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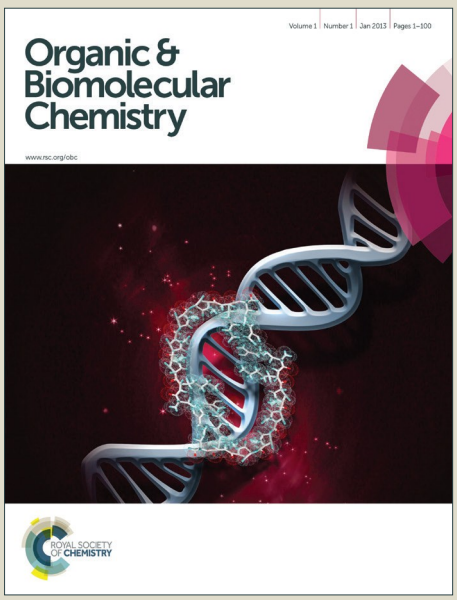

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ARTICLE

Pd-Catalyzed Benzylic C–H Oxidation of Cyclotriveratrylene – Product Diversity

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The inner-rim functionalization of CTV has been examined by employing Pd-catalyzed benzylic oxidation. The outcome of the oxidation depends upon thesolvent and co-oxidants employed. An interesting array of CTV derivatives have been synthesized with a simple change in the conditions.

Introduction

The cyclotriveratrylene (CTV) is an interesting macrocyclic molecule characterized with a crown-like structure having a shallow molecular cavity and a pyramidal shape with the aromatic rings forming the three sides of the pyramid and the methylene hydrogens lying close together at the apex.[1] During the last three decades, CTV and its congeners have been used as precursors for cryptophanes/cavitands, and as components in coordination and self-assembled supramolecularnetworks.[2,3] For example CTV and its derivatives have been extensively studied for their binding with smaller organic (such as benzene, ethanol, DMSO), and organometallic guests.[4] Their ability to host molecules likeC_{60} and anionic C_{70} dimers,[5]lanthanoids, and xenon have led to the development of functionalized CTV derivatives for biomedical applications such as the delivery of fullerenes and their use of MRI-based diagnostic techniques.[6]

Thus, the manipulation of functional and structure/conformational aspects of the CTV holds great promise as increasing number of applications for this classofmolecules are continuously being reported. The functionalization of CTV can be carried out either at the aromatic rings ("outer-rim") or at the methylene bridges ("inner-rim or apex"), which are complementary to each other. The outer-rim functionalization is important in modulating the host-guest properties of the CTV. The apex functionalization which is challenging has been thought to be a handle for tuning the conformational aspects of CTV. The oxidation of the methylene bridges of the CTV is one of the simple means for inner-rim functionalization that has been explored by several groups.[7] Reports for the reliable preparation of the mono- and diketones of the CTV are documented, and the corresponding triketone is known to undergo trans-annular rearrangement.[8] In general, these oxidations are carried out under harsh conditions employing chromium and permanganate based oxidants in solvents such as conc. H_2SO_4 or pyridine.[8] Given the importance of functionalized CTV derivatives and the challenges associated with the inner-rim functionalization, we sought to explore the possibility of metal-catalyzed controlled C–H oxidation of CTV, especially employing Pd-complexes. Unlike the Pd-catalyzed allylic acetoxylation which is very popular, Pd-catalyzed benzylic oxidations are scarcely reported.[9-12]

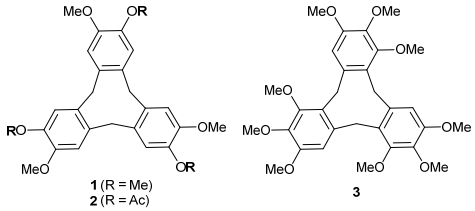


Figure 1. Selected CTV derivatives

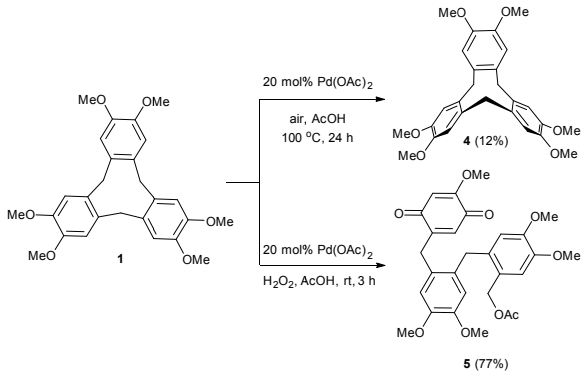
Result and discussion

The three known CTV analogues **1** – **3** have been selected as the substrates and were prepared by following established procedures.[13] Coming to the Pd-catalyzed benzylic oxidations, one of earliest reports by Bryant and co-workers employed air as oxidant for the conversion of xylene to the xylene diacetate.[11] Hydrogen peroxide is another oxidant that has been widely employed in the Pd-catalyzed oxidations.[14] A combination of benzoquinone along with MnO_2 as the co-oxidant has been employed in the Pd-catalyzed allylic oxidations. Considering these reports, our initial experiments are focused on the oxidation of CTV derivatives under these conditions and the characterization of the resulting products.

As shown in Scheme 1, when air was employed as the oxidant,[11] the oxidation of CTV **1** was sluggish and CTV derivative **4** having the saddle conformation was obtained in 12% yield (80% of **1** was recovered). The saddle conformation of **4** is evidenced by its ^{1}H NMR spectrum, in which the methylene bridge hydrogens resonate as a sharp singlet at δ 3.89 ppm and the aromatic proton displays as a singlet at δ 6.83 ppm [in case of **1**, CH_2 as AB doublet at δ 3.55 and 4.77 ppm and aromatic-H as singlet at δ 7.36].[13a] With hydrogen peroxide as a co-oxidant, the reaction proceeded smoothly and provided the quinone **5** resulting from peroxide-mediated oxidative opening of the CTV methylene bridge and subsequent hydroquinone to benzoquinone oxidation. The structure of quinone **5** was confirmed by single crystal *X*-ray structure analysis (Fig. 2a).[15] Considering the mild conditions when H_2O_2 was employed as an co-oxidant, to control oxidation over, various other catalysts such as

$Cu(OAc)_2$, $Ni(OAc)_2$, $CuCl_2$and $FeCl_2$[16] have been examined. Withall the complexes, quinone **5** was isolated as the only product in varying yields.

The formation of the quinone **5** reveals that nuclear hydroxylation (at the more electron rich ring carbon) is preferred over benzylic oxidation in the presence of hydrogen peroxide (Scheme 2).[17]There exist two possibilities for the fragmentation of the resulting bridge-head alcohol; either *via* the acid catalyzed cleavage-rearrangement reaction of the corresponding hydroperoxide[18] or a mechanism operating through a Pd-mediated oxidative fragmentation[19] of the *tert*-alcohol. The stabilization of the released benzylic carbocation through the participation of a *p*-methoxy group along with the release of the steric strain might be playing an important role during these cleavage-rearrangement reactions. Detailed mechanistic studies are required to delineate the role of the Pd-catalyst and its exact mode of action.



Scheme1.Pd–Catalyzed C–H oxidation of CTV **1**employing O_2 or H_2O_2

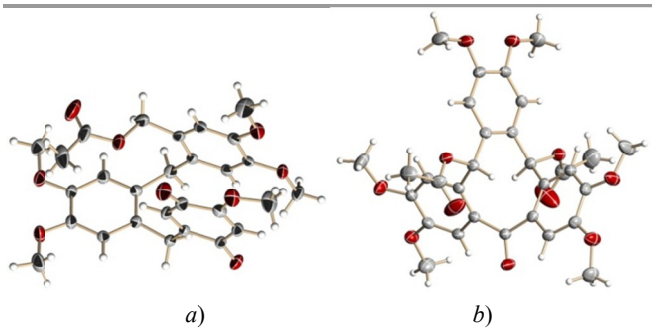
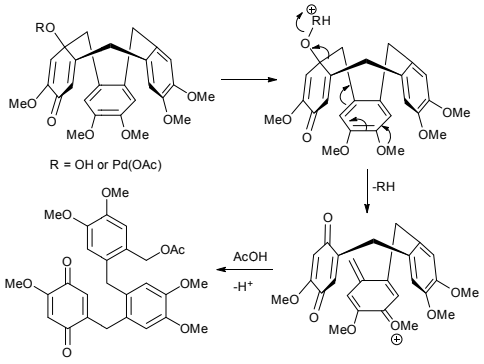
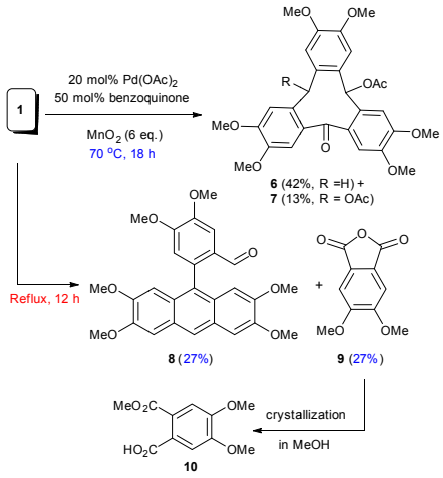


Figure 2. Molecular structure of compounds a) **5** and b) **7**

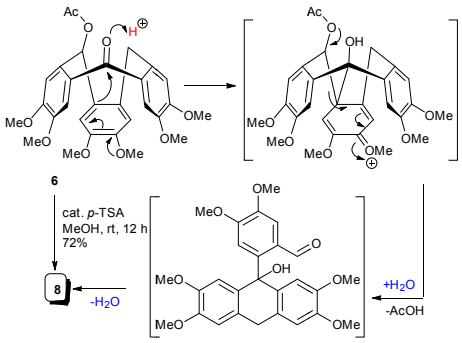


Scheme 2. Possible mechanism for Pd-H_2O_2 mediated oxidation of CTV 1

Next, the Pd-catalyzed benzylic C–H oxidation of CTV **1** was examined by employing benzoquinone as an additive and MnO_2 as a co-oxidant in acetic acid. The conditions employed involve heating of a solution of CTV and $Pd(OAc)_2$ (20 mol%), benzoquinone (0.5 eq.), and MnO_2 (6 eq.) in acetic acid at 70 °C.The complete disappearance of CTV was noticed after 18 h and two new products **6** and **7** were isolated. The structure of the major compound **6** has been confirmed as 10-acetoxycyclotriveratrylene-5-one (42% yield) and that of **7** as 10,15-diacetoxycyclotriveratrylene-5-one (13% yield). The ^{1}H NMR spectrum of **6** displays two AB doublets at δ3.45 and 4.00 (J =15.2 Hz) indicating a crown conformation. The NMR analysis of the diacetate **7** revealed a saddle conformation and this was further substantiated by single crystal *X*-ray structure analysis (Figure 2b).



Scheme 3. Pd-Catalyzed oxidation of CTV **1** using MnO_2

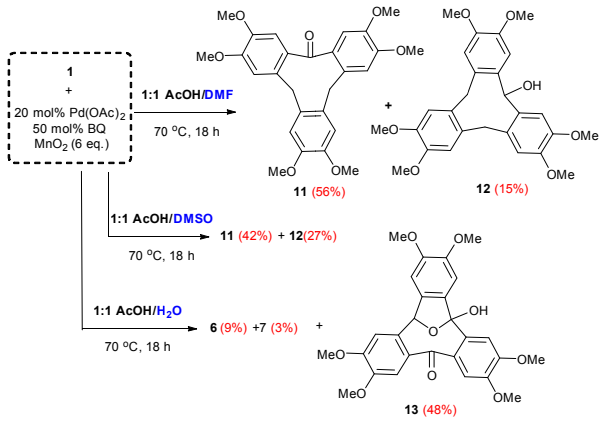


Scheme 4. Transannular rearrangement of ketoacetate **6**

Next, we examined the same reaction at reflux temperature and employed all reagents in the same molar proportions as described above (Scheme 3). Quite interestingly, two new products **8** and **9** that are different from **6/7** were isolated. Compound **8** provided complete unsymmetrical spectra whereas the spectrum of **9** was highly symmetric with only two signals in the ^{1}H NMR and four signals in the ^{13}C NMR spectra. The structure of compound **8** has been assigned as 2'-(9-anthracenyl)benzaldehyde with the help of spectral as well as by single crystal *X*-ray analysis (Figure 3a). Coming to the compound **9**, the single crystal *X*-ray analysis of crystals resulting from recrystallization of **9** in methanol revealed that **9** is 3,4-dimethoxyphthalic anhydride that was converted to its half methyl ester **10** during crystallization.[20] The formation of aldehyde **8** could be accounted from the trans-annular rearrangement of partially oxidized CTV such as **6**. Supporting this argument, it was found that the treatment of compound **6** with catalytic amounts

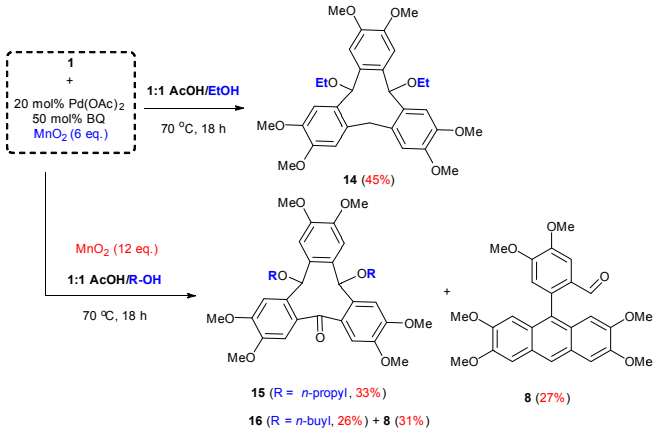
of *p*-TSA in dichloromethane resulted in the isolation of 72% of aldehyde **8** and an uncharacterized mixture (12%, Scheme 4).

Having met with exhaustive oxidation at reflux, we next examined the oxidation of **1** with the BQ-MnO_2 system in combination with other solvents along with AcOH. As shown in Scheme 3, when employed a 1:1 AcOH-DMF as solvent, the Pd-catalyzed oxidation of CTV **1** gave mainly two products which have been characterized as cyclotriveratrylene-5-one (**11**, 56% yield) and cyclotriveratrylene-5-ol (**12**, 15% yield). Changing the solvent from DMF to DMSO also resulted in the isolation of these two products, albeit the proportion of the alcohol **12** was seen to increase.



Scheme 5. Solvent Dependent Pd-catalyzed Oxidation of CTV**1**

When the oxidation of **1** was conducted under similar conditions except that a 1:1 AcOH and water was used as a solvent system, the reaction led to isolation of **6** in 9% and **7** in 3% yield along with the novel hemi-acetal **13** in 48% yield. Next, we examined the oxidation of **1** (Scheme 6) in AcOH-ethanol (1:1). The reaction was incomplete (65% conversion) and provided mainly the 5,10-diethoxycyclotriveratrylene (**14**) in 45% yield.The ^{1}H NMR data of compound **14** revealed that it exists as a stable crown conformer.When we changed the solvent from ethanol to *n*-propanol, and used 12 equivalents of MnO_2, interestingly 10,15-dipropoxy-cyclotriveratrylene-5-one (**15**, 33% yield) was obtained along with the anthracenylbenzaldehyde **8** in 27% yield. A similar result was observed when *n*-butanol was employed as a co-solvent.



Scheme 6. Pd-Catalyzed Oxidation of CTV**1**in protic solvents

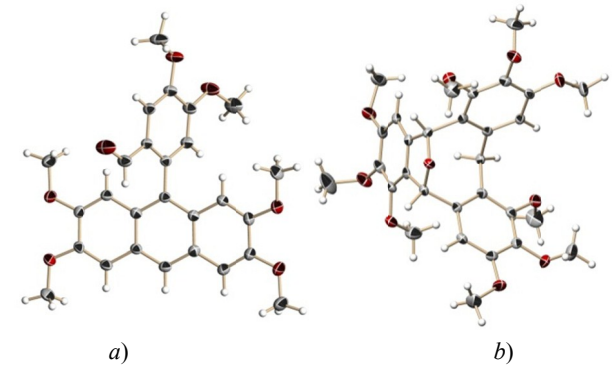
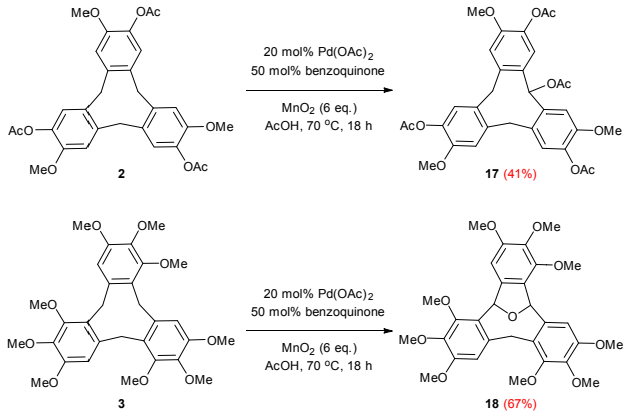


Figure 3. Molecular structure of compounds a) **8** and b) **18**

Next, the Pd-catalyzed oxidation of other CTV analogues **2** and **3** has been examined in acetic acid alone. The C-H oxidation of **2** (Scheme 7) was incomplete and gave mainly 5-acetyloxy-CTV **17** in 41% yield. On the other hand, the C-H oxidation of **3** gave the furan derivative **18** as the main product (67% yield).The structure of compound **18** has been confirmed by NMR and single crystal *X*-ray structure analyses (Figure 3b).



Scheme 7. C–H Oxidation of CTV analogues **2** and **3**

Conclusions

To conclude the Pd-catalyzed C–H oxidation of CTV has been examined with different co-oxidants under different conditions. An interesting array of CTV derivatives have been synthesized with a simple change in the conditions. Some of the oxidations are selective resulting in CTV derivatives with interesting structural features.

Experimental

General Remarks

Reactions were carried out using commercial reagents and solvents were used without purification. Column chromatography was carried out by using Spectrochem silica gel (60–120, 100–200, 230–400 mesh). The purity of the compounds was checked on Merck precoated silica gel 60 F-254. ^{1}H and ^{13}C NMR spectroscopy measurements were carried out on Bruker AC 200 MHz and JEOL 400 spectrometers, and TMS was used as an internal standard. ^{1}H and ^{13}C NMR chemical shifts are reported in ppm downfield from

Chloroform-d (δ = 7.26) or TMS and coupling constants (*J*) are reported in Hertz (Hz). The following abbreviations are used to designate signal multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad. The Multiplicity of ^{13}C NMR signals was assigned with the help of DEPT spectra and the abbreviations used: s = singlet d = doublet t = triplet q = quartet, represent C (quaternary), CH, CH_2 and CH_3 respectively. Mass spectra were recorded on a Thermo Finnigan MSQ LC/MS mass spectrometer. HRMS mass spectra were recorded on a Thermo Scientific Q-Exactive, Accela 1250 pump.

Cyclotriveratrylene Saddle Conformer 4: A solution of cyclotriveratrylene (**1)** (200 mg, 0.4 mmol), $Pd(OAc)_2$ (20 mg, 0.08 mmol) and potassium acetate (42 mg, 0.22 mmol) in 20 mL of acetic acid was stirred at 100 °C for 24 h, while air was blown over its surface. After 24 h, the reaction mixture was cooled and filtrated over the Celite pad. The filtrate was diluted with an equal volume of water and extracted with EtOAc (2 x 20 ml). The combined extract was washed successively with a saturated $NaHCO_3$ solution, water, and brine, dried (Na_2SO4) and evaporated under reduced pressure. The crude was purified by column chromatography (ethyl acetate-petroleum ether 3:7) to obtain starting CTV **1** (160 mg, 80%) and **4** (22 mg, 12%) as a white solid. Mp. 219–220 °C; ^1H NMR (200 MHz, $CDCl_3$): δ 3.84 (s, 18H), 3.89 (s, 6H), 6.62 (s, 6H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ 36.5, 56.0, 113.2, 131.8, 147.7 ppm; HRMS (ESI) Calculated for $C_{27}H_{31}O_6[M+H]^+$: 451.2115, found 451.2103.

Pd-catalyzed Oxidation of CTV 1 in AcOH with H_2O_2 at rt: A solution of CTV **1** (100 mg, 0.2 mmol), $Pd(OAc)_2$ (10 mg, 0.04 mmol) in acetic acid (10 mL) was treated slowly with 30% aqueous H_2O_2 (0.2 ml, 2 mmol,) and stirred at rt for 3 h. The excess peroxide was quenched with MnO_2 and the reaction mixture was filtered over Celite pad and the Celite pad was washed successively with 35 mL of EtOAc and 25 mL of water. The organic layer was separated and the aqueous layer was extracted three times with 15 mL of EtOAc. The combined organic layer was washed successively with water, aq. $NaHCO_3$ and brine, dried (Na_2SO_4) and evaporated under reduced pressure. The crude was purified by column chromatography (ethyl acetate-petroleum ether, 3:7) to afford **5** (86 mg, 77%) as an orange solid. Mp. 120–121°C; ^1H NMR (200 MHz, $CDCl_3$): δ 3.67 (d, *J* = 1.8 Hz, 2H), 3.75 (s, 3H), 3.80 (s, 3H), 3.81 (s, 3H), 3.82 (s, 3H), 3.86 (s, 3H), 3.88 (s, 2H), 4.93 (s, 2H), 5.86 (d, *J* = 2.7Hz, 2H), 6.47 (s, 1H), 6.62 (s, 2H), 6.75 (s, 1H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ 20.8, 32.4, 36.3, 55.7, 55.8, 55.9, 56.0, 56.2, 64.2, 107.3, 113.4, 113.7, 113.9, 114.2, 126.1, 126.5, 130.6, 130.9, 131.9, 147.1, 147.7, 148.0, 148.8, 148.8, 158.4, 170.8, 182.0, 187.4 ppm; FTIR ($CHCl_3$): ν 3435 (br), 3020, 1736, 1651, 1605, 1517, 1216, 1021 cm-1; HRMS (ESI) Calculated for $C_{28}H_{30}O_9Na^+$ $[M+Na]^+$: 533.1782, found 533.1782.

General Procedure for C–H Oxidation with MnO_2 and BQ (A): In a 250-mL round-bottomed, were placed CTV **1** (2.22 mmol), $Pd(OAc)_2$ (0.4 mmol), benzoquinone (1.1 mmol) and 100 mL of acetic acid and heated to 70 °C To this manganese dioxide (13.3 mmol) was added and the reaction mixture was stirred at 70 °C for 18h. The reaction mixture was cooled and diluted with 50 mL of EtOAc and stirred for 10 min. The content was filtrated over Celite pad and the Celite pad was washed successively with 50 mL of EtOAc and 100 mL of water. The organic phase was separated and washed successively with water, 2N NaOH, brine, dried (Na_2SO_4) and evaporated under reduced pressure. The crude product was purified by column chromatography using a mixture of ethyl acetate-petroleum ether as eluent to give corresponding products.

Pd-catalyzed Oxidation of CTV 1 in AcOH at 70 °C: The general procedure **A** was followed **-1** (1 g, 2.22 mmol), $Pd(OAc)_2$ (100 mg, 0.4 mmol), benzoquinone (120 mg, 1.1 mmol) and MnO_2 (1.2 g, 13.3 mmol). The product was purified by column chromatography using ethyl acetate-petroleum ether (4:6) as the eluent to give **6** (490 mg, 42%) and **7** (165 mg, 13%).
Characterization data of **6**: Yellow solid, Mp. 182 – 183 °C; ^1H NMR (200 MHz, $CDCl_3$): δ 2.07 (s, 3H), 3.45 (d, *J* = 15.2 Hz, 1H), 3.80 (s, 3H), 3.82 (s, 3H), 3.93 (s, 3H), 3.96 (s, 6H), 3.98 (s, 3H), 4.00 (d, *J* = 15.2 Hz, 1H), 6.51 (s, 1H), 6.56 (s, 1H), 6.79 (s, 1H), 7.11 (s, 1H), 7.24 (s, 1H), 7.40 (s, 1H), 7.56 (s, 1H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ 21.0, 37.5, 55.8, 55.9, 56.0, 56.1, 56.1, 56.2, 68.6, 107.8, 109.5, 110.7, 111.8, 112.6, 114.2, 131.1, 131.3, 131.8, 132.7, 133.2, 147.6, 147.9, 148.1, 148.8, 152.6, 152.8, 169.0, 192.7 ppm; FTIR ($CHCl_3$): ν 3402 (br), 1597, 1511, 1264, 1218, 1020, 768 cm-1; HRMS (ESI) Calculated for $C_{29}H_{30}O_9Na^+$ $[M+Na]^+$: 545.1782, found 545.1784.
Characterization data of **7**: Mp. 190–191°C, ^1H NMR (200 MHz, $CDCl_3$): δ 2.08 (s, 6H), 3.81 (s, 6H), 3.97 (s, 6H), 3.98 (s, 6H), 6.59 (s, 2H), 6.95 (s, 2H), 7.26 (s, 2H), 7.53 (s, 2H) ppm; 13C NMR (50 MHz, $CDCl_3$): δ 21.0, 55.9 (2C), 56.1 (2C), 56.2 (2C), 68.3, 107.6 (2C), 109.4 (2C), 111. (2C), 129.9 (2c), 131.0 (2C), 133.2 (2C), 147.9 (2C), 149.1 (2C), 153.0 (2C), 168.8, 191.2ppm; FTIR ($CHCl_3$): ν 3414 (br), 3016, 1602, 1514, 1267, 1216, 1094, 1021, 757 cm-1; HRMS (ESI) Calculated for $C_{31}H_{32}O_{11}Na^+$ $[M+Na]^+$: 603.1837, found 603.1838.

Pd-catalyzed Oxidation of CTV 1 in AcOH at reflux: The general procedure A was followed **-1**(100 mg, 0.2 mmol), $Pd(OAc)_2$ (10 mg, 0.04 mmol), benzoquinone (12 mg, 0.1 mmol) and MnO_2 (114 mg, 1.3 mmol), the mixture was refluxed for 12 h. After usual workup, the crude was purified by column chromatography using ethyl acetate-petroleum ether (3:7) as the eluent to give **8** (41 mg, 44%) and **9**(14 mg, 15%) as yellow solid. Mp. 126 °C, ^1H NMR (200 MHz, $CDCl_3$): δ 3.73 (s, 6H), 3.84 (s, 2H), 3.92 (s, 3H), 4.05 (s, H), 4.10 (s, 3H), 6.59 (s, 2H), 6.89 (s, 1H), 7.21 (s, 2H), 7.71 (s, 1H), 8.17 (s, 1H), 9.22 (s, 1H)ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ 55.7 (2C), 55.9, 56.0, 56.1, 56.4, 103.1 (2C), 105.0 (2C), 108.3, 113.1, 113.8, 123.2, 127.0 (2C), 128.6, 131.7, 138.6, 147.7, 149.0, 149.3 (2C), 149.9 (2C), 154.2, 191.11ppm; FTIR ($CHCl_3$): ν 3432 (br), 3020, 2930, 1596, 1509, 1490, 1434, 1267, 1216, 1149, 1095, 1014cm-1; HRMS (ESI) Calculated for $C_{27}H_{26}O_7Na^+$ $[M+Na]^+$: 485.1571, found: 485.1566.

Pd-catalyzed Oxidation of CTV 1 in AcOH-DMF (1:1): The general procedure A was followed **-1**(200 mg, 0.4 mmol), $Pd(OAc)_2$ (20 mg, 0.09 mmol), benzoquinone (24 mg, 0.2 mmol) and MnO_2 (230 mg, 2.6 mmol) in 30 mL of acetic acid and DMF (1:1). After usual workup, the resulting crude was purified by column chromatography (ethyl acetate-petroleum ether 4:6) as the eluent to give **11**(115 mg, 56%) and **12**(31 mg, 15%) as yellow solids
Characterization data of **11**: Mp. 197–198 °C; ^1H NMR (200 MHz, $CDCl_3$): δ 3.62 (d, *J* = 14.0 Hz, 2H), 3.84 (s, 12H), 3.86 (s, 6H), 3.88 (d, *J* = 14.0 Hz, 2H), 6.80 (s, 2H), 6.81 (s, 2H), 7.07 (s, 2H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ 36.9 (2C), 55.8 (2C), 55.9 (2C), 56.1 (2C), 111.4 (2C), 112.6 (2C), 114.2 (2C), 131.9 (2C), 132.7 (2C), 132.9 (2C), 147.4 (2C), 147.8 (2C), 152.5 (2C), 194.0 ppm; HRMS (ESI) Calculated for $C_{27}H_{29}O_7$ [M+H]+: 465.1908, found 465.1909, HRMS (ESI) Calculated for $C_{27}H_{28}O_7Na+$ $[M+Na]^+$: 487.1727, found 487.1725.
Characterization data of **12**: Mp. 144–145 °C, ^1H NMR (200 MHz, $CDCl_3$): δ 3.57 (d, *J* = 14.0 Hz, 2H), 3.83 (s, 6H), 3.84 (s, 6H), 3.87 (s, 6H), 4.77 (d, *J* = 14.0 Hz, 2H), 6.77 (s, 2H), 6.80 (s, 2H), 6.99 (s, 1H), 7.28 (s, 2H)ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ 35.7 (2C), 55.8 (2C), 55.9 (2C), 56.0 (2C), 67.1, 107.9 (2C), 112.3 (2C), 113.1

(2C), 129.7 (2C), 131.3 (2C), 134.3 (2C), 147.8 (2C), 148.1 (2C), 148.2 (2C)ppm; HRMS (ESI) Calculated for $C_{27}H_{29}O_6$ $[M-H_2O]^+$: 449.1959, found 449.1956.

Pd-catalyzed Oxidation of CTV 1 in AcOH-H_2O (1:1): The general procedure A was followed -**1**(200 mg, 0.4 mmol), $Pd(OAc)_2$ (20 mg, 0.09 mmol), benzoquinone (24 mg, 0.2 mmol) and MnO_2 (229 mg, 2.6 mmol) in 30 mL of acetic acid and water (1:1). After usual workup, the crude was purified by column chromatography using ethylacetatepetroleum ether (1:1) as the eluent to give **13**(106 mg, 48%) with **6** (21 mg, 9%) and **7** (9 mg, 3%).
Characterization data of **13**: yellow solid, Mp. 156–157 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.61 (s, 3H), 3.83 (s, 3H), 3.84 (s, 3H), 3.92 (s, 3H), 4.00 (s, 6H), 6.00 (s, 1H), 6.60 (s, 1H), 6.97 (s, 1H), 7.10 (s, 1H), 7.41 (s, 1H), 7.75 (s, 1H), 7.77 (s, 1H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ 55.9 (2C), 56.0 (2C), 56.1 (2C), 60.4, 87.1, 102.0, 103.3, 105.0, 107.9, 108.2, 110.6, 123.4, 124.0, 128.0, 138.7, 139.8, 140.0, 149.1 (2C), 149.7, 151.3, 153.5, 153.6, 181.8 ppm; FTIR ($CHCl_3$): ν 3432 (br), 3020, 1598, 1508, 1465, 1421, 1292, 1292, 1117, 1019 cm-1; HRMS (ESI) Calculated for $C_{27}H_{26}O_9Na^+$ $[M+Na]^+$: 517.1469, found 517.1465.

Pd-catalyzed Oxidation of CTV 1 in AcOH-EtOH (1:1): The general procedure **A** was followed - **1** (100 mg, 0.2 mmol), $Pd(OAc)_2$ (10 mg, 0.04 mmol), benzoquinone (12 mg, 0.1 mmol) and MnO_2 (114 mg, 1.3 mmol) in 20 mL of acetic acid and ethanol (1:1). After usual workup, the crude was purified by column chromatography using ethyl acetate/petroleum ether (3:7) as the eluent to give **1** (35 mg) and **14** as yellow solid (53 mg, 45%), Mp. 97-98°C, ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.31 (tt, *J* = 7.0, 7.0 Hz, 6H), 3.58 (d, *J* = 13.8Hz, 1H), 3.58-3.62 (m, 5H), 3.84 (s,9H), 3.85 (s, 9H), 4.78 (d, *J* = 13.8Hz, 1H), 6.45 (s, 2H), 6.78 (s, 2H), 6.82 (s, 2H), 7.26 (s, 2H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ 15.3 (2C), 35.7, 55.8 (4C), 55.9 (2C), 64.1 (2C), 73.0 (2), 107.3, 107.9, 108.2, 112.3, 113.0, 113.1, 129.6, 130.1, 131.3 (2C), 133.0, 134.5, 147.6, 147.7, 148.0, 148.1, 148.2ppm; HRMS (ESI) Calculated for $C_{31}H_{38}O_8Na^+$ $[M+Na]^+$: 561.2459, found: 561.2449.

Pd-catalyzed Oxidation of CTV 1 in AcOH-*n*Propanol (1:1) with 12 eq. MnO_2: The general procedure **A** was followed -**1** (200 mg, 0.4 mmol), $Pd(OAc)_2$ (20 mg, 0.09 mmol), benzoquinone (24 mg, 0.2 mmol) and with 12 eq. of MnO_2 (418 mg, 4.8 mmol) in 30 mL of acetic acid and propanol (1:1). After usual workup, the crude was purified by column chromatography using ethyl acetate-petroleum ether (2:8) as the eluent to give **8** (50 mg, 27%) and **15** (77mg, 33%) as yellow solid. Mp. 170–172 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.84 (t, *J* = 7.4 Hz, 6H), 1.47 (q, *J*= 6.8 Hz, 4H), 2.97- 3.16 (m, 4H), 3.81 (s, 6H), 3.95 (s, 6H), 3.98 (s, 6H), 5.39 (s, 2H), 6.73 (s, 2H), 7.41 (s, 2H), 7.49 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.7, 22.8 (2C), 55.9 (2C), 56.0 (2C), 56.1 (2C), 69.7 (2C), 73.1 (2C), 107.8 (2C), 109.6 (2C), 110.0 (2C), 132.3 (2C), 133.9 (2C), 134.5 (2C), 147.4 (2C), 148.6 (2C), 153.3 (2C), 192.7ppm; HRMS (ESI) Calculated for $C_{33}H_{40}O_9Na^+$ $[M+Na]^+$: 603.2565, found 603.2557.

Pd-catalyzed Oxidation of CTV 1 in AcOH-*n*Butanol (1:1) with 12 eq. MnO_2:The general procedure **A** was followed -**1** (200mg, 0.4 mmol), $Pd(OAc)_2$ (20 mg, 0.09 mmol), benzoquinone (24 mg, 0.2 mmol) and MnO_2 (418mg, 4.8 mmol) in 30 mL of acetic acid and butanol (1:1).The product was purified by column chromatography using ethyl acetate-petroleum ether (2:8) as the eluent to give **8** (58 mg, 31%) and **16** (64 mg, 26%) as yellow solid; Mp. 165–166 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.83 (t, *J*= 7.0 Hz, 6H), 1.23-1.48 (m, 8H), 3.0-3.17 (m,4H), 3.80 (s. 6H), 3.94 (s, 6H), 3.97 (s, 6H), 5.38 (s, 2H), 6.72 (s, 2H), 7.41 (s, 2H), 7.47 (s, 2H)ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9 (2C), 19.4 (2C), 31.6 (2C), 55.9 (2C), 56.0 (2C), 56.1 (2C), 67.8 (2C), 73.1 (2C), 107.9 (2C), 109.5 (2C), 110.0 (2C), 132.3 (2C), 133.9 (2C), 134.5 (2C), 147.4 (2C), 148.6 (2C), 153.3 (2C), 192.7ppm; HRMS (ESI) Calculated for $C_{35}H_{44}O_9Na^+$ $[M+Na]^+$: 631.2878, found 631.2874.

Pd-catalyzed Oxidation of CTV 2 in AcOH at 70 °C: The general procedure **A** was followed. **2** (100 mg, 0.19 mmol), $Pd(OAc)_2$ (8 mg, 0.04 mmol), benzoquinone (10 mg, 0.09 mmol) and MnO_2 (98 mg, 1.14 mmol) in 20 mL of acetic acid. The product was purified by column chromatography using ethyl acetate-petroleum ether (4:6) as the eluent to give starting compound **2** (32 mg) and **17** as a yellow solid (46 mg, 41%). Mp.101–103 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.03 (s, 9H), 2.16 (3.64 (d, *J* = 13.8 Hz, 2H), 3.79 (s, 6H), 3.81 (s, 3H), 4.82 (d, *J* = 13.8 Hz, 2H), 6.82 (s, 1H), 6.84 (s, 1H), 6.98 (s, 1H), 6.99 (s, 1H), 7.10 (s, 1H), 7.24 (s, 1H), 7.89 (s, 1H)ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 20.6 (3C), 21.2, 35.8 (2C), 56.0, 56.1, 56.1, 68.2, 109.6, 113.3, 114.1, 119.6, 123.6, 124.1, 129.9, 130.7, 130.9, 136.3, 137.2, 137.8, 138.4, 138.8, 139.2, 149.8, 150.1, 150.4, 168.7, 168.8, 169.0, 169.6ppm; HRMS (ESI) Calculated for $C_{32}H_{32}O_{11}Na^+$ $[M+Na]^+$: 615.1837, found: 615.1832.

Pd-catalyzed Oxidation of CTV 3 in AcOH at 70 °C: The general procedure A was followed - **3** (200 mg, 0.37 mmol), $Pd(OAc)_2$ (17 mg, 0.07 mmol), benzoquinone (20mg, 0.18 mmol) and MnO_2 (192 mg, 2.22 mmol) in 30 mL of acetic acid. The product was purified by column chromatography using ethyl acetate-petroleum ether (3:7) as the eluent to give **18**as a yellow solid (138 mg, 67%), Mp. 98–99 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.98 (d, *J* = 14.0 Hz, 1H), 3.56 (s, 3H), 3.72 (d, *J* = 14.0 Hz, 1H), 3.83 (s, 3H), 3.84 (s, 3H), 3.86 (s, 6H), 3.88 (s, 3H), 3.89 (s, 3H), 3.95 (s, 3H), 6.19 (s, 1H), 6.46 (s, 1H), 6.76 (s, 1H), 6.79 (s, 1H), 6.85 (s, 1H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ 27.5, 55.8, 56.0, 56.2, 60.4, 60.6, 60.8, 61.1 (2C), 62.2, 79.6, 87.6, 99.6, 109.7, 112.4, 125.9, 126.1, 127.2, 136.6, 136.9, 137.9, 140.0, 141.8, 141.9, 147.1, 151.1, 152.1, 152.4, 152.7, 155.1ppm; HRMS (ESI) Calculated for $C_{30}H_{34}O_{10}Na^+$ $[M+Na]^+$: 577.2044, found: 577.2036.

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Notes and references

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