Brief Communications

On the mechanism of titanium-catalyzed cyclopropanation of esters with aliphatic organomagnesium compounds. Deuterium distribution in the reaction products of $(CD_3)_2CHMgBr$ with ethyl 3-chloropropionate in the presence of titanium tetraisopropoxide

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The reaction of $(CD_3)_2CHMgBr$ with ethyl 3-chloropropionate in the presence of catalytic amounts of $Ti(OPr)_4$ results in (E)-1-(2-chloroethyl)-3,3-dideuterio-2-trideuterio-methylcyclopropanol and $(CD_3)_2CDH$, identified by mass spectrometry. The reaction mechanism is discussed.

Key words: cyclopropanation, cyclopropanols, titanium alkoxides, Grignard reagents, esters, β -elimination, titanacyclopropanes.

The addition of monoalkylated titanium derivatives to carbonyl compounds is characterized by high chemoand stereoselectivity.¹ Organotitanium compounds containing two and more alkyl residues are usually unstable and could not find use in organic synthesis for a long time. Tebbe and co-authors have first reported² the use of the Me₂AlCl·CH₂TiCp₂ complex, the product of interaction of 2 equivs. of Me₃Al with Cp₂TiCl₂, as a reactant for homologization of alkenes and methylenation of ketones. As applied to esters, this reaction was described by Pine and co-authors.³ Later, simplified procedures have been used^{4,5} for the preparation of titanium-methylene complexes, including thermolysis of easily accessible dimethyltitanocene.⁵ It is assumed that these complexes are formed from the corresponding dimethyltitanium derivatives by α -elimination of the H atom from one of the Me groups, and the elimination of the CH₄ molecule occurs as the intramolecular process by a concerted mechanism or through the formation of the corresponding titanium hydride.⁶

A novel and experimentally very simple version of using dialkyltitanium derivatives as 1,2-dicarbanionic organometallic equivalents has recently been found.^{7,8} In the simplest variant, the reaction of ester with 2 equivs. of EtMgBr is carried out in the presence of catalytic amounts of (PrⁱO)₄Ti to yield 1-substituted cyclopropanols.⁷ We have postulated⁸ that β -elimination of the H atom (cf. Refs. 1 and 9) from one of the ethyl radicals of the intermediate dialkyltitanium derivative occurs under the reaction conditions to afford ethane and diisopropoxytitanacyclopropane, which further functions as a 1,2-dicarbanionic organometallic reagent. Although the mechanism of decomposition of alkyl derivatives of transition metals by β -elimination of the H atom with the intermediate formation of metal hydrides has been commonly accepted, 1,9,10 the possibility of formation of titanacyclopropane intermediates in consecutive reactions of α -elimination of the H atom from the alkyl radical followed by the rearrangement of the titaniumalkylidene complex cannot be a priori ruled out.11

In this work, we studied the reaction of $Cl(CH_2)_2CO_2Et$ (1) with $(CD_3)_2CHMgBr$ (2) in the presence of $(PrO)_4Ti$ and obtained data that agree with the mechanism of β elimination during the formation of titanacyclopropane

Translated from Izvestiya Akademii Nauk. Seriya Khimicheskaya, No. 2, pp. 376-378, February, 2000.

1066-5285/00/4902-0378 \$25.00 © 2000 Kluwer Academic/Plenum Publishers

reagents. Compound 1 was chosen as the starting substrate due to the possibility of unambiguous identification of the reaction product by ¹H NMR spectroscopy.

Provided the mechanism of β -elimination in the formation of titanacyclopropane 3 is valid, pentadeuterated cyclopropanol 4 should be formed as the final product. In this case, titanacyclopropane 3 can be generated directly from dialkylitanium derivative 5 or intermediate titanium hydride 6 (Scheme 1). At the same time, stepwise mechanism of α -elimination followed by carbene-olefin isomerization of titanium-carbene complex 7 suggests the formation of hexadeuterated cyclopropanol 8 by the alkylation of ester 1 with completely deuterated titanacyclopropane 9 (Scheme 2).



The ¹H NMR spectral data of the obtained cyclopropanol derivative make it possible to establish unambiguously that the compound that formed is (E)-1-(2chloroethyl)-3,3-dideuterio-2-trideuteriomethylcyclopropanol (4). The cis-arrangement of the alkyl substituents in the ring was suggested from the analysis of the ¹H NMR spectrum of nondeuterated (E)-1-(2chloroethyl)-2-methylcyclopropanol (10) obtained under the same conditions by the reaction of ester 1 with PrⁱMgBr. The spectrum of compound 10 exhibits an insignificant difference in chemical shifts of the methine protons and one of the protons of the methylene group of the three-membered cycle, which is characteristic of 1,2-disubstituted cyclopropanols.¹² As compared to the nondeuterated analog, the ¹³C NMR spectrum of compound 4 recorded under the conditions of broad-band spin-spin decoupling with protons contains no signals at δ 14.2 and 20.5, which confirms the presence of deuterium atoms in the Me group and in the methylene unit of the cycle,¹³ while the signal at δ 18.8 confirms the absence of deuterium at the C(2) atom of the cycle.



Comparison of the relative intensities of the peaks with m/z 33 ((CD₃)₂CDH - CD₃) and 32 ((CD₃)₂CH₂ - CD₃) in the mass spectrum of the gaseous product obtained in the reaction under study with those in the spectrum of the reaction product of Grignard reagent 2 with the corresponding amount of (PrⁱO)₄Ti in the absence of ester 1 shows that, in the first case, the side product, (CD₃)₂CH₂, is formed in much greater amount. In our opinion, this fact can be due to the partial deprotonation of the starting ester 1 by an organomagnesium reagent or the occurrence of other side processes.

Experimental

 1 H and 13 C NMR spectra were recorded on a Bruker AC-200 instrument with a working frequency of 200.13 and 50.32 MHz, respectively. Mass spectra of gaseous products were obtained on a Hewlett Packard GC MS 5890/5972 instrument with an electron impact energy of 70 eV. 2-Bromo-1,1,1,3,3,3hexadeuteriopropane was prepared by the previously published procedure.¹⁴

(E)-1-(2-Chloroethyl)-3,3-dideuterio-2-trideuteriomethylcyclopropanol (4). A solution of the Grignard reagent (obtained from 2-bromo-1,1,1,3,3,3-hexadeuteriopropane (1 mL, 10 mmol) and Mg chips (0.5 g, 21 mg-at.) in ether (6 mL) was added over 30 min to a solution of ethyl 3-chloropropionate (1) and (PriO), Ti (0.15 mL, 0.5 mmol) in anhydrous Et₂O (3 mL) with boiling of the reaction mixture. Gaseous products that evolved in the reaction were collected over a saturated solution of NaCl and analyzed by mass spectrometry. The reaction mixture was poured in 20 mL of 10% H₂SO₄ cooled to 0 °C, the organic layer was separated, and the aqueous layer was extracted with ether (10 mL). The combined ethereal extracts were successively washed with saturated solutions of NaHCO₃ and NaCl and dried with Na₂SO₄. The solvent was removed in vacuo, and the residue was chromatographed on silica gel (hexane-ethyl acetate, 3:1). The yield of cyclopropanol 4 was 0.29 g (46%). ¹H NMR (CDCl₂), δ : 1.04 (s, 1 H): 1.92-2.16 (m, 3 H): 3.77 (t, 2 H, J = 7.2 Hz). ¹³C NMR (CDCl₃), *δ*: 18.8, 36.0, 41.8, 58.2.

Mass spectrum of the gaseous reaction product. m/c (I_{rel} (%)): 51 (CD₃CDHCD₃ [M⁺]) (9.7), 50 (CD₃CH₂CD₃ [M⁺]) and CD₃CDHCD₃ – H) (29.7), 49 (31.7), 48 (4.9), 47 (15), 46 (16.1), 45 (21.5), 44 (5), 43 (4.1), 42 (25.2), 41 (12.8), 40 (8.5), 39 (2.4), 38 (5.5), 34 (10.8), 33 (CD₃CDHCD₃ – CD₃) (85.3), 32 (CD₃CH₂CD₃ – CD₃) (100), 31 (62.7), 30 (74.9), 29 (48.1), 28 (23.1), 27 (9.8), 26 (2.5).

Mass spectrum of the gaseous reaction product in the absence of ester 1. m/z (I_{rel} (%)): 51 (CD₃CDHCD₃ [M⁺]) (10.8), 50 (CD₃CH₂CD₃ [M⁻] and CD₃CDHCD₃ – H) (28.5), 49 (25.4), 48 (7.1), 47 (17.6), 46 (20.9), 45 (25.2), 44 (6.8), 43 (5.4), 42 (33.2), 41 (16.2), 40 (11.6), 39 (3.1), 38 (7.6), 34 (14.1), 33 (CD₃CDHCD₃ – CD₃) (100), 32 (CD₃CH₂CD₃ – CD₃) (85.9), 31 (67.9), 30 (75.7), 29 (53.3), 28 (31.4), 27 (12.3), 26 (3.6).

(*E*)-1-(2-Chloroethyl)-2-methylcyclopropanol was obtained by a similar procedure in 51% yield from ester 1 (0.61 mL, 4.5 mmol), (Pr^{IO})₄Ti (0.15 mL, 0.5 mmol), and Grignard reagent obtained from 2-bromopropane (1 mL, 10 mmol) and Mg (0.5 g, 21 mg-at.) in Et₂O (6 mL). ¹H NMR (CDCl₃), δ : 0.12 (t, 1 H, J = 5.5 Hz); 0.83-0.98 (m, 2 H); 1.02 (s, 3 H); 1.92-2.18 (m, 2 H); 2.28 (br.s, 1 H); 3.77 (t, 2 H, J = 7.2 Hz). ¹³C NMR (CDCl₃), δ : 14.2, 19.4, 20.5, 36.7, 42.0, 57.2.

This work was financially supported by the International Science Foundation (INTAS, Grant 96-1325).

References

- M. T. Reetz, Organotitanium Reagents in Organic Synthesis, Springer-Verlag, Berlin-Heidelberg, 1986.
- F. N. Tebbe, G. W. Pazrshall, and G. S. Reddy, J. Am. Chem. Soc., 1978, 100, 3611.
- S. H. Pine, R. J. Petit, G. D. Geib, S. J. Gru, C. H. Gallego, T. Tijerina, and R. D. Pine, *J. Org. Chem.*, 1985, 50, 1212;
 S. H. Pine, *Organic Reactions*, 1992, 43, 1.

- J. R. Stiele and R. H. Grubbs, J. Am. Chem. Soc., 1983, 105, 1664; L. Clawson, S. L. Buchwald, and R. H. Grubbs, Tetrahedron Lett., 1984, 25, 5733.
- N. A. Petasis and E. I. Browej, J. Am. Chem. Soc., 1990, 112, 6392.
- J. Cheon, D. M. Rogers, and G. S. Girolani, J. Am. Chem. Soc., 1997, 119, 6804; J. Cheon, L. H. Dubois, and G. S. Girolani, J. Am. Chem. Soc., 1997, 119, 6814.
- O. G. Kulinkovich, S. V. Sviridov, and D. A. Vasilevskii, Synthesis, 1991, 234.
- O. G. Kulinkovich, S. V. Sviridov, D. A. Vasilevskii, and T. S. Pritytskaya, *Zh. Org. Khim.*, 1989, 25, 2244 [*J. Org. Chem. USSR*, 1990, 25, 2027 (Engl. Transl.)]; O. G. Kulinkovich, D. A. Vasilevskii, A. I. Savchenko, and S. V. Sviridov, *Zh. Org. Khim.*, 1991, 27, 1428 [*J. Org. Chem. USSR*, 1992, 27, 1429 (Engl. Transl.)].
- P. J. Davidson, M. F. Lappert, and R. Pearce, *Chem. Rev.*, 1976, **76**, 219; M. L. Steierwald and W. A. Goddard, III, *J. Am. Chem. Soc.*, 1984, **106**, 308.
- R. R. Schrock and G. W. Parshall, Chem. Rev., 1976, 76, 243; B. J. Burger, M. E. Thompson, W. D. Cotter, and J. E. Bercaw, J. Am. Chem. Soc., 1990, 112, 1566.
 O. M. Nefedov, A. I. Joffe, and L. G. Mcnchikov, Khimiya
- O. M. Nefedov, A. I. Ioffe, and L. G. Mcnchikov, *Khimiya karbenov* [*Chemistry of Carbenes*], Khimiya, Moscow, 1990, p. 233 (in Russian).
- E. J. Corey, S. A. Rao, and M. C. Noe, J. Am. Chem. Soc., 1994, 116, 9345; J. Lee, H. Kim, and J. K. Cha, J. Am. Chem. Soc., 1996, 118, 4198.
- E. Breitmaier and W. Voelter, Carbon-13 NMR Spectroscopy: High Resolution Methods and Application in Organic Chemistry and Biochemistry, VCH, New York, 1987, 337.
- 14. R. F. Nystrom, W. H. Yanks, and W. G. Brown, J. Am. Chem. Soc., 1948, 70, 441.

Received March 5, 1999; in revised form October 26, 1999

Formation of formic and acetic acids by low-temperature condensation of a mixture of methane and water vapor dissociated in MW discharge

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Formic and acetic acids are formed by the low-temperature (77 K) condensation of a mixture of methane and water vapor dissociated by MW discharge at a low pressure. The effect of experimental conditions on the yield of HCOOH and AcOH was studied under different experimental conditions. The yields of H⁺, OH⁺, and O₂ from MW discharge in the CH₄+H₂O mixture were determined by ESR in the gas phase under the experimental conditions in the conditions used to synthesize HCOOH and AcOH. The kinetics of the gas phase reactions in the connecting channel was simulated. The mechanism of formation of HCOOH and AcOH through the interaction of active species from the gas phase on the condensate surface was suggested.

Key words: electric discharge in gases, low-temperature condensation, formic acid, acetic acid, methane, water, ESR in gas phase, hydrogen atoms, oxygen atoms, hydroxyl radicals.

Low-temperature condensation (LTC) of gas mixtures dissociated by electric discharges is a unique method for synthesis of inaccessible compounds, for example, higher hydrogen polyoxides H_2O_3 and H_2O_4 (Ref. 1).

Translated from Izvestiya Akademii Nauk. Seriya Khimicheskaya, No. 2, pp. 379-382, February, 2000.