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Palladium(II)-catalyzed dicarboxymethylation of chiral allylic alcohols: chirality transfer affording optically active diesters containing three contiguous chiral centers

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1. Introduction

Enantiopure chiral materials are of key importance, particularly in the preparation of bioactive pharmaceuticals and more recently in liquid crystals, and palladium catalysis can be used in the construction of new asymmetric centers, either asymmetric catalysis or through the intramolecular transfer of existing chirality within a molecule. The directing influence of the hydroxyl group has been demonstrated for a number of reactions of chiral allylic alcohols, and stereoselectivities of over 98% have been demonstrated for some reactions. We presently wish to report the extension of chirality transfer from chiral allylic alcohols utilizing Stille’s palladium-catalyzed olefin dicarbonylation reaction. In this context it is noteworthy that a number of groups have explored the use of chiral catalysts with the Stille bis-alkoxycarbonylation for the asymmetric construction of chiral bis-esters. Inomata and coworkers recently reported the palladium-catalyzed asymmetric bis(alkoxycarbonylation) of cyclic olefins in the presence of copper triflate. Liang et al. have described a palladium-catalyzed asymmetric bisis(alkoxycarbonylation) of terminal olefins using chiral S,N-heterobideterminate ligands. Takeuchi described a palladium-catalyzed asymmetric bis(alkoxycarbonylation) reaction of terminal olefins in the presence of copper(I) triflate using a chiral bioxazoline ligand to give optically active mono-substituted succinates with enantioselectivities up to 66% ee. While Sperrle reported the enantioselective bis-alkoxycarbonylation of 1-olefins to substituted succinates using cationic palladium(II) complexes with C2 symmetric chelating ligands, and also the use of cationic palladium(II) complexes to catalyze multiple carbonylation of 1-olefins to 2-oxopentanepoate and to butanedioates. The dicarbonylation reaction is catalyzed by a PdCl2–CuCl2 system in methanol under basic conditions at low CO pressures (3 atm) to give diesters with an overall syn addition. While chirality transfer generally involves transfer of optical activity from one carbon to another, this allylic dicarbonylation that we now report involves a double insertion of CO to give diesters containing three contiguous chiral centers.

2. Results and discussion

The bis-carbonylation with chirality transfer was first tested with the chiral cyclic allylic alcohol (R)-(+)-cyclopent-2-en-1-ol in 78.3% isolated yield and 71% ee by reduction with (R)-oxazaborolidine and borane. Kita reported a similar asymmetric reduction of a cyclic enone with an oxazaborolidine and Matusuo recently reported the oxazaborolide-catalyzed asymmetric reduction of α-methylene ketones using borane-diethylaniline as a stoichiometric reducing agent. The absolute configuration of 1 was determined based upon measurement of rotation and comparison with literature values. Treatment of (R)-(−)-1 with PdCl2 and CuCl2 in methanol at room temperature under an atmosphere of CO (3 atm) in the presence of trimethyl orthoformate to remove adventitious water gave two products in 65% and 35% relative yields as determined by gas chromatography. The two products were identified by 1H and 13C NMR to be (1S,2S,3R)-dimethyl 3-hydroxycyclopentane-1,2-dicarboxylate and (S)-methyl 3-oxocyclopentanecarboxylate, respectively (Scheme 1). The ee of 2 was established to be 69.7% as determined by 1H NMR in the presence of lanthanide shift reagent Eu(hfc)3, thus the reaction proceeded in 98% diastereoselectivity (Table 1), representing the efficiency of chirality transfer from the asymmetric carbinol center. As noted, allylic alcohol (R)-(+)-1 was utilized with 71% ee, such that complete diastereoselectivity.
in the bis-alkoxycarbonylation would yield diester of ee identical to the starting allylic alcohol. The relative stereochemistry of the dicarbonylation product 2 was established by \( ^1H \) NMR, and NOE studies. The \( J \) values of \( H_a \) with \( H_b \) and \( H_c \), respectively are 8.0 and 15.6 Hz. These values are consistent with the syn stereochemistry between \( H_a \), \( H_b \), and \( H_c \). Since the absolute configuration at C-1 is known to be \( R \), the absolute configuration at C-1 and C-2, bearing the carbomethoxy groups, must both be \( S \). The relative stereochemistries of \( H_a \), \( H_b \), and \( H_c \) were also confirmed on the basis of NOE studies (Fig. 1). The all-syn relative stereochemistry evident by the 10.2% enhancement of the signal for \( H_a \) upon irradiation of \( H_b \) and \( H_c \) shows that the carbomethoxy groups, which are cis, have the same absolute configuration. This suggests that the hydroxyl group directs the palladium to the face that produces \( S \), which is consistent with the mechanism proposed by Uenishi\(^{13}\) for an intramolecular palladium-catalyzed oxypalladation and 1,3-chirality transfer. Thus, the hydroxyl group directs the palladium to the face that produces the most stable \( \pi \)-complex 4, which in turn depends on the absolute configuration of the starting allylic alcohol 1.\(^4\) Addition of carbon monoxide to complex 4 followed by insertion of methanol yields the olefin-carbomethoxypalladium intermediate 5, which undergoes insertion of the carbomethoxy group to produce the \( \pi \)-complex 6.\(^{14,19}\) Adduct 6 then either undergoes further syn addition of CO to give desired 2, or loses a proton and eliminates palladium yielding an enol which tautomerizes to ketone 3.

Next we examined the carbomethoxylation of (R)-(Z)-pent-3-en-2-ol [(Z)-9] and (R)-(E)-pent-3-en-2-ol [(E)-9]. Both isomers were prepared from the reduction of (R)-(Z)-3-yne-2-ol (8) (Scheme 3). (R)-(+)pent-3-yne-2-ol (8) was prepared in 85% yield by the reduction of 3-pentyn-2-one 7 with chiral [(SS)-RuCl\{N-(tosyl)-1,2-diphenylethynediylamine\}[p-cymene]] reagent in formic acid/triethylamine isotropic mixture according to the general method of Bogliotti.\(^{36}\) A sample of (R)-(Z)-9 was prepared in 86% ee by reduction of the triple bond with Lindlar’s catalyst\(^{37}\) while (R)-(E)-9 was prepared in 83% ee by reduction with LiAlH\(_4\).\(^{38}\) GLC and \( ^1H \) NMR analysis showed that each sample was greater than 95% of the desired double bond geometric isomer.

Dicarbomethoxylation of each geometric isomer of 9 independently was carried out in the same manner as for the substrate (R)-(+)1 (Table 1). (R)-(Z)-9 afforded three products as shown by GLC, which were identified by NMR spectroscopy to be the desired (2R,3R)-dimethyl 2-((R)-1-hydroxyethyl)-3-methylsuccinate [(R,R,R)-9].
in 80% relative yield, plus 4-methoxy-pentan-2-one in 10% yield, and 4-acetoxy-pentan-2-one in 10% yield. A pure sample of \((R,R,R)-10\) was obtained by gas chromatography and the enantiomeric excess was determined by \(^1\text{H}\) NMR in the presence of chiral shift reagent Eu(hfc)_3 to be 82.7%, thus the diastereoselectivity was 96%. The dicarbonylation of \((R)-E)-9\) afforded the desired dicarboxymethylation product \((R,R,S)-10\) in 45% relative yield, plus 4-methoxy-pentan-2-one, 4-acetoxy-pentan-2-one, and 4-carboxymethoxy-pentan-2-one, and 5%, 20%, and 30% relative yields, respectively. A pure sample of \((R,R,S)-10\) was collected by GLC and analyzed by \(^1\text{H}\) NMR in the presence of the lanthanide shift reagent Eu(hcf)_3 to establish an ee of 64.7%, representing a diastereoselectivity of 78%. The relative configurations of stereogenic centers in the carbonylated products \((R,R,S)-10\) of \((R)-E)-9\) and \((R)-Z)-9\) were confirmed by NOE. NOE has been used previously to assign absolute configurations of cyclic systems and the theory for acyclic systems such as 9 with restricted rotation has also been presented. Shown in Figure 2 are the NOE assignments for the most stable rotamers of the two products. These assignments are in agreement with all the information from \(^1\text{H}\) NMR. The assignment of absolute configuration is consistent with the expected initial syn addition of the elements of the carboxymethoxy-Pd(II) moiety shown in Scheme 2.

Carbonylation of allylic alcohols \((R)-(Z)-4\)-phenyl-but-3-ene-2-ol \([\((R)-(Z)-13\)]\) and \((R)-(E)-4\)-phenyl-3-buten-2-ol \([\((R)-(E)-13\)]\) were then evaluated. Propargyl alcohol 12 was prepared in 87% ee with (R) absolute configuration by the reduction of propargyl ketone 11 again using \((S,S)-\text{RuCl}[\text{N}-(\text{tosyl})]-1,2\)-diphenylethlyenediamine)\([p\text{-cymene}]\) as outlined in Scheme 3. Allylic alcohol \((R)-(Z)-13\) was prepared in 87% ee by the reduction of propargyl alcohol \((R)-(E)-13\) using Lindlar’s catalyst. Allylic alcohol \((R)-(E)-13\) was prepared in 75% ee by the reduction of 12 using LiAlH₄.
Carbomethylation of (R)-(Z)-13 afforded three products that were isolated and purified by flash chromatography. NMR analysis showed the compounds to be 4-methoxy-4-phenylbutan-2-one, 4-acetoxy-4-phenylbutan-2-one, and the desired (2R,3S)-dimethyl 2-((R)-1-hydroxyethyl)-3-phenylsuccinate (R,R,R)-14, in 41% yield. The ee of (R,R,R)-14 was determined by 1H NMR in the presence of the lanthanide shift reagent Eu(hcf)3 to be 64.7%, thus the diastereoselectivity of 93%. Dicarbomethylation of (R)-13 showed the compounds to be 4-methoxy-4-phenylbutan-2-one, 4-acetoxy-4-phenylbutan-2-one, and the (2R,3R)-dimethyl 2-((R)-1-hydroxyethyl)-3-phenylsuccinate (R,R,R)-14 in 17%, 27% and 56% yield, respectively. The diastereomeric ratio for (R,R,R)-14 was determined by 1H NMR in the presence of the lanthanide shift reagent Eu(hcf)3 to be 64.7%, thus the dicarbomethylation proceeded in 86% diastereoselectivity.

We also attempted to prepare (R)-1-phenyl-3-butyn-1-ol and (R)-1-hydroxyethyl)-3-phenylsuccinate (R,S,R)-13 from the corresponding p-cymene) from the corresponding materials containing three contiguous asymmetric centers in good to excellent (78–98%) diastereoselectivities.

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Supplementary data


References and notes