanes with orthoformates as a new route to 1-functionalized 4-methylalkanes

O. S. Vostrikova,[a] E. F. Dekhtyar´,[b] S. S. Zlotskii,[b] and V. A. Dokichev[a]*

[a]*Institute of Organic Chemistry, Ufa Research Center of the Russian Academy of Sciences, 71 prosp. Oktyabrya, 450054 Ufa, Russian Federation. Fax: +7 (347 2) 35 6066. E-mail: dokichev@anrb.ru*

[b]*Research Institute of Small-Scale Products and Reagents, 75 ul. Ul´yanovykh, 450029 Ufa, Russian Federation. Fax: +7 (347 2) 43 1731. E-mail: reaktiv@soros.bashedu.ru*

The reactions of triethyl, diethyl phenyl, or tributyl orthoformate with 1,3-dialkylaluminacyclopentanes results in regioselective cleavage of the sterically less hindered Al—C(5) bond; hydrolysis of the reaction mixture gives 4-methyl aldehyde acetals. In the case of more inert orthoformates, the process is activated with catalytic amounts of $ZrCl_4$.

Key words: organoaluminum compounds, 1,3-dialkylaluminacyclopentanes, orthoformates, catalysis, 4-methyl-substituted aldehyde acetals.

It is known[1] that functional derivatives of 4-methylalkanes are valuable low-molecular bioregulators and find use in organic synthesis. For example, 4-methylnonan-1-ol is a sex pheromone of big meal worm,[2] and 4,8-dimethyldecan-1-al is a pheromone of little and *Rhopalocera* meal worms.[3] The known syntheses of these compounds[1,2] include many steps or are inconvenient.

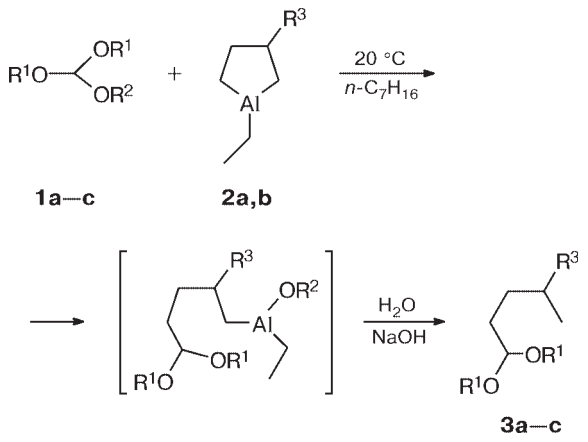
The present work was intended to continue our investigations of the reactions of organoaluminum compounds with substrates containing geminal RO groups[4,5] and to develop a preparative method for the synthesis of inaccessible 1-functionalized 4-methylalkanes. For this purpose, we studied the reactions of 3-alkyl-1-ethylaluminacyclopentanes with orthoformates.

Results and Discussion

It should be noted[6,7] that the reactivities of both endocyclic Al—C bonds in β-alkylaluminacyclopentanes (ACPs) toward nucleophilic reagents are usually almost the same, significantly exceeding the reactivity of the exocyclic Al—C bond. Thus, 1,3-dialkylaluminacyclopentanes oxidize nonselectively to give an approximately equimolar mixture of isomeric 3- and 4-alkyl alcohols.[6]

We found that the reactions of orthoformates **1a—c** with 3-alkyl-1-ethylaluminacyclopentanes **2a,b** result in regioselective ring opening *via* cleavage of the sterically least hindered endocyclic Al—C(5) bond (Scheme 1).

Scheme 1



a: $R^1 = R^2 = Et$, $R^3 = n\text{-}C_5H_{11}$
b: $R^1 = R^2 = Bu^n$, $R^3 = n\text{-}C_6H_{13}$
c: $R^1 = Et$, $R^2 = Ph$, $R^3 = n\text{-}C_6H_{13}$

For example, the reaction of ethyl orthoformate (**1a**) with an equimolar amount of compound **2a** in heptane at 20 °C followed by hydrolysis of the reaction mixture gives 1,1-diethoxy-4-methylnonane (**3a**) (Table 1). As in the case of organomagnesium compounds,[8—10] diethyl phenyl orthoformate (**1c**) reacts with aluminacyclopentane **2b** with elimination of only the phenoxy group, the ethoxy groups remaining untouched. 1,1-Diethoxy-3-ethylnonane and 1,1-diethoxypropane that would form upon cleavage of the Al—C(2) and Al—Et

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 5, pp. 828—830, May, 2002.

1066-5285/02/5105-901 $27.00

Table 1. Reaction conditions and the yields of acetals **3a—c** (20 °C, heptane as a solvent)

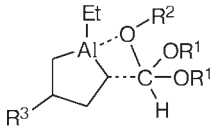
Starting compounds	Time /h	Acetal	Yield (%)
1a + **2a**	6	**3a**	45 (55*)
1a + **2b**	6	**3c**	42 (50*)
1b + **2b**	96	**3b**	5
	6	**3b**	19*
	24	**3b**	64*
1c + **2b**	6	**3c**	53 (62*)

* In the presence of $ZrCl_4$ (3 mol. %).

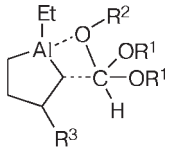
bonds were not detected in the reaction products. Under analogous conditions, butyl orthoformate (**1b**) proved to be substantially more inert, as evidenced by a low yield of dibutyl acetal **3b** (see Table 1).

Earlier,[4] it has been shown that splitting of cyclic acetals with triethyl- or triisobutylaluminum is catalyzed by $ZrCl_4$. In connection with this, it was interesting to study the influence of this catalyst on the reactions of orthoformates with ACP. It turned out that $ZrCl_4$ (3 mol. %) catalyzes the process, providing the greatest effect for the most inert orthoformate **1b** (the yield of compound **3b** was 64%).

High regioselectivity of the reactions of ACP with orthoformates, as well as a low reactivity of butyl orthoformate compared to ethyl orthoformate, is probably due to steric hindrances in the transition state. Assuming that the reaction can proceed through the formation of four-membered intermediates[11] **4** and **5**, one should believe that structure **4** is sterically more preferable; its decomposition yields 4-methyl-substituted aldehyde acetals.



4



5

The structures of acetals **3a—c** were proved using ^1H and ^{13}C NMR spectroscopy. The ^1H NMR spectra of these compounds shows a characteristic doublet at δ 0.85—0.9 for the methyl protons at the tertiary C atom. Attention should also be given to magnetic nonequivalence of the CH_2 protons at the O atoms in $OC\underline{H}_2CH_3$ and $OC\underline{H}_2CH_2CH_2CH_3$.

Experimental

Chromatographic analysis of the reaction mixtures was carried out on a Chrom-5 chromatograph (stainless steel column 370×0.5 cm, 5% S-30 on Chromaton N-AW, flame ionization detector, helium as a carrier gas). ^1H and ^{13}C NMR spectra were recorded on a Bruker AM-300 spectrometer (300 and 75 MHz, respectively) in $CDCl_3$ with Me_4Si as the internal standard. The starting aluminacyclopentanes **2a,b** were prepared according to the known procedure.[6] Orthoformates **1a—c** were synthesized as described in Ref. 12, distilled in a flow of argon over NaOH, and kept in an inert atmosphere; their physicochemical parameters are identical with those reported in the literature.[12]

Reactions of orthoformates 1a—c with 1-ethyl-3-*n*-pentyl- (2a) and 1-ethyl-3-*n*-hexylaluminacyclopentanes (2b) (general procedure). A solution of ACP **2a** or **2b** (20 mmol) in 10 mL of dry heptane was added dropwise at −20 °C in an atmosphere of dry argon to the corresponding orthoformate (20 mmol). The reaction mixture was warmed to 20 °C, stirred for 6—96 h (see Table 1), cooled to −20 °C, and decomposed by adding 20 mL of aqueous 10% NaOH. The organic layer was separated, dried with $MgSO_4$, and analyzed by GLC. Products **3a—c** were isolated by distillation *in vacuo*.

1,1-Diethoxy-4-methylnonane (3a), b.p. 74—75 °C (1 Torr), n_D^{20} 1.4389. Found (%): C, 72.81; H, 12.94. $C_{14}H_{30}O_2$. Calculated (%): C, 72.99; H, 13.12. ^1H NMR, δ: 0.86 (d, 3 H, H(10), $CHCH_3$, J = 6.5 Hz); 0.88 (t, 3 H, H(9), $CH_2C\underline{H}_3$, J = 6.9 Hz); 1.17 (t, 6 H, H(2′), H(2″), $OCH_2C\underline{H}_3$, J = 7.0 Hz); 1.33 (m, 1 H, H(4), C<u>H</u>); 1.10—1.40 (m, 10 H, H(3), H(5), H(6), H(7), H(8), CH_2); 1.61 (m, 2 H, H(2), $CHC\underline{H}_2$); 3.48 (dq, 2 H, H(1′a), H(1″a), $OC\underline{H}_aH_b$, J = 9.7 Hz, J = 7.0 Hz); 3.62 (dq, 2 H, H(1′b), H(1″b), $OCH_a\underline{H}_b$, J = 9.7 Hz, J = 7.0 Hz); 4.45 (t, 1 H, H(1), $C\underline{H}(OEt)_2$, J = 6.0 Hz). ^{13}C NMR, δ: 14.1 (C(9), Me); 15.4 (C(2′), C(2″), $OCH_2\underline{C}H_3$); 19.7 (C(10), Me); 22.8 (C(8)); 26.8 (C(3)); 31.2 (C(6)); 31.9 (C(7)); 32.3 (C(2)); 32.8 (C(4)); 37.0 (C(5)); 60.8 (C(1′), C(1″), $O\underline{C}H_2CH_3$); 103.4 (C(1)).

1,1-Dibutoxy-4-methyldecane (3b), b.p. 100—103 °C (1 Torr), n_D^{20} 1.4245. Found (%): C, 75.72; H, 13.64. $C_{19}H_{40}O_2$. Calculated (%): C, 75.94; H, 13.42. ^1H NMR, δ: 0.86 (d, 3 H, H(11), $CHC\underline{H}_3$, J = 6.4 Hz); 0.92 (t, 6 H, H(4′), H(4″), $O(CH_2)_3C\underline{H}_3$, J = 7.3 Hz); 0.93 (t, 3 H, H(10), $(CH_2)_3C\underline{H}_3$); 1.37 (m, 1 H, H(4), CH); 1.30—1.45 (m, 18 H, H(5) H(6), H(7), H(8), H(9), H(2′), H(2″), H(3′), H(3″), CH_2); 1.56 (m, 4 H, H(2), H(3)); 3.41 (dq, 2 H, H(1′a), H(1″a), $OC\underline{H}_aH_b$, J = 9.4 Hz, J = 6.4 Hz); 3.56 (dq, 2 H, H(1′b), H(1″b), $OCH_a\underline{H}_b$, J = 9.4 Hz, J = 6.4 Hz); 4.44 (t, 1 H, H(1), $C\underline{H}(OBu^n)_2$, J = 5.7 Hz). ^{13}C NMR, δ: 13.9 (C(4′), C(4″), $O(CH_2)_3\underline{C}H_3$); 14.1 (C(10)); 19.4 (C(3′), C(3″), $O(CH_2)_2\underline{C}H_2CH_3$); 19.6 (C(11)); 22.7 (C(9)); 27.0 (C(3)); 29.6 (C(7)); 30.9 (C(6)); 31.8 (C(8), C(2)); 32.0 (C(2′), C(2″), $OCH_2\underline{C}H_2Et$); 32.6 (C(4)); 36.9 (C(5)); 65.0 (C(1′), C(1″), $O\underline{C}H_2(CH_2)_2Me$); 103.4 (C(1)).

1,1-Diethoxy-4-methyldecane (3c), b.p. 84—85 °C (1 Torr), n_D^{20} 1.4325. Found (%): C, 73.83; H, 13.08. $C_{15}H_{32}O_2$. Calculated (%): C, 73.71; H, 13.20. ^1H NMR, δ: 0.86 (d, 3 H, H(11), $CHC\underline{H}_3$, J = 6.5 Hz); 0.88 (t, 3 H, H(10), $CH_2C\underline{H}_3$, J = 6.6 Hz); 1.09 (t, 6 H, H(2′), H(2″), $OCH_2C\underline{H}_3$, J = 6.4 Hz); 1.12 (m, 2 H, H(3)); 1.28 (m, 1 H, H(4), C<u>H</u>); 1.20—1.37 (m, 12 H, H(2), H (5), H(6), H(7), H(8), H(9), CH_2); 3.48 (dq, 2 H, H(1′a), H(1″a), $OC\underline{H}_aH_b$, J = 9.4 Hz, J = 7.1 Hz); 3.63 (dq, 2 H, H(1′b), H(1″b), $OCH_a\underline{H}_b$, J = 9.4 Hz, J = 7.1 Hz); 4.32 (t, 1 H, H(1), $C\underline{H}(OEt)_2$, J = 6.0 Hz). ^{13}C NMR, δ: 14.3 (C(10)); 15.5 (C(2′), C(2″), $OCH_2\underline{C}H_3$); 19.5 (C(11), Me); 22.6 (C(9)); 26.9 (C(6)); 29.6 (C(7)); 31.0 (C(3)); 31.7 (C(8)); 31.8 (C(5)); 32.5 (C(4)); 36.8 (C(2)); 60.6 (C(1′), C(1″), $O\underline{C}H_2Me$); 130.4 (C(1)).

Catalytic reactions of orthoformates 1a—c with 1-ethyl-3-*n*-pentyl- (2a) and 1-ethyl-3-*n*-hexylaluminacyclopentane (2b) (general procedure). A solution of ACP **2a** or **2b** (20 mmol) in 10 mL of dry heptane was added dropwise at −20 °C in an atmosphere of dry argon to a solution of $ZrCl_4$ (0.14 g, 0.6 mmol) in orthoformate **1a—c** (20 mmol). The reaction mixture was warmed to 20 °C, stirred for 6—24 h, cooled to −20 °C, and decomposed by adding 20 mL of aqueous 10% NaOH. The organic layer was separated, dried with $MgSO_4$, and analyzed by GLC (see Table 1).

Products **3a**, **3b**, and **3c** were also obtained from compounds **1a** + **2a**, **1b** + **2b**, and **1c** + **2b**, respectively; they were found to be identical with those described above.

This work was financially supported by the Russian Foundation for Basic Research, Project "State Support for Integration of Highest Education and Fundamental Science" (Project No. 425).

References

1. G. Yu. Ishmuratov, M. P. Yakovleva, R. Ya. Kharisov, and G. A. Tolstikov, *Monoterpenoidy v sinteze opticheski aktivnykh feromonov nasekomykh* [*Monoterpenoids in the Synthesis of Optically Active Insect Pheromones*], Gilem, Ufa, 1999, 99 pp. (in Russian).
2. Y. Tanaka, H. Honda, K. Ohsawa, and J. Yamamoto, *Pestic. Sci.*, 1989, **14**, 197.
3. K. Kori and H. Takikawa, *Liebigs. Ann. Chem.*, 1991, **4**, 497.
4. O. S. Vostrikova, Yu. T. Gafarova, V. A. Dokichev, and S. S. Zlotskii, *Izv. Akad. Nauk, Ser. Khim.*, 1999, 1550 [*Russ. Chem. Bull.*, 1999, **48**, 1530 (Engl. Transl.)].
5. O. S. Vostrikova, Yu. T. Gafarova, V. A. Dokichev, and S. S. Zlotskii, *Dokl. Akad. Nauk*, 1999, **368**, 201 [*Dokl. Chem.*, 1999 (Engl. Transl.)].
6. U. M. Dzhemilev, A. G. Ibragimov, and A. P. Zolotarev, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1989, 207 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1989, **38**, 194 (Engl. Transl.)].
7. U. M. Dzhemilev, A. G. Ibragimov, A. P. Zolotarev, and G. A. Tolstikov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1990, 2831 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1990, **39**, 2570 (Engl. Transl.)].
8. F. Barbot, L. Poncini, B. Randrianoelina, and P. Miginiac, *J. Chem. Research (S)*, 1981, 343.
9. H. Stetter and H. Kuhlman, *Synthesis,* 1975, 379.
10. H. Stetter and E. Reske, *Chem. Ber.,* 1970, **103**, 643.
11. G. A. Tolstikov and V. P. Yur´ev, *Alyuminiiorganicheskii sintez* [*Organoaluminum Synthesis*], Nauka, Moscow, 1979, 292 pp. (in Russian).
12. V. V. Mezheritskii, E. P. Olekhnovich, S. M. Luk´yanov, and G. N. Dorofeenko, *Ortoefiry v organicheskom sinteze* [*Orthoesters in Organic Synthesis*], Rostov Univ., Rostov-na-Donu, 1976, 176 pp. (in Russian).

Received October 5, 2001;
in revised form December 5, 2001