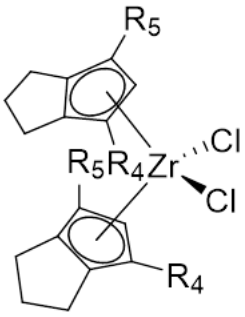
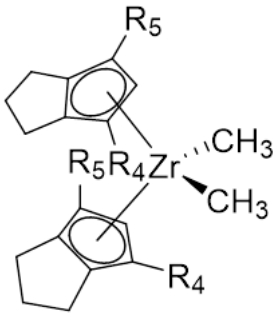
reaction product thereof; or a combination of a polyphosphoric acid (PPA) and a P_2O_5/H_3CSO_3H mixture, or a reaction product of thereof.

[0008b] In another aspect, the present disclosure refers to a compound of formula (8a):



(8a), wherein R_4 and R_5 are methyl.

[0008c] In another aspect, the present disclosure refers to a compound of formula



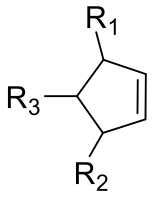
, wherein R_4 and R_5 are methyl.

DETAILED DESCRIPTION

[0009] The Summary and Abstract are incorporated here by reference.

[0010] Certain inventive embodiments are described below as numbered aspects for easy cross-referencing. Additional embodiments are described elsewhere herein.

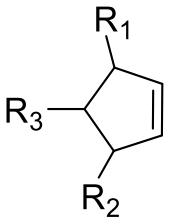
[0011] Aspect 1. A method of synthesizing a bicyclo[3.3.0]octene compound, the method comprising (A) contacting a compound of formula (1) ("compound (1)"):



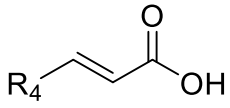
(1), wherein R1, R2, and R3 are independently H or $(C_1\text{-}C_4)$alkyl, or R1 and R3 are bonded together to form a $(C_1\text{-}C_4)$alkylene and R2 is H or $(C_1\text{-}C_4)$alkyl, with a compound of

CLAIMS

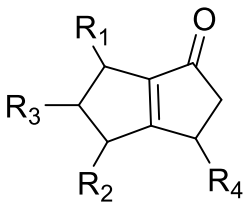
1. A method of synthesizing a bicyclo[3.3.0]octene compound, the method comprising (A) contacting a compound of formula (1) ("compound (1)"):



(1), wherein R1, R2, and R3 are independently H or (C_1-C_4)alkyl, or R1 and R3 are bonded together to form a (C_1-C_4)alkylene and R2 is H or (C_1-C_4)alkyl, with a compound of formula (2) ("compound (2)"):

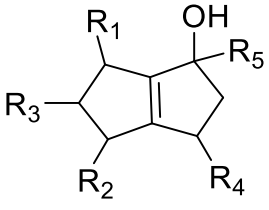


(2), wherein R4 is H or (C_1-C_4)alkyl, in the presence of an effective amount of a phosphoric and sulfonic acid reagent and under reaction conditions sufficient to make a compound of formula (3) ("compound (3)"):

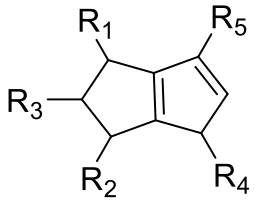


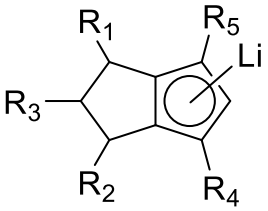
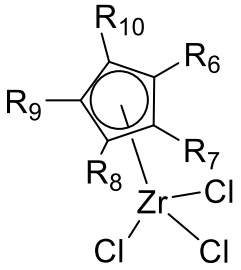
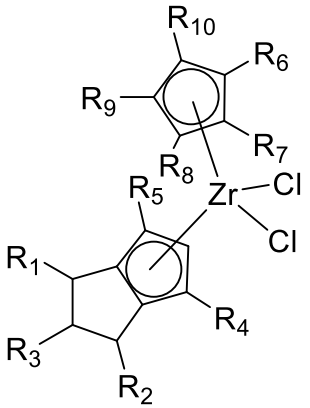
(3) and/or its oxo/R4 regioisomer; wherein R1 to R4 are as defined above; and wherein the phosphoric and sulfonic acid reagent is a mixture of a phosphorous pentoxide and methanesulfonic acid ("P_2O_5/H_3CSO_3H mixture"), or a reaction product thereof; or a combination of a polyphosphoric acid (PPA) and a P_2O_5/H_3CSO_3H mixture, or a reaction product of thereof.

2. The method of claim 1 further comprising (B) contacting the compound (3) and/or its oxo/R4 regioisomer with either a hydride-functional reducing agent or a (C_1-C_4)alkyl lithium, under reaction conditions sufficient to make a compound of formula (4) ("compound (4)"):

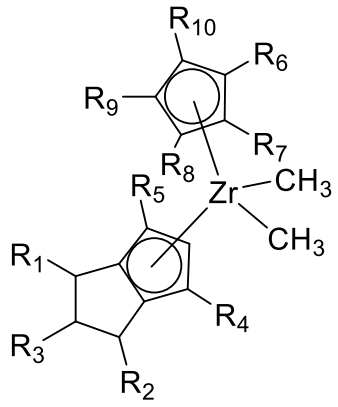


(4) and/or its (HO,R5)/R4 regioisomer, respectively, wherein R1 to R4 are as defined above and R5 is either H or (C_1-C_4)alkyl, respectively; and (C) contacting the compound (4) and/or its (HO,R5)/R4 regioisomer with dehydration reaction conditions to make a compound of formula (5)

(“compound (5)”):  (5), and/or its R5/R4 regioisomer, respectively; wherein R1 to R5 are as defined above.

3. The method of claim 2 further comprising (D) contacting the compound (5) and/or its R5/R4 regioisomer with an alkyl lithium under reaction conditions sufficient to make a compound of formula (6) (“compound (6)”):  (6) and/or its R5/R4 regioisomer, wherein R1 to R5 are as defined in claim 2; and (E) contacting the compound (6) and/or its R5/R4 regioisomer with a compound of formula (7) (“compound (7)”):  (7), wherein R6 to R8 independently are H or (C_1-C_4)alkyl and R9 and R10 independently are H, (C_1-C_4)alkyl, or R9 and R10 are bonded together and are a (C_3-C_5)alkylene, under reaction conditions sufficient to make a compound of formula (8) (“compound (8)”):  (8) and/or its R5/R4 regioisomer, wherein R1 to R10 are as defined above.

4. The method of claim 3 further comprising (F) contacting the compound (8) and/or its R5/R4 regioisomer with an effective amount of methyl magnesium bromide under reaction conditions sufficient to make a compound of formula (9) (“compound

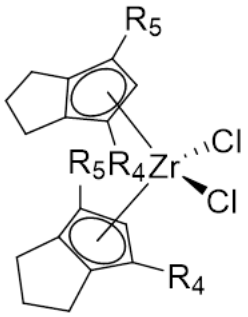
(9)"):  (9) and/or its R5/R4 regioisomer, wherein R1 to R10 are as defined above.

5. The method of any one of claims 1 to 4, wherein the phosphoric and sulfonic acid reagent is the P_2O_5/H_3CSO_3H mixture, or a reaction product thereof.

6. The method of any one of claims 1 to 4, wherein the phosphoric and sulfonic acid reagent is the combination of the PPA and the P_2O_5/H_3CSO_3H mixture, or a reaction product thereof.

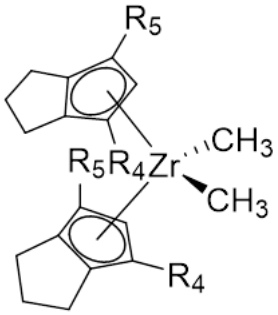
7. The method of any one of claims 1 to 6, characterized by any one of limitations (i) to (ix): (i) wherein at least one of R1 to R3 is a (C_1-C_4)alkyl or R4 is H; (ii) wherein each of R1 to R4 is H; (iii) wherein each of R1 to R3 is H and R4 is methyl; (iv) wherein in compound (1) each of R2 and R3 is H and R1 is methyl; in compound (2) R4 is methyl; and in compound (3) each of R2 and R3 is H and each of R1 and R4 is methyl; and in its oxo/R4 regioisomer each of R1 and R3 is H and each of R2 and R4 is each methyl; (v) wherein R1 and/or R2 is methyl and R3 is H; (vi) wherein R1 is methyl, R2 is 1-methylethyl (i.e., isopropyl), and R3 is H; (vii) wherein R1 is 1-methylethyl (i.e., isopropyl), R2 is methyl, and R3 is H; (viii) wherein R1 and R2 independently are (C_1-C_4)alkyl, R3 is H, and the stereochemistry of the carbon atom bonded to R1 is (R) and the stereochemistry to the carbon atom bonded to R2 is (S); and (ix) wherein R1 and R2 independently are (C_1-C_4)alkyl, R3 is H, and the stereochemistry of the carbon atom bonded to R1 is (S) and the stereochemistry to the carbon atom bonded to R2 is (R).

8. A compound of formula (8a):



(8a), wherein R_4 and R_5 are methyl.

9. A compound of formula



, wherein R_4 and R_5 are methyl.