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NOTE

Synthesis of 2-(*t*-Butyl)dimethyl-silyloxy-2-cyclopropyl-1-ethyl-triphenylphosphonium iodide and Its Crystal Structure

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Compound of 2-(*t*-butyl)dimethyl-silyloxy-2-cyclopropyl-1-ethyl-triphenylphosphonium iodide ($C_{29}H_{38}IOPSi$) has been synthesized through five steps and the structure was determined by X-ray diffraction. The crystal is monoclinic, space group $P2_1/n$ with unit cell parameters: a = 13.6074(2) Å, b = 13.0416(2) Å, c = 17.0381(2) Å. α = 90º, β = 95.5280(10) º, γ = 90º, v = 3009.56(7) Å^3, z = 4, Dc = 1.299 Mg/m^3, Mr = 588.55, F(000) = 1208 and μ = 1.175 mm^{-1}. The final R and wR are 0.0444 and 0.1178, respectively for 5312 observed reflections with I > 2σ(I).

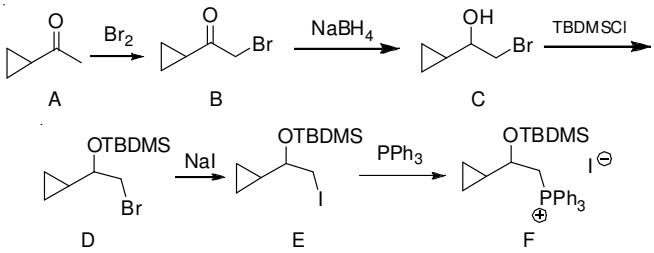
Key Words: Calcipotriol, Triphenylphosphine, Bromoacetylcyclopropane, Crystal structure.

1a,25-Dihydroxyvitamin (vitamin D_3) is recognized as a calcium- and phosphorous-regulating hormone and plays a pivotal role in bone homeostasis[1]. [20(R)-[3'(S)-Cyclopropyl-3'-hydroxyprop-1'(E)-enyl]-1(S),3(R)-dihydroxy-9,10-seco pregna-5(Z),7(E),10(19)-triene (Calcipotriol) is an analog of vitamin D_3 which has strong activity in inhibiting undesirable proliferation of epidermal keratinocites and used as a dermatologic drug in clinical application[2,3]. Scientists have attached more attention to the synthesis of calcipotriol[4,5]. One important intermediate in synthesis of calcipotriol is 2-(*t*-butyl)dimethyl-silyloxy-2-cyclopropyl-1-ethyl-triphenylphosphonium iodide. Herein, the new route for synthesis of the 2-(*t*-butyl)-dimethyl-silyloxy-2- cyclopropyl-1-ethyl-triphenylphosphonium iodide and its crystal structure are reported.

All the reagents were of AR grade and used without further purification. ^{1}H NMR spectra were recorded on a Bruker ACF-400 spectrometer with $CDCl_3$ as solvent unless otherwise specified. For X-ray Crystallographic analysis, the X-ray diffraction intensities and the unit cell parameters were determined on a Brucker SMART APEXII CCD diffractometer.

General procedure

Bromoacetylcyclopropane (B): A solution of 21 g cyclopropyl methyl ketone (A), 150 mL methanol was added to a 500 mL round bottom flask. The reaction solution was stirred and cooled below 5 ºC. 40 g bromine was added slowly. After the reaction was completed, the mixture was diluted with water and extracted four times with ethyl ether. The ether extracts were washed with 10 % Na_2CO_3, water, brine and dried with $MgSO_4$. Afer removing Et_2O, the residue was distilled to give the product 35 g (b.p. 60-65 ºC 10 mmHg).



Scheme-I: Synthesis of 2-(*t*-butyl)dimethyl-silyloxy-2-cyclopropyl-1-ethyl-triphenylphosphonium iodide

2-Bromo-1-cyclopropylethanol (C): To a stirred, ice-cooled solution of 20 g of **B**, 100 mL methanol was added 14.4 g sodium borohydride. After addition, the mixture was stirred under room temperature for 2 h and then methanol was removed *in vacuo*. The residue was poured into 100 mL water and extracted three times with Et_2O. The ether extracts were dried with $MgSO_4$ and then the residue was concentrated and distilled to give the product 12.4 g (b.p. 63-65 ºC 5 mmHg).

***t*-Butyl(1-cyclopropyl-2-bromoethoxy)dimethylsilane (D):** To a stirred, ice-cooled solution of 8.7g of **C**,3.2g 4-dimethylaminopyridine (DMAP), 5.4 g imidazole, 100 mL DMF was added a mixture of 16.1 g *t*-butyl(dimethyl)-

silyltrifluormethanesulfonate (TBDMSCl) and 30 mL N,N-dimethyl formamide. After 24 h, stirring at room temperature, 100 mL water was added. The mixture was extracted with hexane, then it was dried over $MgSO_4$. Hexane was removed under reduced pressure. The crude product (18.8 g, GC content: 50.7 %) was direct used without further purification.

***t*-Butyl(1-cyclopropyl-2-iodoethoxy)dimethylsilane (E):** 18.8 g **D**, 15.9 g NaI and 60 mL acetone were mixed and reflux 1 day. Then acetone was removed and 100 mL of water was added. The mixture was extracted with hexane, then it was washed by 50 mL of $KHCO_3$ (10 %), 50 mL water and dried over with $MgSO_4$. It gives 15.2 g (GC content: 63.6 %) crude product and it was used to the next step directly.

2-(*t*-Butyl)dimethyl-silyloxy-2-cyclopropyl-1-ethyl-triphenylphosphosphonium iodide (F): 1.54 g (63.6 %) **E** was placed in a 50 mL flask under nitrogen atmosphere. Triphenylphosphine 1.25 g was added. The mixture was warmed at 90-100 ºC for 2 h and then was cooled to rom temperature. The solid was washed with anhydrous cyclohexanne for three times. The crude product was purified by column chromatography on silica gel (300-400 m, 20 % CH_2Cl_2/hexane). Yellow solid 1.26 g was obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69-8.10 (m, 15H), 4.18 (s, 1H), 3.98 (dd, 1H, J = 27.2, 13.2 Hz), 3.48 (s, 1H), 1.69 (s, 3H), 1.12 (s, 1H), 0.65 (s, 12H), 0.45 (s, 1H), -0.38 (s, 3H).

Crystal structure detection method: A yellow single crystal (0.168 mm × 0.164 mm × 0.152 mm) was mounted on a glass fiber capillary for intensity data collection with a graphite-monochromated (Mo-K_α) radiation (λ = 0.71073 Å) and operating in the ω/2θ scan mode. The intensity data were collected in the range of $1.83^o \le \theta \le 25.00^o$ using φ-ω mode at 296(2) K. Total reflections of 38232 were collected, of which 5312 reflections with $R_{int} = 0.0379$ were unique in the ranges of $-16 \le h \le 16$, $-15 \le k \le 15$, $-20 \le l \le 20$. Data collection and cell refinement were performed with APEX2 software. Structures were solved by direct methods and refined by full-matrix least-squares on F_2 with SHELXTL 97. Non-hydrogen atoms were refined by anisotropic displacement parameters and the positions of all H-atoms were fixed geometrically and included in estimated positions using a riding model. The final full-matrix least-squares refinements including 292 parameters for 5312 reflections with $I > 2\sigma(I)$ gave $R_1 = 0.0444$, $wR_2 = 0.1178$.

The selected bond lengths and bond angles are given in Table-1. Fig. 1 shows the molecular structure of the present compound. The interplanar angles of the three phenyl rings to each other are 83.1(4)°, 76.0(7)°, 65.7(2)°. The bond distance of the three Si-C bonds ranging from 1.844(6)-1.855(6) Å. The bond distance of P-C25 bond is 1.787(4) Å and it is a little shorter than normal distance of P-C bond (1.80 Å)[6].

TABLE-1
SELECTED BOND DISTANCES (Å) AND ANGLES (º)

Si-O	1.650(3)	O-Si-C(11)	110.6(2)
Si-C(11)	1.844(6)	O-Si-C(10)	106.58(17)
Si-C(10)	1.853(4)	C(11)-Si-C(10)	109.7(3)
Si-C(6)	1.855(6)	O-Si-C(6)	110.1(2)
P-C(25)	1.787(4)	C(11)-Si-C(6)	111.9(3)
P-C(19)	1.791(4)	C(10)-Si-C(6)	107.8(3)
P-C(13)	1.793(4)	C(25)-P-C(19)	109.5(2)
P-C(12)	1.799(4)	C(25)-P-C(12)	109.47(19)
O-C(2)	1.423(5)	C(2)-O-Si	134.0(3)

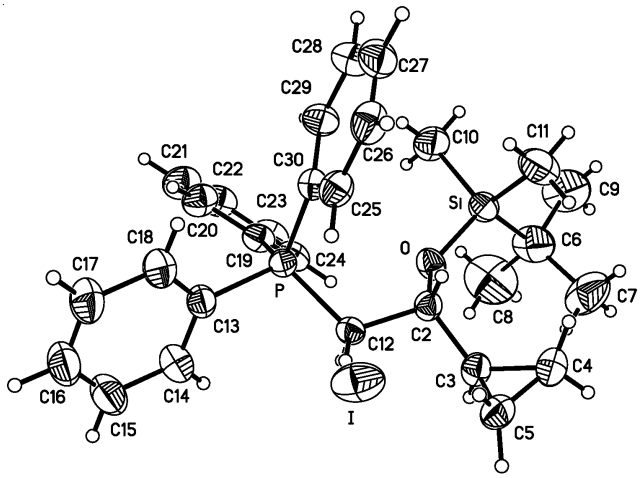


Fig. 1. Molecular structure of the present compound

Conclusion

Crystal structure of 2-(*t*-butyl)dimethyl-silyloxy-2-cyclopropyl-1-ethyl-triphenylphosphonium iodide has been synthesized and characterized by ^{1}H NMR and X-ray diffraction analysis.

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