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Research Article

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Synthesis of new alpha–methylene–gamma–butyrolactone skeleton using cobaloxime(pseudo vitamin B_{12}) as catalyst

K. Tabatabaeian*, R. Alipour and N. O. Mahmoodi

Chemistry Department, Faculty of Sciences, University of Guilan, Rasht, Iran

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ABSTRACT

The alpha–methylene–gamma–butyrolactone skeleton belongs to a group of natural compounds, which are called sesquiterepenes. These compounds, have already been known to possess biological activities for example anti-tumor, antimicrobial, allergenic, etc. Here a new route to synthesize of this skeleton is reported using allybenzene and premade cobaloxime catalyst in three steps, such as bromoetherification of alkene , cyclization in the presence of cobaloxime and ultimate oxidation lead to preparation of target alpha–methylene–gamma–butyrolactone. Main products were isolated and characterized via IR, ^{1}HNMR and GC-Mass.

Keywords: Alpha–methylene–gamma–butyrolactone, Cobaloxime, Cyclization, Alkene

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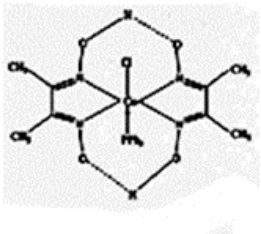
INTRODUCTION

A large number of research activities concerning presence of alpha–methylene–gamma–butyrolactone have been reported [1,2,3]. These squiterepenes style skeleton is reported as anti-HIV, anti-cancer, anti-allergenic, etc [4]. However, for synthesis of this type of compounds several different methods were reported. One of these methods is to use electro-organic chemistry [5]. The advantage of this method in comparison to other reported methods is to produce super-nucleophilic particles such as (Co^+) ion which have sufficient ability for alkylation [6]. Cobalt complex alkyltion was used for synthesis of organic compounds as a one of powerful radical sources. Cobaloxime compounds of bis (dimethylglyoximato) cobalt(III) which were generally called pseudo vitaminB_{12}, was used to synthesize sequentially numbered key rings and to provide targets alpha–methylene–gamma–butyrolactone(Scheme1) [7,8]. Similar products were also reported from aldehydes [9].



Scheme 1

These complexes perform the cyclization process via ions (Co^+) , (Co^{2+}) and (Co^{3+}) [10,11].Here, we are reporting a new route for synthesis of alpha–methylene–gamma–butyrolactone. For this purpose we utilized premade fresh cobaloxime as catalyst in an electron transfer cycle via three steps; initially, preparing of bromoether from allybenzene in the presence of NBS and propargyle alcohol. Next step preparation of methylene oxalone from bromoether in the presence of cobaloxime catalyst . Lastly, oxidation of the methylene oxalone to target alpha–methylene–gamma–butyrolactone utilizing Jones reagent.

EXPERMENTAL SECTION

In general , each step was isolated through [SiO_2:60-7730 mesh]. IR spectra were taken with KBr disk for solid and CCl_4 for a solution using Shimadzu 470 spectrometer.^{1}HNMR spectra were recorded on a Bruker DRX-500 MHz Advance instrument with internal standard TMS and $CDCl_3$.GC-Mass was performed using instrument 689 HP in acetone.

Preparation of bis(dimethyl glyoximato) triphenyl phosphine cobalt (III).

Dry EtOH96% (40 ml), DH (1.129 g, 9.4 mmol), $CoCl_2$, $6H_2O$ (1.28 g, 4.3 mmol) were added to round-bottom flask the mixture was heated and stirred at 60°C. To this mixture was added PPh_3 (2.36 g,9 mmol). At this stage the color of solution gradually was turned from dark green to purple and finally to stable brownish. After the solution was cooled by remaining 30 min at room temperature. Filtered and the precipitate was washed with H_2O, Et_2O and dry EtOH (1.336 g, 2.53 mmol, 53.2%).IR (KBr):518(Co-N), 698 (bend aromatic), 1085 (N-O), 1285,1438,1550 (C=N), 2945 (C-H), 3400 (O-H) cm^{-1}.^{1}HNMR (500 MHz, $CDCl_3$):δ: 2.02 (s, 12H , CH_3), 7.3-7.5 (m ,15H) ppm.

Preparation 3-bromo-2-prop-2-enyloxy-propyl-benzene 3

NBS (4.3g, 24 mmol) was dissolved in propargyl alcohol (20 ml). The solution was stirred at -35°C.Allybenzene (3.5 ml) in CH_2Cl_2 (20 ml) was added for 1h.The reaction was maintained at16°C for 1h and allowed to come to room temperature for 24h. After this time to this solution was added NaOH (1 N, 25 ml). The mixture was extracted with CH_2Cl_2 (3×20 ml). Organic phase was washed with NaOH (1 N, 10 ml), separated and dried over anhydride $MgSO_4$.The solvent was removed. Oily phase was monitored through TLC and isolated through[SiO_2:60-7730mesh, CH_2Cl_2: petroleum ether (4:17)] compound **3** (0.95g, 3.74 mmol, 14.8%) as center cut was recovered. IR(CCl_4):665(C-Br),1075 (C-Ostreh), 2900 (C-Haliphatic), 3010 (Ar-H), 3300 (C≡H) cm^{-1}.^{1}HNMR (500 MHz, $CDCl_3$):δ: 2.5 (t, 1H, J=2.4Hz), 2.5 (t, 1H, J=2.4Hz, C≡H), 2.6 (d, J=5.4Hz, 2H), 3.3 (dd, J=4.3, 10.8Hz, 1H, HC-Br), 3.4 (dd, J=5, 10.8Hz, 1H, HC-Br), 3.9 (m, 1H, HC-O-C), 4.2 (d, J=2.4Hz, 2H, CH_2-O), 7.2 (m, 5H) ppm.

Prapration2-benzyle-4-methylene-tetrahydrofuran 7

To a stirred solution of **3** (0.85g, 3.34 mmol) in EtOH (20 ml) was added NaOH (10N, 0.5 ml) and $NaBH_4$ (127 mg, 3.34 mmol) at 50°Cunder argon atmosphere. Then, to this mixture cobaloxime catalyst (0.5 mg, 0.85 mmol) for 1.5 h was added and stirred for additional 3h. After that EtOH solution was evaporated and the remaining oily residue was washed with saturated NaCl and excracted with petroleum ether: Et_2O (1:4), (3×15 ml).The organic phase was dried over anhydride $MgSO_4$ and evaporated. The reside was chromatographed [SiO_2:60-7730 mesh, petrolumether:Et_2O (1:8)] to isolate center cut oily compound **7** (0.61 g, 3.5 mmol, 34%).

IR (CCl_4):1090 (C-O, ether), 1450 (C=C , Ar-H), 1640 (C=C), 3000 (C-H, aliph) cm^{-1} .^{1}HNMR (500MHz, $CDCl_3$):δ: 2.9 (d, J=6.3Hz,2H), 3.39 (dd, J=4.38, 15.9 Hz, 1H), 3.9 (m, J=4.9Hz, 1H,O-C-H), 3.4 (dd, J=5,15.9Hz, 1H), 6.4 (d, J=15.9Hz,1H,=C-H) , 6.2 (dt, J=4.38, 15.9Hz , 1H, =C-H), 7.2 (m, 5H, Ar-H) ppm.

Preparation of 5-benezyle-3-methylene-dihydrofuran-2-one 9

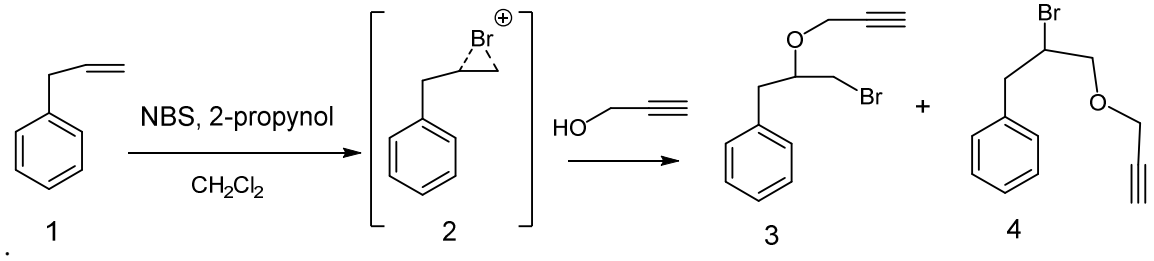
Mixture solution of CH_2Cl_2 (24 ml), pyridine (2 ml) and CrO_3 (1.5 g, 15 mmol) was stirred for 20 min. To this solution was added compound **7** (0.32 g, 1.38 mmol), CH_2Cl_2 (10 ml) and was refluxed at 60°C for a further 3 h and then filtered. The filtered was washed with CH_2Cl_2 and saturated $NaHCO_3$. The mixture was extracted with CH_2Cl_2 (3×20 ml) and washed with HCl (2 N) for a second time. The mixture was purified through (SiO_2:60-7733 mesh) column chromatography. The column was washed with $CHCl_3$ and evaporated to dryness.

The organic phase was chromatographed [SiO_2:60-7730 mesh, n-hexane:Et_2O (1:8)] to isolated center cut butyrolactone**9** (0.289, 1.106 mmol, 65%);IR (CCl_4):695,1090(C-O, ether),1450 (C=C, Ar-H), 1640 (C=C)cm^{-1}.^{1}HNMR (500 MHz, $CDCl_3$):δ: 3.3(d, J=4.5Hz, 2H), 3.8 (m, 2H, =C-H), 4.2 (m, 1H), 6.4 (m, 1H) , 6.8 (d , J=14Hz, 2H), 7.2 (m, 5H , Ar-H) ppm. MS,m/z (%): 188 $[C_{12}H_{12}O]^+$ (17%), 160 $[C_{11}H_{12}O]^+$ (48%), 144 $[C_{11}H_{12}O]^+$ (63%), 91 $[C_7H_7]^+$ (97%).

RESULTS AND DISCUSSION

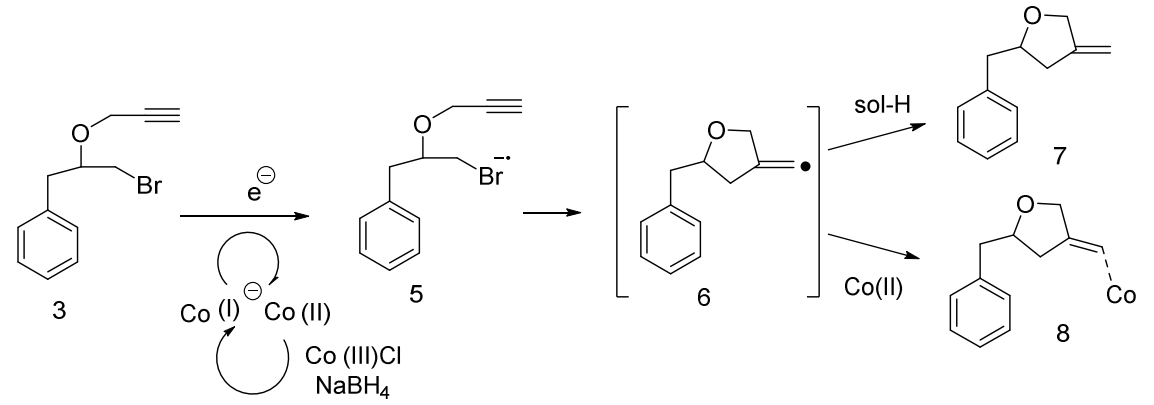
Our aim was to obtain an organic compound with new alpha–methylene–gamma– butyrolactone skeleton using cobaloxime complex. Cobaloxime belongs to a group of bis[(dimethylglyoximato) cobalt(III)] (bis-DH), which was

reduced to supernucleophile(Co^+). Here cobaloxime was prepared through mixing $CoCl_2$, $6H_2O$, DH ligand and PPH_3 in EtOH.Bis[DH] was formed under vigorous stream of air [12]with 53.2% yield. IR spectrum reveals the C=N, at 1550, Co-N at 518, N-O at 1085, and O-H stretching at 3400cm^{-1}.^{1}HNMR spectrum of bis[DHCo(III)] reveals δ 2.02 (s, 12H), δ 7.3-7.5 (m,15H) ppm. In other efforts we used allybenzene**1**for the production of alpha-methylene-gamma–butyrolactone**9**via compounds **2**, **3** and **7** in three steps. For preparation of bromoether**3** a mixture of allylbenzene**1**, propargyle alcohol and NBS was stirred at -35°C for 3h according to the reported literature with minor modification(in order to increase the reaction yield the mixture was stirred for 24h at room temperature)[13,14].Isomers **3** and **4** were recovered via bromonium ion **2** (Schem2). The main product **3**was prepared through more stable secondary carbocation. In IR spectrum of **3**acetylenic band at 3300 C-O at 1075 and C-Br at 665$cm^{-1}$was observed and in ^{1}HNMR δ 2.5 (t, 1H), δ 2.6 (d, 2H), δ 4.2 (d,2H) and aromatic protons at δ 7.2 (m,5H) ppm were appeared.



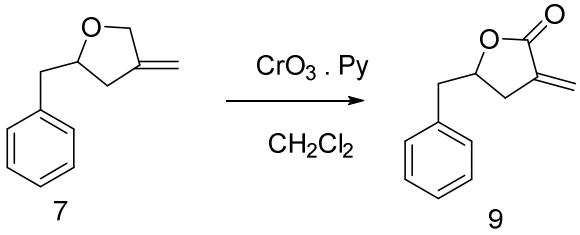
Scheme 2

Intramolecular preparation of THF derivative **7** was achieved from bromoether **3** in the presence of cobaloxime and $NaBH_4$via intermediate radical **6** (Scheme3). Since super nucleophile $(Co^+)^-$ is susceptive to air oxidation therefore was performed under argon atmosphere. To avoid C=C bond dimerization of prepared THF derivative **7** the temperature of reaction was maintained at 60$^{°C}$.IR spectra of **7** were characterized C-H aromatic bending at 695 C=C alkene at 1450 and C-O at 1090 cm^{-1}.^{1}HNMR reveals C=C protons atδ 6.4(d,1H)atδ 6.2(m,1H) protons of THF ring at δ 2.9 (d, 1H), δ 3.3 (dd, 1H), (dt, 2H) and aromatic protons at δ 7.2 (m, 5H) ppm.



Scheme 3

Lastly for preparation of target alpha–methylene–gamma–butyrolactone **9,** THF derivative **7** was refluxed at 60^{oC} for 3h with CrO_3.py and oxidized to alpha–methylene-gamma–butyrolactone **9** (Scheme4) [14].The IR spectrum of **9** reveals C=O of lactone as strong bond at 1770 cm^{-1} , aromatic protons at 1440, 1500 , 1600$cm^{-1}$and C=C aliphatic at 1645 cm^{-1}. In ^{1}HNMR the terminal geminal protons of C=C appeared at δ 6.8 (d, 1H), δ 6.4 (m,1H), benzilic protons at δ 3.3 (d, 2H) and aromatic protons δ 7.25 (m, 5H) ppm were appeared. The GC–Mass $C_7H_7^+$(67%), $C_{11}H_{22}O^+$(48%) were characterized.



Scheme 4

CONCLUSION

In this short note, we report a simple new procedure for preparation of alpha-methelene-gamma-butyrolaton **9** in the presence of allybenzene and premade cobaloxime catalyst in three steps, such as bromoetherification of alkene, cyclization in the presence of cobaloxime and ultimate oxidation for preparation of this target gamma butyrolactone.

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