Platinum(II)-Catalyzed Isomerization of Alkoxycyclopropanes to Alkylated Ketones

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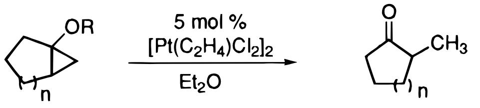
Received March 4, 1996[⊗]

Summary: Conversion of alkoxycyclopropanes to 2-methyl ketones has been accomplished using catalytic platinum. Mechanistic studies revealed that the conversion involves platinum insertion into the cyclopropane followed by rearrangement to produce the methyl ketone.

The reaction of cyclopropanes with organometallic complexes represents an effective means to convert simple, readily available substrates into more elaborate molecules.[3] Because a cyclopropyl unit possesses "double-bond character", the high level of strain lends itself to chemical reactivity not otherwise attainable.[4] Lately, new methodologies have provided excellent stereo- and regioselective products making cyclopropanes a useful synthon in organic synthesis.[5] Interest in cyclopropane transformations using platinum complexes has prompted us to explore the influence of various functional groups on cyclopropanes.[6] This note describes the results of our recent investigations on the platinum-*catalyzed* conversion of alkoxy-substituted cyclopropanes as shown in eq 1.

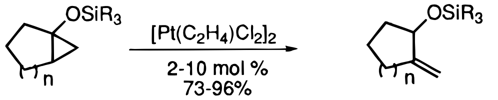


(1)

1a n=1, R=Et
1b n=2, R=Et
1c n=2, R=H
1d n=4, R=Et

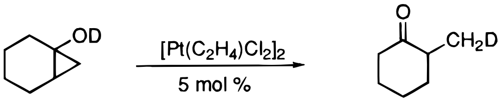
2a 65%
2b 85%
2c 82%
2d 80%

Reaction of **1b** was initially carried out using stoichiometric amounts of platinum at room temperature. However, it was subsequently determined that only catalytic amounts were needed. Thus, treating 1-ethoxybicyclo[4.1.0]heptane with 5 mol % of Zeise's dimer in diethyl ether resulted in complete conversion to 2-methylcyclohexanone in 18 h at room temperature. The reaction appears to be general as various ring sizes and both ethoxy ethers and alcohols are converted. Furthermore, solvents such as THF and CH_2Cl_2 (or without solvent) can be used to carry out the transformation. The isomerization is also carried out in air without any special precautions, as exposure to air does not terminate the reaction. This in contrast to many organometallic reactions. It is interesting to note that 1-ethoxybicyclo[6.1.0]nonane (**1d**) produced the desired product, whereas bicyclo[6.1.0]nonane has been shown to be inert to platinum insertion under these conditions.[7] Thus, platinum insertion appears to be facilitated by the electron-releasing affect of the ethoxy functionality.[8] Finally, this work compliments the work of Sonoda et al., in which the use of silyl ether cyclopropanes resulted in the formation of exocyclic methylenes (eq 2).[9]



(2)

Even though the results in eqs 1 and 2 give precedence for platinum insertion, the source of the proton for the methyl moiety was in question. Therefore to gain insight into the mechanism of the transformation, we carried out a deuterium labeling experiment in which the hydroxy proton was replaced by a deuterium (eq 3). Reaction of **1e** with Zeise's dimer in dry ether (or no solvent) produced **2e** in which the ^2H spectrum displayed a single resonance at 1.0 ppm. Deuterium labeling in the product was further verified by mass spectrometry which exhibited a molecular ion at *m*/*e* 113.



1e **2e** (3)

Further support for a platinum-catalyzed reaction is obtained from an intramolecular olefin trapping experiment. Reaction of **3** with stoichiometric amounts of platinum resulted in generation of an orange solid which upon dissolution in acetonitrile gave complex **5** (eq 4). Verification of this structure was accomplished by

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[⊗] Abstract published in *Advance ACS Abstracts,* August 1, 1996.

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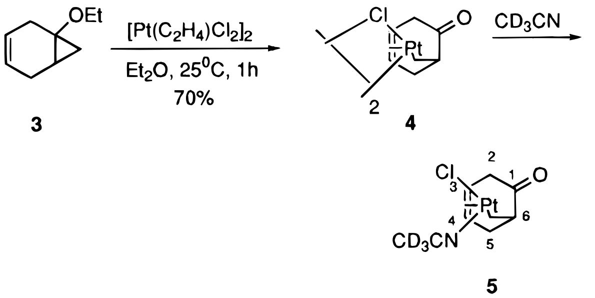
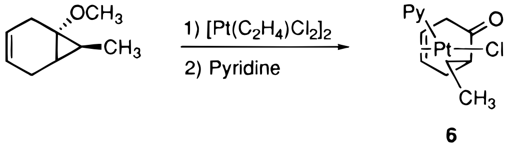
S0276-7333(96)00157-4 CCC: $12.00



(4)

comparing the NMR data of complex **5** to complex **6** (eq 5), which has been established by X-ray crystallography



(5)

(Table 1).[10] The NMR assignments for **5** were garnered using COSY and HETCOR spectroscopy. A Pt(II) oxidation state for the platinum was established from observation of a resonance at 1026 ppm in the ^{195}Pt NMR spectrum.[11] Additionally, ^{13}C CP/MAS experiments on solid **4** exhibit downfield resonances at 75 and 215 ppm suggesting the formation of a platinum-bound olefin and the carbonyl moiety in the solid. IR spectroscopy confirmed the carbonyl functionality with a resonance at 1715 cm^{-1}. The structure of **4** is believed to be a dimer of **5**.

With the above information, we propose the mechanism for this isomerization as depicted in Scheme 1. Insertion of platinum into the methylene-methoxy bearing carbon produces platinacycle **7**. Rearrangement of **7** with loss of EtCl or DCl generates **8**. At this point, unsaturated molecules such as **3** undergo platinum coordination to the olefin altering the cycle to produce complex **4**. For the saturated systems, oxidative addition of RCl leads to **9** which undergoes elimination to provide the observed products and completes the catalytic cycle. In the case of an ethoxy substituent, we believe β-hydride elimination from a σ-bound ethyl group produces **3** and generates an ethylene molecule.[12] Finally, excellent precedence for this mechanism can be found in the work of Ryu and Sonoda.[13]

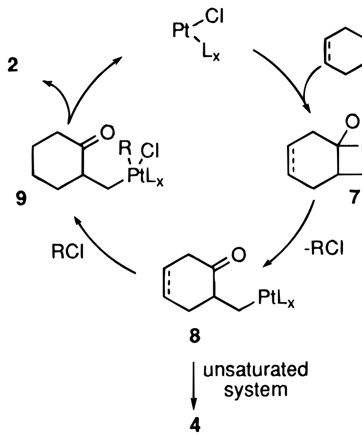
In conclusion, a facile method for the isomerization of alkoxy- and hydroxycyclopropanes to alkylated ketones has been found. Current studies are underway to further elaborate this methodology and to incorporate additional functionality.

Table 1. ^{13}C NMR Data for 5 and 6

C no.	6^a ($J_{Pt,C}$)	5^b	C no.	6^a ($J_{Pt,C}$)	5^b
1	211.0 (*)^{c,d}	210.6 (27)	5	31.0	35.2
2	39.2 (26)	38.0 (34)	6	60.8 (28)	51.5 (5)
3	75.1 (*)	74.7 (257)	7	25.7 (723)	17.0 (720)
4	81.0 (*)	84.3 (233)	Me	22.9 (37)	

^{a} Relative to CDCl$_3$. ^{b} Relative to CD$_3$CN. ^{c} Coupling in hertz. ^{d} Asterisk indicates unresolved coupling.

Scheme 1



Experimental Section

General Methods. ^{1}H, ^{2}H, ^{13}C, and ^{195}Pt NMR spectra were collected on Bruker WM250, AC300, and AM500 spectrometers. ^{195}Pt NMR chemical shifts are given relative to external 1 M Na$_2$Pt(CN)$_4$. CP/MAS spectra were obtained at 50.2 MHz for ^{13}C on a Chemagnetics spectrometer. Mass spectral data were collected on VG-MM-16 and 7070 spectrometers, numbers in (parentheses) represent intensity. Infrared spectra were obtained on a Nicolet SDX FT-IR spectrometer. Diethyl ether was distilled from sodium benzophenone prior to use, and pentane was distilled from LiAlH$_4$. Zeise's dimer was prepared from K$_2$PtCl$_4$ on loan from Johnson-Matthey Corp. Cyclopropanes **1a**–**d** were prepared by literature procedures.[14] 1-Deuterioxybicyclo[4.1.0]heptane (**1e**) was prepared by modifing Murai's procedure[14c] with NaOD and CD$_3$OD. Key NMR data for **1e** displayed a broad resonance at 3.5 ppm (CHCl$_3$) in the ^{2}H spectrum and the absence of the OH resonance in the ^{1}H spectrum; integration revealed 100% labeling.

General Procedure for the Isomerization of 1a–e. In a 10 mL flask was placed 140.2 mg (1.00 mmol) of **1** and 5 mL of freshly distilled ether. Zeise's dimer (29.4 mg, 0.050 mmol) was added, and the mixture was stirred at room temperature for 10–20 h. The product (**2**) was isolated by chromatography on silica gel with Et$_2$O/pentane (1:1). Physical data for compounds **2a** [1120-72-5], **2b** [583-60-8], and **2d** [10363-27-6] were identical in all respects to authentic material.

Deuterated 1-Methylcyclohexanone (2e). **2e** was isolated as a colorless oil in 81% yield: ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.02 (d, J = 6.6, 2H), 1.4 (m, 1H), 1.6–1.9 (m, 3H), 2.1 (m, 2H), 2.4 (m, 3H); ^{2}H NMR (46 MHz, CHCl$_3$) δ 1.0; IR (neat) 2931, 2861, 1715, 1453, 922, 730 cm^{-1}; MS (GCMS) m/e 113 (30), 112 (30), 97 (10), 85 (10), 84 (35), 69 (100).

1-Ethoxybicyclo[4.1.0]hept-3-ene (3). Under argon, a 100 mL flask equiped with condensor and side arm was loaded

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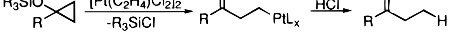
[11] Pt(IV) complexes are found between 2500–3400 ppm whereas Pt(II) complexes range from 680–1800 ppm relative to Na$_2$Pt(CN)$_4$. See ref 3b and: (a) Ekeland, R. A.; Jennings, P. W. *J. Organomet. Chem.* **1985**, *281*, 397. (b) Hanks, T. W.; Ekeland, R. A.; Emerson, K.; Larsen, R. D.; Jenning, P. W. *Organometallics* **1987**, *6*, 28. (c) Hanks, T. W.; Jennings, P. W. *J. Am. Chem. Soc.* **1987**, *109*, 5023.

[12] Reaction of 1-methoxybicyclo[4.1.0]heptane requires stoichiometric amounts of platinum implying the formation of a carbene type ligand.

[13] Ikura, K.; Ryu, I.; Ogawa, A.; Sonoda, N.; Harada, S.; Kasai, N. *Organometallics* **1991**, *10*, 528. The platinum complex was established by X-ray crystallography:



For additional evidence see: Stahl, S. S.; Labinger, J. A.; Bercaw, J. E. *J. Am. Chem. Soc.* **1995**, *117*, 9371.

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with 811 mg of Zn (12.4 mmol), 1.23 g of CuCl (12.4 mmol), and 50 mL of ether. The mixture was brought to reflux for 30 min, and then 0.988 mL of CH_2I_2 was added followed by 1.03 g (8.26 mmol) of 1-ethoxy-1,4-cyclohexadiene [55983-17-0] in 10 mL of ether. The mixture was maintained at reflux for 48 h and then cooled and filtered. The ether layer was washed with saturated NH_4Cl, Na_2CO_3, water and dried ($MgSO_4$). Distillation (72 °C, 10 mm) provided 694 mg (5.02 mmol, 61%) of colorless oil. Preparative GC (20 ft SE30 on Chromosorb W) was required to obtain pure **3**: ^1H NMR (300 MHz, $CDCl_3$) δ 0.48 (m, 1H), 0.76, m, 1H), 1.13 (t, $J = 6.6$, 3H), 1.22 (m, 1H), 2.11−2.70 (m, 4H), 3.45 (q, $J = 6.6$, 2H), 5.35−5.52 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 15.7, 18.0, 25.6, 28.0, 59.7, 61.5, 123.5, 123.6. Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 77.99; H, 10.01.

Complex 4. In a 10 mL flask was placed 58.1 mg (0.420 mmol) of **3** and 3 mL of dry ether. The mixture was cooled to 0 °C, Zeise's dimer was added, and the mixture was stirred under nitrogen for 1 h. The yellow solid was triturated 3× with 10 mL of pentane and dried under vacuum to give 106.9 mg of **4** (70% yield). ^{13}C CP/MAS (200 MHz) δ 27, 34, 52, 75, 215; IR (KBr) 1715 cm^{-1}. Anal. Calcd for $C_{14}H_{18}Cl_2O_2Pt_2$: C, 24.75; H, 2.67; Cl, 10.44. Found: C, 24.38; H, 3.01; Cl, 10.79.

Complex 5. Complex **4** was dissolved in CD_3CN to produce **5** as a yellow solution. Attempted recrystallization or precipitation of **5** resulted in decomposition: ^1H NMR (500 MHz, CD_3CN) δ 1.13 (dd, $J = 3.7$, 8.9 Hz, $J_{Pt,H} = 113.4$, H7a), 1.64 (m, $J_{Pt,H} = 85$ Hz, H6), 1.72 (m, H5a), 2.10 (dd, $J = 3.7$, 7.0 Hz, H7b), 2.31 (m, H5b), 2.61 (dd, $J = 21.7$, 1.8Hz, H2a), 2.97 (dd, $J = 21.7$ Hz, 2.2H, H2b), 4.65 (m, $J_{Pt,H} = 80.9$ Hz, H4), 4.80 (m, $J_{Pt,H} = 76.3$ Hz, H3); ^{195}Pt NMR (CD_3CN) δ 1026; IR (neat) 2950, 2230, 1715, 1080, 822 cm^{-1}.

Acknowledgment. Support from the Petroleum Research Fund, administered by the American Chemical Society, the National Science Foundation, and Johnson-Matthey is gratefully acknowledged.

Supporting Information Available: Figures displaying IR, NMR, and mass spectra (18 pages). Ordering information is given on any current masthead page.

OM960157T