High Selectivity from Configurational Match/Mismatch in Carbon−Hydrogen Insertion Reactions of Steroidal Diazoacetates Catalyzed by Chiral Dirhodium(II) Carboxamidates

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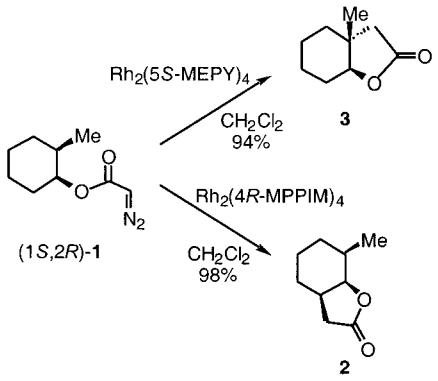
Diazo decomposition of steroidal diazoacetates, where the point of attachment is the 3-position of the steroid A-ring, catalyzed by chiral dirhodium(II) carboxamidates results in products from carbon−hydrogen insertion in high yield and selectivities. Use of *S*-configured catalysts shows a distinctive preference for insertion into the 3-position to form *β*-lactone products. The *R*-configured catalysts direct insertion preferentially to the equatorial C−H bond at the 2-position. Substituents or functional groups at the 5/6-position prevent C−H insertion from taking place at the 4-position. Even in the best case with the 5/6-positions fully saturated, however, insertion into the 3-position remains competitive with insertion into the 4-position. Corresponding 3-substituted phenyldiazoacetates give only *β*-lactone products, and selectivity here is highest with chiral dirhodium(II) prolinate catalysts. A model is presented to explain these results. Overall, this methodology is versatile for functionalization of the steroid A-ring at positions 2 and 3.

We previously reported exceptional diastereoselection and regioselection in chiral catalyst controlled intramolecular carbon−hydrogen insertion reactions of cyclohexyl diazoacetates.[1,2] Using enantiomerically pure 2-substituted cyclohexyl diazoacetates and a series of chiral dirhodium(II) carboxamidates, virtually complete diastereocontrol was achieved when there was a match between substrate and catalyst configurations (e.g., Scheme 1).[1] When there was a significant mismatch, mixtures of products were obtained. Similar selectivities were obtained for reactions of conformationally restricted 4-substituted cyclohexyl diazoacetates;[2,3] there are no reported examples using 3-substituted cyclohexyl diazoacetates.

Carbon−hydrogen insertion normally takes place to form five-membered ring products,[4−7] but there is an increasing number of examples of four-membered ring formation, especially when insertion can occur adjacent to a heteroatom, especially oxygen and nitrogen.[4,8−10] Furthermore, reactivity for insertion into C−H bonds

Scheme 1



follows the order tertiary > secondary ≫ primary,[11] but conformational influences can and do override electronic preferences.[12] Insertion into an equatorial C−H bond is favored over insertion into an axial C−H bond,[1,2] although an exception has been noted.[13]

Although there has continued to be a flurry of activity in metal-catalyzed C−H insertion reactions,[4] and high selectivity continues to be achieved,[14] there have been few reports of the influence of remote substituents on selectivity.[4−7] Steroidal systems are especially useful

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(5) (a) Padwa, A.; Krumpe, K. E. *Tetrahedron* **1992**, *48*, 5385. (b) Padwa, A.; Austin, D. J. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1797.
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(14) (a) Wee, A. G. H. *Tetrahedron Lett.* **2000**, *41*, 9025. (b) Taber, D. F.; Malcolm, S. C.; Bieger, K.; Lahuerta, P.; Sanaú, M.; Stiriba, S.-E.; Pérez-Prieto, J.; Monge, M. A. *J. Am. Chem. Soc.* **1999**, *121*, 860. (c) Taber, D. F.; Song, Y. *J. Org. Chem.* **1997**, *62*, 6603. (d) Davies, H. M. L.; Hansen, T.; Churchill, M. R. *J. Am. Chem. Soc.* **2000**, *122*, 3063. (e) Davies, H. M. L.; Antoulinakis, E. G. *Org. Lett.* **2000**, *2*, 4153. (f) Anada, M.; Watanabe, N.; Hashimoto, S. *J. Chem. Soc. Chem. Commun.* **1998**, 1517.

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Table 1. Products from Catalytic Diazo Decomposition of Cholesteryl Diazoacetate (8)[a]

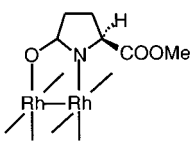
		rel yield, %	
catalyst	product yield,[b] %	**9**	**10**
$Rh_2(5R\text{-MEPY})_4$	81	94	6
$Rh_2(4R\text{-MEOX})_4$	81	89	11
$Rh_2(5S\text{-MEPY})_4$	74	33	67
$Rh_2(4S\text{-MEOX})_4$	80	10	90
$Rh_2(4S\text{-MEAZ})_4$	69	27	73
$Rh_2(4S\text{-IBAZ})_4$	31[c]	32	68
$Rh_2(OAc)_4$	<5[c]		

[a] Reactions were performed in refluxing CH_2Cl_2 using 1.0 mol % of catalyst. [b] Weight yield after chromatographic separation of catalyst. [c] Major product was that from O−H insertion.

substrates for such investigations because of their conformational rigidity, but they have previously received only a minimum of attention with diazo decomposition reactions.[4] We wish to report that exceptional diastereoselectivity and regiocontrol can be achieved in chiral dirhodium(II) carboxamidate catalyzed reactions of steroidal-3-diazoacetates and that there exists a surprising effective competition between γ- and β-lactone formation that is dependent on the configurational match between substrate and catalyst.

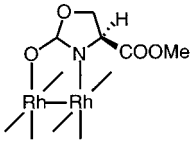
Results and Discussion

Cholest-5-en-3β-yl diazoacetate (**8**) was selected for the initial survey. Prepared from cholesterol by diketene condensation, diazo transfer, and deacetylation in 68% overall yield, this diazoacetate was subjected to standard conditions for diazo decomposition[1] with the series of chiral dirhodium(II) carboxamidate catalysts **4**-**7**.[15−17]



$Rh_2(5S\text{-MEPY})_4$

4



$Rh_2(4S\text{-MEOX})_4$

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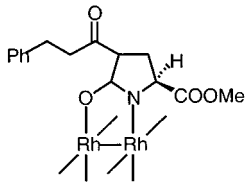
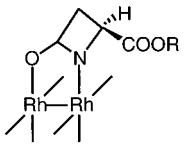


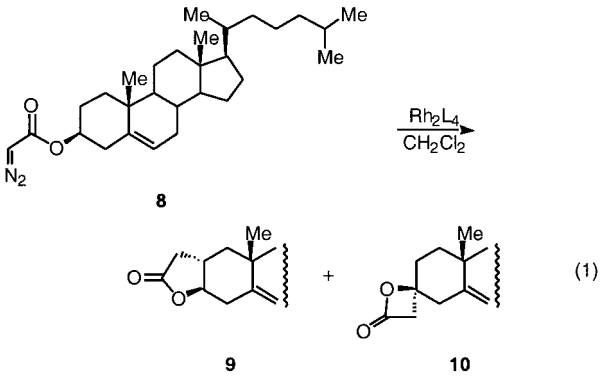
$Rh_2(4S\text{-MPPIM})_4$

6

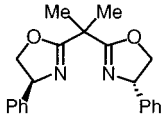


7a : $Rh_2(4S\text{-MEAZ})_4$, R = Me
7b : $Rh_2(4S\text{-BNAZ})_4$, R = Bn
7c : $Rh_2(4S\text{-IBAZ})_4$, R = *i*Bu

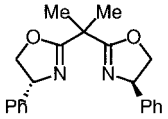
Two products were obtained (eq 1) with γ-lactone **9** favored by the *R*-configured catalysts and β-lactone **10** dominant with the *S*-configured catalysts (Table 1). A product from C−H insertion into the steroidal 4-position could not be confirmed and, if present, was only a trace constituent. The reason for the absence of insertion into the 4-position is not obvious. Significantly, the use of the achiral catalyst $Rh_2(OAc)_4$ resulted in a low yield of insertion products when reactions were performed under the same conditions. The γ-lactone product (**9**) stereochemistry was ascertained by NMR analyses.



High product yields and high selectivities (≥9:1) can be achieved with $Rh_2(MEPY)_4$ and $Rh_2(MEOX)_4$ catalysts. Lower selectivities and lower product yields occur in reactions catalyzed by $Rh_2(IBAZ)_4$ and $Rh_2(MPPIM)_4$.[18] Use of chiral bis-oxazoline ligands **11** for copper(I) complexes[19] from $Cu(MeCN)_4PF_6$ allowed C−H insertion to take place, but selectivities were low (**9**/**10** = 72:28 with *S*-**11** and 37:63 with *R*-**11**).

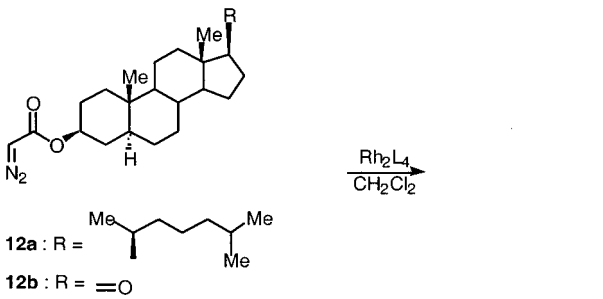


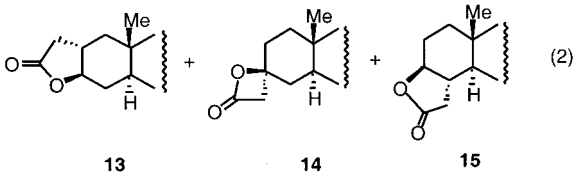
***S*-11**



***R*-11**

With the dihydrogen analogue of **8**, 5α-cholestan-3β-yl diazoacetate (**12a**), a strikingly different outcome occurred as a result of competition for C−H insertion at the 4-position. Three products were isolated in excellent yields (eq 2), and the results from reactions with a series of dirhodium(II) carboxamidate catalysts are reported in Table 2. That the stereochemistry of the γ-lactone products was trans in **13a** and **15a** was confirmed by NMR through 2D HSQC and 1D NOE experiments.





13 **14** **15**

The *R*-configured ligands on dirhodium(II) do favor attack at the equatorial C−H bond at the 2-position, and the formation of **15a** also occurs through attack at an equatorial C−H bond. This is consistent with prior

(15) Doyle, M. P.; Zhou, Q.-L.; Raab, C. E.; Roos, G. H. P.; Simonsen, S. H.; Lynch, V. *Inorg. Chem.* **1996**, *35*, 6064.
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(18) With $Rh_2(4S\text{-MPPIM})_4$, the yield of **9** + **10** was 54% with 30% of unreacted diazoacetate; selectivity for **9**/**10** was 20:80.
(19) The first report of the effective use for C−H insertion of copper(I) complexes with chiral bis-oxazoline ligands: Lim, H.-J.; Sulikowski, G. A. *J. Org. Chem.* **1995**, *60*, 2326.

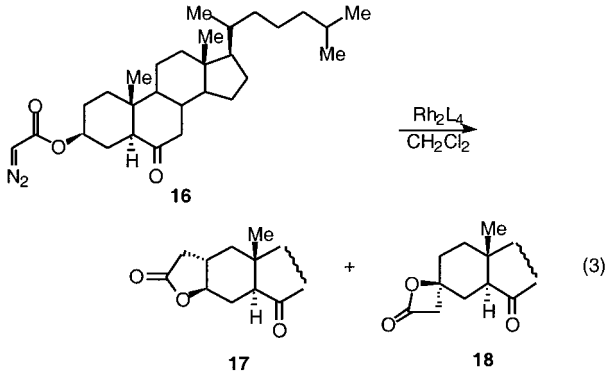
Table 2. Products from Catalytic Diazo Decomposition of Cholestanyl Diazoacetate (12a)[a]

		rel yield, %		
catalyst	product yield,[b] %	**13a**	**14a**	**15a**
$Rh_2(5R\text{-MEPY})_4$	89	72	20	8
$Rh_2(4R\text{-MEOX})_4$	86	60	33	7
$Rh_2(4R\text{-MPPIM})_4$	86	87	8	5
$Rh_2(5S\text{-MEPY})_4$	87	6	62	32
$Rh_2(4S\text{-MEOX})_4$	91	4	70	26
$Rh_2(4S\text{-MPPIM})_4$	76	16	66	20
$Rh_2(4S\text{-MEAZ})_4$	85	6	39	55
$Rh_2(4S\text{-BNAZ})_4$	80	7	44	49

[a] Reactions were performed in refluxing CH_2Cl_2 using 1.0 mol % of catalyst. [b] Weight yield after chromatographic separation of catalyst.

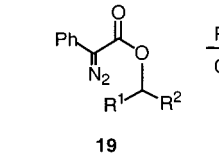
investigations.[1,4] However, the competition between β-lactone (**14a**) and γ-lactone (**15a**) formation with the *S*-configured catalysts is surprising and probably results from constraints placed on the configuration of the reacting metal carbene in its approach to the equatorial C−H bond at the 4-position. These constraints could be from substitution at the 5-position or from the angular methyl group at the 10-position. In any case, the fact that one or both of these remote substituents profoundly influences regiocontrol is an indication of the strength of these catalyst interactions. Virtually identical results were obtained with 5α-androstan-17-on-3β-yl diazoacetate (**12b**), and these data are reported in Table 3; however, note that $Rh_2(OAc)_4$ offers virtually no selectivity for insertion.

Diazo decomposition of the 6-keto analogue of cholesteryl diazoacetate (**16**) for which the stereoelectronic influence of the 6-keto group was expected to inhibit C−H insertion β to this functional group[20] gave results that greatly favored formation of the β-lactone product (eq 3).



Results from catalytic reactions with representative chiral dirhodium carboxamidates are reported in Table 4. In only one other case, that of the diazo decomposition of nonracemic 2-octyl diazoacetate,[1] have we seen such a high tendency to undergo β-lactone formation.

We have recently reported that intramolecular C−H insertion of phenyldiazoacetates exhibited preferential formation of β-lactones with secondary alkyl esters (eq 4).[10] Enantiocontrol approached 50% ee, but diastereocontrol was low. To ascertain the applicability of phenyldiazoacetates in the steroidal series we prepared the 3β-cholesteryl ester. Prior investigations had established that dirhodium(II) carboxylates and the reactive dirhodium(II) azetidinone-carboxylate catalysts (**7**) were active toward phenyldiazoacetate decomposition, but other carboxamidate catalysts (**4**−**6**) were not.[16] Diazo decomposition resulted in the formation of two products, both β-lactones, in good yield (eq 5).



(4)

Table 3. Products from Catalytic Diazo Decomposition of Androstan-17-on-3-yl Diazoacetate (12b)[a]

		rel yield, %		
catalyst	product yield,[b] %	**13b**	**14b**	**15b**
$Rh_2(5R\text{-MEPY})_4$	84	73	23	4
$Rh_2(4R\text{-MEOX})_4$	89	60	37	3
$Rh_2(5S\text{-MEPY})_4$	83	3	65	32
$Rh_2(4S\text{-MEOX})_4$	86	3	87	19
$Rh_2(4S\text{-MEAZ})_4$	76	1	42	57
$Rh_2(OAc)_4$	62	22	32	46

[a] Reactions were performed in refluxing CH_2Cl_2 using 1.0 mol % of catalyst. [b] Weight yield after chromatographic separation of catalyst.

Table 4. Products from Catalytic Diazo Decomposition of 16[a]

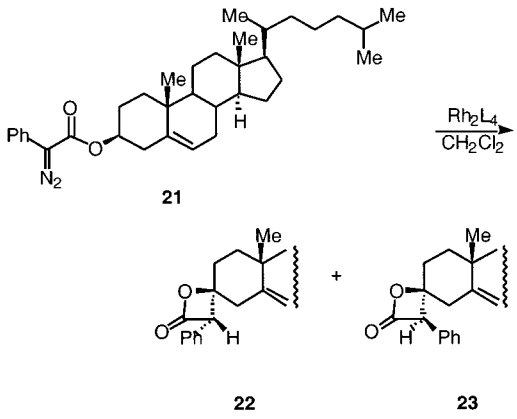
		rel yield, %	
catalyst	product yield,[b] %	**17**	**18**
$Rh_2(5R\text{-MEPY})_4$	85	61	39
$Rh_2(4R\text{-MEOX})_4$	88	43	57
$Rh_2(5S\text{-MEPY})_4$	76	8	92
$Rh_2(4S\text{-MEOX})_4$	90	3	97

[a] Reactions were performed in refluxing CH_2Cl_2 using 1.0 mol % of catalyst. [b] Weight yield after chromatographic separation of catalyst.

Table 5. Products from Catalytic Diazo Decomposition of Cholesteryl Phenyldiazoacetate 21[a]

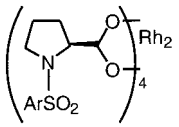
		rel yield, %	
catalyst	product yield,[b] %	**22**	**23**
$Rh_2(OAc)_4$	69	22	78
$Rh_2(4R\text{-MEAZ})_4$	69	16	84
$Rh_2(4S\text{-MEAZ})_4$	66	38	62
$Rh_2(S\text{-DOSP})_4$	58	16	84
$Rh_2(S\text{-DOSP})_4$[c]	69	10	90

[a] Unless specified otherwise, reactions were performed in refluxing CH_2Cl_2 using 1.0 mol % of catalyst. [b] Weight yield after chromatographic separation of catalyst. [c] Reaction performed in refluxing pentane.



The influence of the catalyst on diastereoselectivity (Table 5) was substantial with the greatest selectivity

achieved with Davies' Rh_2(*S*-DOSP)$_4$ (**24**) in pentane.[21] Once again, remote substituents control diastereoselectivity to a substantial degree.[22]

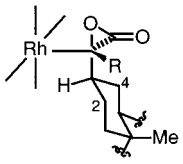


24: Ar = *p*-$CH_3(CH_2)_{11}C_6H_4$

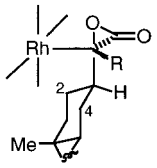
What is obvious from the data presented here is that steric factors play a significant role in determining product selectivity. Access to the 4-position for C−H insertion is possible only with the least sterically demanding azetidinone-ligated dirhodium(II) catalysts (Tables 2 and 3). However, insertion into a C−H bond at the 2-position occurs with high selectivity using sterically more robust dirhodium(II) carboxamidate catalysts. In each case, insertion takes place into an equatorial C−H bond.

The formation of β-lactone product is favored by *S*-configured catalysts. This process occurs in synthetically meaningful yields even though there is significant ring strain introduced by the process. The driving force here is, in part, insertion into an oxygen-activated tertiary C−H bond, but steric factors must also contribute.

One way of understanding the selectivities that have been achieved is through the use of models for the reactant metal carbene.[23] Preference for insertion at the 2-position over insertion at the 4-position may be understood by comparison of **25** with **26**. We have previously documented the preference for the conformation in which the carbonyl group is anti to the dirhodium(II) core.[24,25]



25



26

In **25**, a slight rotation of the steroid brings the C−H bond at the 3-position into close contact with the carbene carbon. In **26**, the rotation required to bring the C−H bond at the 2- or 4-positions into contact with the carbene carbon also twists the bulk of the steroid away from the ligated metal (envision motion of the methyl group at C-10 clockwise or counterclockwise). That placement of a double bond between carbons 5 and 6 completely inhibits insertion into the C−H bond at C-4 is not obvious even with these models. However, competition between insertion at the 3-position and the 4-position (Tables 2 and 3) is consistent with **26** elaborated to describe the stereochemistry of the ligands on rhodium.

Experimental Section

General Methods. ^{1}H NMR (300, 500, or 600 MHz) and ^{13}C NMR (75, 125, or 150 MHz) were recorded from solutions in $CDCl_3$, and chemical shifts are reported in parts per million (ppm, δ) downfield from internal Me_4Si (TMS). Mass spectra were obtained using electron ionization on a quadrapole instrument. Infrared spectra were recorded by an FT-IR instrument either as a thin film on sodium chloride plates or as solutions as indicated, and absorptions are reported in wavenumbers (cm^{-1}). Melting points are uncorrected. Elemental analysis was performed by Atlantic Microlab, Inc. Dichloromethane was distilled from calcium hydride prior to use in catalytic reactions. Tetrahydrofuran was distilled from sodium and benzophenone. Methanesulfonyl azide was prepared from methanesulfonyl chloride and sodium azide and was not distilled.[26] Synthetic reagents were purified by distillation or crystallization prior to use. The preparation of Rh_2(5*R*-MEPY)$_4$ and Rh_2(5*S*-MEPY)$_4$,[24] Rh_2(4*R*-MEOX)$_4$ and Rh_2(4*S*-MEOX)$_4$,[27] Rh_2(4*S*-MPPIM)$_4$,[15] and Rh_2(4*S*-MEAZ)$_4$,[16] Rh_2(4*S*-IBAZ)$_4$,[28] and Rh_2(4*S*-BNAZ)$_4$[28] by acetate displacement from $Rh_2(OAc)_4$ have been reported.

Cholest-5-en-3β-yl diazoacetate (8) was prepared by a two-pot modification of the standard three-step procedure.[12] To a stirred solution of cholesterol (3.00 g, 7.75 mmol) and triethylamine (98 μL, 0.70 mmol) in dry THF (30 mL) at 0 °C was added diketene (0.975 g, 11.6 mmol) via syringe over 5 min. The resulting yellow solution was stirred for 1 h at 0 °C and then warmed to room temperature. After 24 h, the mixture was again cooled to 0 °C, at which time triethylamine (1.57 g, 15.5 mmol) and methanesulfonyl azide (1.88 g, 15.5 mmol) were added via syringe. The reaction mixture was allowed to warm slowly to room temperature. After 24 h, the reaction was diluted with water (25 mL), and the diazoacetoacetate was isolated by extraction with ethyl acetate (3 × 20 mL). The organic layers were combined, washed with water (3 × 20 mL) and brine (50 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Flash column chromatography on silica gel (15% ethyl acetate in hexanes) afforded the diazoacetoacetate in 87% overall yield (3.35 g, 6.75 mmol) as a yellow oil. **Cholest-5-en-3β-yl diazoacetoacetate:** ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.40 (d, J = 5.1 Hz, 1H), 4.81−4.68 (m, 1H), 2.47 (s, 3H), 2.42−2.34 (comp, 2H), 2.06−0.95 (comp, 29H), 1.03 (s, 3H), 0.92 (d, J = 6.3 Hz, 3H), 0.87 (d, J = 6.6 Hz, 3H), 0.86 (d, J = 6.6 Hz, 3H), 0.68 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.2, 160.8, 139.0, 123.1, 76.4, 75.4, 56.6, 56.1, 49.9, 42.2, 39.6, 39.4, 38.2, 36.8, 36.5, 36.1, 35.7, 31.8, 31.7, 28.2, 28.1, 28.0, 27.9, 24.2, 23.8, 22.8, 22.5, 21.0, 19.2, 18.6, 11.8.

Acetyl cleavage of cholest-5-en-3β-yl diazoacetoacetate was performed by the addition of LiOH monohydrate (0.979 g, 23.3 mmol) to a biphasic solution of the diazoacetoacetate (3.35 g, 6.75 mmol) in THF (15 mL) and distilled water (10 mL). The dark brown solution was stirred at room temperature until acetyl cleavage was complete. The reaction mixture was extracted with ethyl acetate (3 × 20 mL). The organic layers were combined and washed with water (3 × 15 mL), brine (3 × 15 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Flash column chromatography on silica gel (3% ethyl acetate in hexanes) afforded cholest-5-en-3β-yl diazoacetate (**8**) as a pale yellow solid in 68% yield (1.93 g, 5.27 mmol): mp 138−139 °C; $[\alpha]^{26}_D$ = −24.5 (*c* 2.79, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.38 (d, J = 5.1 Hz, 1H), 4.74−4.68 (m, 1H), 4.70 (bs, 1H), 2.38−2.28 (comp, 2H), 2.02−

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1.94 (comp, 2H), 1.89−1.79 (comp, 3H), 1.63−0.90 (comp, 21H), 1.01 (s, 3H), 0.91 (d, J = 6.6 Hz, 3H), 0.87 (d, J = 6.6 Hz, 3H), 0.86 (d, J = 6.6 Hz, 3H), 0.67 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.3, 139.5, 122.7, 74.6, 56.7, 56.1, 50.0, 46.3, 42.3, 39.7, 39.5, 38.3, 36.9, 36.6, 36.2, 35.8, 31.9, 31.8, 28.2, 28.0, 27.9, 24.3, 23.8, 22.8, 22.6, 21.0, 19.3, 18.7, 11.9; IR (film) 2120 (C═N_2), 1698 (C═O), 1404, 1196 cm^{-1}. Anal. Calcd for $C_{29}H_{46}N_2O_2$: C, 76.6; H, 10.20; N, 6.16. Found: C, 76.67; H, 10.28; N, 6.06.

Diazo Decomposition of Cholest-5-en-3β-yl Diazoacetate. To a stirred solution of Rh_2(4*R*-MEOX)$_4$ (1.9 mg, 0.0011 mmol) in dry CH_2Cl_2 (5 mL) heated at reflux under a nitrogen atmosphere was added cholesteryl diazoacetate **8** (50.0 mg, 0.111 mmol) in dry CH_2Cl_2 (3 mL) over 5 h via syringe pump. The reaction mixture was heated at reflux for an additional half hour. After being cooled to room temperature, the reaction solution was filtered through a short silica plug, which was subsequently washed with 10 mL of 30% ethyl acetate in hexanes. The solvent was removed under reduced pressure to afford 34 mg of product (72% yield) consisting of γ-lactone **9** and β-lactone **10**. The ratio of products in the crude reaction mixture was determined by ^{1}H NMR spectroscopy. Column chromatography on silica gel (3% ethyl acetate in hexanes) afforded 30 mg of 2-(3β-hydroxy-5-cholesten-2α-yl)acetic acid lactone **(9)** (63% yield) and 3 mg of 3-(3β-hydroxy-5-cholesten-3α-yl)acetic acid lactone **(10)** (6% yield). The Rh_2(4*S*-MEOX)$_4$-catalyzed reaction of diazoacetate **8** afforded 4 mg of 2-(3β-hydroxy-5-cholesten-2α-yl)acetic acid lactone **(9)** and 30 mg of 3-(3β-hydroxy-5-cholesten-3α-yl)acetic acid lactone **(10)** (65% yield). 4-(3β-Hydroxy-5-cholesten-4α-yl)acetic acid lactone, the product from C−H insertion at the 4-position, did not form to an appreciable amount in any diazo decomposition reaction.

2-(3β-Hydroxy-5-cholesten-2α-yl)acetic acid lactone (9): mp 137−138 °C; $[\alpha]^{22}_D$ = −11.4 (*c* 1.75, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.49 (d, J = 5.2 Hz, 1H), 3.69 (ddd, J = 12.2, 10.3, 4.7 Hz, 1H), 2.58 (dd, J = 12.2, 4.4 Hz, 1H), 2.53 (dd, J = 15.2, 5.2 Hz, 1H, lactone α-H_{eq}), 2.57−2.49 (comp, 1H), 2.19 (t, J = 15.2, 1H, lactone α-H_{ax}), 2.34−2.13 (comp, 1H), 2.07−1.98 (comp, 3H), 1.88−1.80 (comp, 1H), 1.61−0.70 (comp, 20H), 1.07 (s, 3H), 0.91 (d, J = 6.5 Hz, 3H), 0.87 (d, J = 6.6 Hz, 3H), 0.86 (d, J = 6.6 Hz, 3H), 0.68 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 176.6, 138.1, 125.6, 84.9, 56.6, 56.1, 50.1, 42.3, 40.9, 40.4, 39.6, 39.5, 38.6, 37.7, 36.1, 35.9, 35.7, 31.8, 31.6, 28.2, 28.0, 24.2, 23.8, 22.8, 22.5, 21.0, 20.6, 18.7, 11.8; IR ($CDCl_3$) 1787 (C═O) cm^{-1}; HRMS (FAB$^+$) calcd for $C_{29}H_{47}O_2$ 427.3576, found 427.3589 (M^{+1}).

3-(3β-Hydroxy-5-cholesten-3α-yl)acetic acid lactone (10): mp 119−121 °C; $[\alpha]^{26}_D$ = −24.0 (*c* 0.35, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.42 (d, J = 5.1 Hz, 1H), 3.03 (d, J = 16.2 Hz, 1H, lactone α-H), 2.95 (d, J = 16.2 Hz, 1H, lactone α-H), 2.24−1.73 (comp, 8H), 1.61−0.97 (comp, 20H), 1.05 (s, 3H), 0.91 (d, J = 6.3 Hz, 3H), 0.87 (d, J = 6.6 Hz, 3H), 0.86 (d, J = 6.6 Hz, 3H), 0.68 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 138.5, 124.2, 79.2, 56.6, 56.1, 50.0, 46.2, 42.7, 42.3, 39.6, 39.5, 36.7, 36.5, 36.2, 35.7, 32.0, 31.9, 31.8, 28.2, 28.0, 24.2, 23.8, 22.8, 22.5, 21.1, 19.2, 18.7, 11.8; IR ($CDCl_3$) 1818 (C═O) cm^{-1}; HRMS (FAB$^+$) calcd for $C_{29}H_{47}O_2$ 427.3576, found 427.3581 (M^{+1}).

5α-Cholestan-3β-yl diazoacetate (12a) was prepared by the standard method.[12] To a stirred solution of 5α-cholestan-3β-ol (3.00 g, 7.72 mmol) and triethylamine (11 μL, 0.077 mmol) in dry THF (35 mL) at 0 °C was added diketene (0.973 g, 11.6 mmol) via syringe over 5 min. The resulting yellow solution was stirred for 1 h at 0 °C and then warmed to room temperature. After 24 h, the mixture was again cooled to 0 °C, at which time triethylamine (1.17 g, 11.6 mmol) and methanesulfonyl azide (1.40 g, 11.6 mmol) were added via syringe. The reaction mixture was allowed to warm slowly to room temperature. After 24 h, the reaction was diluted with water (25 mL), and the diazoacetoacetate was isolated by extraction with ethyl acetate (3 × 75 mL). The organic layers were combined, washed with 1 M NaOH (25 mL), water (3 × 50 mL), and brine (50 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Flash column chromatography on silica gel (15% ethyl acetate in hexanes) afforded the diazoacetoacetate in 87% overall yield (3.37 g, 6.72 mmol) as a yellow oil. **5α-Cholestan-3β-yl diazoacetoacetate:** ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.90−4.77 (m, 1H), 2.47 (s, 3H), 2.04−0.95 (comp, 30H), 0.90 (d, J = 6.6 Hz, 3H), 0.87 (d, J = 6.6 Hz, 3H), 0.86 (d, J = 6.6 Hz, 3H), 0.84 (s, 3H), 0.74−0.60 (comp, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.4, 161.0, 75.3, 56.4, 56.2, 54.1, 44.7, 42.5, 39.9, 39.5, 36.7, 36.1, 35.8, 35.4, 34.2, 31.9, 28.6, 28.3, 28.2, 28.0, 27.6, 24.2, 23.8, 22.8, 22.5, 21.2, 18.6, 12.2, 12.0.

Acetyl cleavage of 5α-cholestan-3β-yl diazoacetoacetate was performed as previously described by the addition of LiOH monohydrate (0.421 g, 10.0 mmol) to a biphasic solution of the diazoacetoacetate (3.55 g, 6.68 mmol) in THF (25 mL) and distilled water (25 mL). Flash column chromatography on silica gel (5% ethyl acetate in hexanes) afforded 5α-cholestan-3β-yl diazoacetate **(12a)** in 88% yield (2.67 g, 5.89 mmol) as a pale yellow solid: mp 141−144 °C; $[\alpha]^{34}_D$ = +15.4 (*c* 1.22, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.83−4.70 (m, 1H), 4.69 (bs, 1H), 2.05−0.92 (comp, 30H), 0.90 (d, J = 6.6 Hz, 3H), 0.86 (d, J = 6.6 Hz, 6H), 0.82 (s, 3H), 0.74−0.55 (comp, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 74.4, 56.4, 56.2, 54.2, 46.3, 44.6, 42.6, 39.9, 39.5, 36.7, 36.1, 35.8, 35.5, 35.4, 34.2, 32.0, 28.6, 28.2, 28.0, 27.7, 24.2, 23.8, 22.8, 22.5, 21.2, 18.6, 12.2, 12.0; IR (film) 2117 (C═N_2), 1672 (C═O) cm^{-1}. Anal. Calcd for $C_{29}H_{48}N_2O_2$: C, 76.27; H, 10.59; N, 6.13. Found: C, 76.34; H, 10.73; N, 6.01.

Diazo Decomposition of 5α-Cholestan-3β-yl Diazoacetate. To a stirred solution of Rh_2(5*R*-MEPY)$_4$ (1.0 mg, 0.0011 mmol) in dry CH_2Cl_2 (5 mL) heated at reflux under a nitrogen atmosphere was added diazoacetate **12a** (50.0 mg, 0.110 mmol) in dry CH_2Cl_2 (3 mL) over 5 h via syringe pump. The reaction mixture was heated at reflux for an additional 0.5 h to complete the reaction. After being cooled to room temperature, the reaction mixture was filtered through a short silica plug, which was subsequently washed with 10 mL of 20% ethyl acetate in hexanes. The solvent was removed under reduced pressure to afford 45 mg of product (95% yield) consisting of γ-lactone **13a**, 2-(3β-hydroxy-5α-cholestan-2α-yl)acetic acid lactone; β-lactone **14a**, 3-(3β-hydroxy-5α-cholestan-3α-yl)acetic acid lactone; and γ-lactone **15a**, 4-(3β-hydroxy-5α-cholestan-4α-yl)acetic acid lactone. The relative ratio of products in the crude reaction mixture was determined by ^{1}H NMR spectroscopy. Column chromatography on silica gel (3% ethyl acetate in hexanes) afforded 27 mg of a mixture of 2-(3β-hydroxy-5α-cholestan-2α-yl)acetic acid lactone (**13a**) and 4-(3β-hydroxy-5α-cholestan-4α-yl)acetic acid lactone (**15a**) (90:10 ratio respectively, 58% yield) and 6 mg of 3-(3β-hydroxy-5α-cholestan-3α-yl)acetic acid lactone (**14a**) (13% yield). Using the same procedure, the Rh_2(5*S*-MEPY)$_4$ catalyzed reaction of diazoacetate **12a** afforded 14 mg **13a** and **15a** (13:87 ratio respectively, 30% yield) and 19 mg of (**14a**) (41% yield). The Rh_2(4*S*-MEOX)$_4$ catalyzed reaction of diazoacetate **12a** afforded 12 mg of **13a** and **15a** (9:91 ratio respectively, 26% yield) and 21 mg of (**14a**)-(45% yield).

2-(3β-Hydroxy-5α-cholestan-2α-yl)acetic acid lactone (13a): mp 178−180 °C; $[\alpha]^{28}_D$ = +38.8 (*c* 1.96, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.78 (dt, J = 11.0, 4.0 Hz, 1H), 2.46 (dd, J = 14.1, 4.6 Hz, 1H, lactone α-H_{eq}), 2.17 (t, J = 14.1 Hz, 1H, lactone α-H_{ax}), 2.15−2.08 (comp, 1H), 1.98 (dt J = 12.8, 3.4 Hz, 1H), 1.92 (dd, J = 12.8, 2.9 Hz, 1H), 1.86 (dt, J = 12.0, 3.6 Hz, 1H), 1.84−1.78 (m, 1H), 1.69 (dq, J = 13.2, 3.5 Hz, 1H), 1.62−1.20 (comp, 14H), 1.19−0.83 (comp, 9H), 0.90 (d, J = 6.3 Hz, 3H), 0.89 (s, 3H), 0.87 (d, J = 6.6 Hz, 3H), 0.86 (d, J = 6.6 Hz, 3H), 0.72 (dt, J = 6.6, 2.7 Hz, 1H), 0.66 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.8, 85.6, 56.3, 56.2, 54.3, 45.7, 42.6, 40.4, 40.1, 39.9, 39.5, 37.9, 36.2, 36.1, 35.7, 35.4, 32.8, 32.0, 28.6, 28.2, 28.0, 24.1, 23.8, 22.8, 22.5, 21.4, 18.6, 14.1, 12.1; IR (film) 1799 (C═O) cm^{-1}; HRMS (FAB$^+$) calcd for $C_{29}H_{49}O_2$ 429.3733, found 429.3731 (M^{+1}).

3-(3β-Hydroxy-5α-cholestan-3α-yl)acetic acid lactone (14a): mp 136−138 °C; $[\alpha]^{30}_D$ = +14.0 (*c* 1.34, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.07 (s, 2H, lactone α-H), 2.05 (dt, J = 13.6, 4.2 Hz, 1H), 1.98 (dt. J = 12.7, 3.3 Hz, 1H), 1.93 (t, J = 13.0 Hz, 1H), 1.84 (dt, J = 12.9, 3.6 Hz, 1H), 1.84−1.76 (m, 1H), 1.74 (dq, J = 13.1, 3.1 Hz, 1H), 1.69, (dq, J = 13.2,

3.5 Hz, 1H), 1.69−1.44 (comp, 4H), 1.40−1.20 (comp, 8H), 1.18−0.80 (comp, 11H), 0.90 (d, J = 6.5 Hz, 3H), 0.87 (d, J = 6.6 Hz, 3H), 0.86 (d, J = 6.6 Hz, 3H), 0.85 (s, 3H), 0.65 (s, 3H), 0.63 (ddd, J = 12.3, 10.7, 4.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.5, 79.3, 56.4, 56.2, 54.1, 47.6, 44.6, 42.6, 39.9, 39.5, 38.4, 36.3, 36.1, 35.8, 35.4, 35.3, 32.0, 31.9, 28.5, 28.2, 28.0, 24.2, 23.8, 22.8, 22.5, 21.3, 18.6, 12.1, 11.8; IR (film) 1836 (C=O) cm^{-1}; HRMS (FAB$^+$) calcd for $C_{29}H_{49}O_2$ 429.3733, found 429.3731 (M^{+1}).

4-(3β-Hydroxy-5α-cholestan-4α-yl)acetic acid lactone (15a): mp 117−119 °C; $[\alpha]^{30}_D$ = +0.8 (*c* 0.57, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.77 (ddd, J = 11.8, 10.2, 4.2 Hz, 1H), 2.43 (dd, J = 15.6, 6.0 Hz, 1H, lactone α-H$_{eq}$), 2.09 (t, J = 15.6 Hz, 1H, lactone α-H$_{ax}$), 2.22−1.37 (comp, 10H), 1.36−1.20 (comp, 8H), 1.25 (s, 3H), 1.19−0.92 (comp, 9H), 0.91−0.80 (comp, 2H), 0.89 (d, J = 5.6 Hz, 3H), 0.87 (d, J = 6.6 Hz, 3H), 0.86 (d, J = 6.6 Hz, 3H), 0.71 (dt, J = 11.0, 4.2 Hz, 1H), 0.66 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.0, 85.9, 56.4, 56.2, 54.2, 49.0, 43.9, 42.5, 39.8, 39.5, 36.4, 36.1, 35.8, 35.1, 34.5, 31.5, 29.7, 28.2, 28.0, 26.2, 25.4, 24.2, 23.8, 22.8, 22.6, 21.2, 18.6, 13.5, 12.1; IR (film) 1789 (C=O) cm^{-1}; HRMS (FAB$^+$) calcd for $C_{29}H_{49}O_2$ 429.3733, found 429.3731 (M^{+1}).

5α-Androstan-17-one-3β-yl diazoacetate (12b) was prepared as described for **12a**. To a stirred solution of 5α-androstan-17-on-3β-ol (3.00 g, 10.3 mmol) and triethylamine (15.7 mg, 0.155 mmol) in dry THF (50 mL) at 0 °C was added diketene (1.30 mg, 15.5 mmol). Triethylamine (1.57 mL, 15.5 mmol) and methanesulfonyl azide (1.88 g, 15.5 mmol) were added. Flash column chromatography on silica gel (25% ethyl acetate in hexanes) afforded the diazoacetoacetate in 88% overall yield (3.62 g, 9.03 mmol) as a yellow oil. **5α-Androstan-17-on-3β-yl diazoacetoacetate:** ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.89−4.77 (m, 1H), 2.46 (s, 3H), 2.42 (dd, J = 18.9, 9.0 Hz, 1H), 2.05 (dd, J = 19.0, 9.0 Hz, 1H), 2.00−0.95 (comp, 19H), 0.88 (s, 3H), 0.86 (s, 3H), 0.75 (dt, J = 11.7, 3.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 220.4, 189.7, 160.5, 76.0, 74.6, 53.8, 50.9, 47.3, 44.3, 36.2, 35.4, 35.2, 34.6, 33.7, 31.1, 30.4, 27.9, 27.2, 21.4, 20.1, 13.4, 11.9.

Acetyl cleavage of 5α-androstan-17-on-3β-diazoacetoacetate was performed as previously described by the addition of LiOH monohydrate (0.566 g, 13.5 mmol) to a biphasic solution of the diazoacetoacetate (3.60 g, 8.99 mmol) in THF (30 mL) and distilled water (30 mL). Flash column chromatography on silica gel (25% ethyl acetate in hexanes) afforded 5α-androstan-17-on-3β-yl diazoacetate (**12b**) in 77% yield (2.51 g, 6.97 mmol) as a pale yellow solid: mp 163−165 °C; $[\alpha]^{34}_D$ = +16.6 (*c* 2.53, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.82−4.70 (m, 1H), 4.69 (bs, 1H), 2.42 (dd, J = 19.2, 9.0 Hz, 1H), 2.03 (dd, J = 19.2, 9.0 Hz, 1H), 1.97−1.12 (comp, 17H), 1.05−0.89 (comp, 2H), 0.84 (s, 6H), 0.75 (dt, J = 11.4, 4.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 221.2, 166.4, 74.1, 54.2, 51.3, 47.7, 46.2, 44.6, 36.6, 35.8, 35.6, 35.0, 34.1, 31.5, 30.7, 28.2, 27.6, 21.7, 20.4, 13.8, 12.2; IR (film) 2142 (C=N$_2$), 1720 (C=O), 1657 (C=O) cm^{-1}. Anal. Calcd for $C_{21}H_{30}N_2O_3$: C, 70.36; H, 8.44; N, 7.81. Found: C, 70.48; H, 8.55; N, 7.61.

Diazo Decomposition of 5α-Androstan-17-on-3β-yl Diazoacetate. To a stirred solution of Rh_2(5*R*-MEPY)$_4$ (2.4 mg, 0.0028 mmol) in dry CH_2Cl_2 (5 mL) heated at reflux under a nitrogen atmosphere was added diazoacetate **12b** (100 mg, 0.278 mmol) in dry CH_2Cl_2 (3 mL) over 5 h via syringe pump. The reaction mixture was heated at reflux for an additional 0.5 h to complete the reaction. After being cooled to room temperature, the reaction mixture was filtered through a short silica plug, which was subsequently washed with 10 mL of 30% ethyl acetate in hexanes. The solvent was removed under reduced pressure to afford 84 mg of product (91% yield) consisting of γ-lactone **13b** [2-(3β-hydroxy-5α-androstan-17-on-2α-yl)acetic acid lactone], β-lactone **14b** [3-(3β-hydroxy-5α-androstan-17-on-3α-yl)acetic acid lactone], and γ-lactone **15b** [4-(3β-hydroxy-5α-androstan-17-on-4α-yl)acetic acid lactone]. The relative ratio of products in the crude reaction mixture was determined by ^{1}H NMR spectroscopy. Column chromatography on silica gel (2% ethyl acetate in CH_2Cl_2) afforded 56 mg of a mixture of **13b** and **15b** (95:5 ratio respectively, 61% yield) and 14 mg of **14b** (15% yield). Using the same procedure, the Rh_2(4*S*-MEAZ)$_4$-catalyzed reaction of diazoacetate **12b** afforded 35 mg of **13b** and **15b** (5:95 ratio respectively, 38% yield) and 26 mg of **14b** (38% yield). The Rh_2(4*S*-MEOX)$_4$-catalyzed reaction of diazoacetate **12b** afforded 18 mg of **13b** and **15b** (13:87 ratio respectively, 20% yield) and 42 mg of **14b** (46% yield).

2-(3β-Hydroxy-5α-androstan-17-on-2α-yl)acetic acid lactone (13b): mp 208−210 °C; $[\alpha]^{29}_D$ = +86.8 (*c* 1.74, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.79 (dt, J = 10.9, 3.9 Hz, 1H), 2.47 (dd, J = 14.7, 4.6 Hz, 1H, lactone α-H$_{eq}$), 2.42 (d, J = 9.4 Hz, 1H), 2.18 (t, J = 14.7 Hz, 1H, lactone α-H$_{ax}$), 2.25−1.76 (comp, 7H), 1.72−1.15 (comp, 11H), 1.01 (t, J = 12.2 Hz, 1H), 0.94 (s, 3H), 0.87 (s, 3H), 0.90−0.75 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 220.9, 176.6, 85.3, 54.4, 51.2, 47.7, 45.7, 40.4, 40.1, 38.0, 36.1, 35.8, 34.9, 32.7, 31.4, 30.8, 28.2, 21.7, 20.6, 14.1, 13.8; IR (film) 1777 (C=O), 1732 (C=O) cm^{-1}; HRMS (FAB$^+$) calcd for $C_{21}H_{31}O_3$ 331.2273, found 331.2278 (M^{+1}).

3-(3β-Hydroxy-5α-androstan-17-on-3α-yl)acetic acid lactone (14b): mp 145−147 °C; $[\alpha]^{30}_D$ = +72.4 (*c* 1.59, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.08 (s, 2H, lactone α-H), 2.46 (dd, J = 19.2, 8.9 Hz, 1H), 2.16−1.72 (comp, 7H), 1.71−1.43 (comp, 4H), 1.42−1.18 (comp, 5H), 0.89 (s, 3H), 0.87 (s, 3H), 1.17−0.79 (comp, 4H), 0.72 (dt, J = 12.0, 8.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 221.0, 168.3, 79.0, 54.1, 51.3, 47.7, 47.6, 44.6, 38.3, 36.2, 35.6, 34.9, 31.9, 31.4, 30.7, 29.7, 28.2, 21.8, 20.5, 13.8, 11.8; IR (film) 1824 (C=O), 1738 (C=O) cm^{-1}; HRMS (FAB$^+$) calcd for $C_{21}H_{31}O_3$ 331.2273, found 331.2277 (M^{+1}).

4-(3β-Hydroxy-5α-androstan-17-on-4α-yl)acetic acid lactone (15b): mp 136−138 °C; $[\alpha]^{30}_D$ = +31.3 (*c* 0.98, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.79 (ddd, J = 11.8, 10.2, 4.2 Hz, 1H), 2.47 (dd, J = 16.0, 6.5 Hz, 1H, lactone α-H$_{eq}$), 2.53−2.44 (comp, 1H), 2.16 (t, J = 15.8 Hz, 1H, lactone α-H$_{ax}$), 2.17−0.90 (comp, 19H), 0.93 (s, 3H), 0.87 (s, 3H), 0.81 (dt, J = 12.0, 4.2, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 220.9, 176.7, 85.7, 54.2, 51.3, 48.9, 47.7, 43.8, 37.4, 36.3, 35.7, 34.6, 34.4, 31.4, 30.3, 26.2, 25.1, 21.7, 20.5, 13.8, 13.6; IR (film) 1786 (C=O), 1734 (C=O) cm^{-1}; HRMS (FAB$^+$) calcd for $C_{21}H_{31}O_3$ 331.2273, found 331.2269 (M^{+1}).

5α-Cholestan-6-on-3β-yl Diazoacetate (16). To a stirred solution of 5α-cholestan-6-on-3β-ol (1.00 g, 2.48 mmol) and triethylamine (2.5 mg, 0.25 mmol) in dry THF (10 mL) at 0 °C was added diketene (0.313 g, 3.72 mmol). Triethylamine (0.377 g, 3.72 mmol) and methanesulfonyl azide (0.451 g, 3.72 mmol) were added. Flash column chromatography on silica gel (25% ethyl acetate in hexanes) afforded diazoacetoacetate in 59% overall yield (0.755 g, 1.47 mmol) as a yellow solid. **5α-Cholestan-6-on-3β-yl diazoacetatoacetate:** ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.89−4.76 (m, 1H), 2.47 (s, 3H), 2.39−2.25 (comp, 2H), 2.10−0.96 (comp, 27H), 0.91 (d, J = 6.3 Hz, 3H), 0.87 (d, J = 6.6 Hz, 3H), 0.86 (d, J = 6.6 Hz, 3H), 0.79 (s, 3H), 0.67 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.9, 189.8, 160.6, 74.2, 56.4, 56.1, 55.8, 53.4, 46.3, 42.7, 42.6, 40.6, 39.2, 39.1, 37.6, 36.0, 35.8, 35.4, 28.0, 27.8, 27.7, 26.8, 26.1, 23.7, 23.5, 22.6, 22.3, 21.2, 18.4, 12.8, 11.7.

Acetyl cleavage of 5α-cholestan-6-on-3β-yl diazoacetoacetate was performed as previously described by the addition of LiOH monohydrate (0.141 g, 2.93 mmol) to a biphasic solution of the diazoacetoacetate (0.752 g, 1.47 mmol) in THF (8 mL) and distilled water (8 mL). Flash column chromatography on silica gel, (25% ethyl acetate in hexanes) afforded 5α-cholestan-6-on-3β-yl diazoacetate (**16**) in 80% yield (0.546 g, 1.17 mmol) as a pale crystalline yellow solid: mp 166−168 °C; $[\alpha]^{25}_D$ = −4.6 (*c* 0.34, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.83−4.66 (m, 1H), 4.71 (bs, 1H), 2.38−2.22 (comp, 2H), 2.10−0.96 (comp, 27H), 0.91 (d, J = 6.3 Hz, 3H), 0.87 (d, J = 6.6 Hz, 3H), 0.86 (d, J = 6.6 Hz, 3H), 0.77 (s, 3H), 0.66 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.3, 166.3, 73.4, 56.6, 56.4, 56.0, 53.7, 46.6, 46.3, 42.9, 40.9, 39.4, 39.5, 37.9, 36.3, 36.0, 35.6, 28.0, 27.9, 27.0, 26.3, 23.9, 23.7, 22.8, 22.5, 21.4, 18.6, 13.0, 11.9; IR (film) 2109 (C=N$_2$), 1709 (C=O), 1689 (C=O) cm^{-1}. Anal. Calcd for $C_{29}H_{46}N_2O_3$: C, 74.00; H, 9.85; N, 5.95. Found: C, 73.80; H, 9.83; N, 5.69.

Diazo Decomposition of 5α-Cholestan-6-on-3β-yl Diazoacetate (16). To a stirred solution of Rh_2(5*R*-MEPY)$_4$ (0.9

mg, 0.0011 mmol) in dry CH_2Cl_2 (5 mL) heated at reflux under a nitrogen atmosphere was added diazoacetate **16** (50.0 mg, 0.107 mmol) in dry CH_2Cl_2 (3 mL) over 5 h via syringe pump. The reaction mixture was heated at reflux for an additional 0.5 h to ensure completion of the reaction. After cooling to room temperature, the reaction was filtered through a short silica plug, which was subsequently washed with 10 mL of 35% ethyl acetate in hexanes. The solvent was removed under reduced pressure to afford 43 mg of product (90% yield) consisting of γ-lactone **17** [2-(3β-hydroxy-5α-cholestan-6-on-2α-yl)acetic acid lactone] and β-lactone **18** [3-(3β-hydroxy-5α-cholestan-6-on-3β-yl)acetic acid lactone]. The relative ratio of products in the crude reaction mixture was determined by ^{1}H NMR spectroscopy. Column chromatography on silica gel (2% ethyl acetate in CH_2Cl_2) afforded 20 mg of **17** and 12 mg of **18** (25% yield). The $Rh_2(4S\text{-MEOX})_4$ catalyzed reaction of diazoacetate **12** afforded 35 mg of **18** (74% yield). 4-(3β-Hydroxy-5α-cholestan-6-on-4α-yl)acetic acid lactone did not form to an appreciable extent in any decomposition.

2-(3β-Hydroxy-5α-cholestan-6-on-2α-yl)acetic acid lactone (17): mp 173−176 °C; $[\alpha]^{31}_D = +3.3$ (*c* 1.25, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.78 (ddd, *J* = 11.8, 10.8, 3.9 Hz, 1H), 2.51 (dd, *J* = 15.4, 5.8 Hz, 1H, lactone α-H_{eq}), 2.39−2.32 (comp, 2H), 2.23 (t, *J* = 15.4 Hz, 1H, lactone α-H_{ax}), 2.24−1.72 (comp, 6H), 1.62−1.04 (comp, 19H), 1.00 (q, *J* = 9.1 Hz, 1H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 6.7 Hz, 3H), 0.86 (d, *J* = 6.7 Hz, 3H), 0.85 (s, 3H), 0.67 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.1, 176.1, 84.8, 57.3, 56.6, 56.1, 53.9, 46.5, 43.0, 42.9, 39.9, 39.6, 39.5, 39.4, 37.6, 36.0, 35.8, 35.7, 29.7, 28.0, 25.4, 23.9, 23.8, 22.8, 22.5, 21.6, 18.6, 14.7, 12.0; IR (film) 1806 (C═O), 1709 (C═O) cm^{-1}; HRMS (FAB$^+$) calcd for $C_{29}H_{47}O_3$ 443.3525, found 443.3523 (M^{+1}).

3-(3β-Hydroxy-5α-cholestan-6-on-3α-yl)acetic acid lactone (18): mp 158−160 °C; $[\alpha]^{30}_D = -8.3$ (*c* 0.93, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.07 (d, *J* = 15.8 Hz, 1H, lactone α-H), 3.01 (d, *J* = 15.8 Hz, 1H, lactone α-H), 2.37 (dd, *J* = 13.4, 4.5 Hz, 1H), 2.15−2.02 (comp, 3H), 1.96 (t, *J* = 12.8 Hz, 1H), 1.95−1.76 (m, 4H), 1.65−1.47 (comp, 4H), 1.45−1.04 (comp, 15H), 0.99 (q, *J* = 9.1 Hz, 1H), 0.91 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 3H), 0.81 (s, 3H), 0.67 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.1, 167.5, 78.8, 56.7, 56.2, 56.1, 53.7, 47.2, 46.5, 43.0, 40.8, 39.5, 39.4, 37.8, 36.1, 35.9, 35.7, 31.4, 30.6, 29.7, 28.0, 24.0, 23.8, 22.8, 22.5, 21.5, 18.6, 12.7, 12.0; IR (film) 1842 (C═O), 1710 (C═O) cm^{-1}; HRMS (FAB$^+$) calcd for $C_{29}H_{49}O_2$ 443.3525, found 443.3523 (M^{+1}).

Preparation of 5-Cholesten-3β-yl Phenyldiazoacetate (21). To a stirred solution of cholesterol (4.0 mL, 10 mmol) and triethylamine (2.2 mL, 11 mmol) in freshly distilled CH_2Cl_2 (50 mL) at 0 °C under an argon atmosphere was added phenylacetyl chloride (1.5 mL, 16 mmol) via syringe pump over 10 min. After being stirred at 0 °C for 1 h, the reaction mixture was warmed to room temperature and stirred overnight. The reaction mixture was diluted with CH_2Cl_2 (200 mL) and extracted with 10% aqueous HCl (2 × 50 mL), water (25 mL), and brine (25 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Purification by column chromatography on silica gel (0−7.5% ethyl acetate in hexanes) afforded 3.4 g (6.7 mmol, 64% yield) of **5-cholesten-3β-yl phenylacetate:** ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39−7.22 (comp, 5H), 5.39−32 (m, 1H), 4.65−4.56 (m, 1H), 3.59 (s, 2H), 2.33−2.26 (comp, 2H), 2.05−1.76 (comp, 6H), 1.62−0.87 (comp, 20H), 1.01 (s, 3H), 0.91 (d, *J* = 6.5 Hz, 3H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.67 (s, 3H).

To a stirred solution of 5-cholesten-3β-yl phenylacetate (3.4 g, 6.7 mmol) and 4-acetamidobenzenesulfonyl azide (1.8 g, 7.7 mmol) in HPLC grade acetonitrile (50 mL) at 0 °C under an argon atmosphere was added DBU (2.0 mL, 13.4 mmol) portion wise. The reaction mixture was warmed to room temperature and stirred overnight. The reaction mixture was concentrated under reduced pressure, dissolved with ethyl acetate (100 mL), washed with saturated aqueous NH_4Cl (3 × 15 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Purification by column chromatography (0−10% ethyl acetate in hexanes) afforded 2.7 g (5.3 mmol, 80% yield) of phenyldiazoacetate **21** as a yellow solid: mp 129−131 °C; $[\alpha]^{25}_D = -11.0$ (*c* = 0.95 in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.6 Hz, 2H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.16 (t, *J* = 7.6 Hz, 1H), 5.42−5.36 (m, 1H), 4.43−4.23 (m, 1H), 2.47−2.32 (comp, 2H), 2.05−1.77 (comp. 6H), 1.71−0.80 (comp, 20H), 1.03 (s, 3H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 3H), 0.68 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.4, 139.4, 128.8, 125.7, 125.5, 123.8, 122.8, 74.7, 63.3, 56.6, 56.1, 50.0, 42.2, 39.7, 39.5, 38.3, 36.9, 36.5, 36.3, 35.8, 31.9, 31.8, 28.2, 28.0, 27.9, 24.2, 23.8, 22.8, 22.5, 21.0, 19.3, 18.7, 11.8; IR (film, cm^{-1}) 2087 (C═N_2) and 1705 (C═O). Anal. Calcd for $C_{35}H_{50}N_2O_2$: C, 79.2; H, 9.49. Found: C, 79.31; H, 9.56.

Diazo Decomposition of 5-Cholesten-3β-yl Phenyldiazoacetate. The procedure for the diazo decomposition of **21** with $Rh_2(OAc)_4$ is representative. To a stirred solution of $Rh_2(OAc)_4$ (2.1 mg, 0.0047 mmol) in dry CH_2Cl_2 (5 mL) heated at reflux under an argon atmosphere was added phenyldiazoacetate **2** (250 mg, 0.47 mmol) in dry CH_2Cl_2 (3 mL) over 2 h via syringe pump. The reaction mixture was heated at reflux for an additional 30 min upon completion of the addition. After cooling to room temperature, the reaction was filtered through a short silica plug, which was subsequently washed with 10 mL of 25% ethyl acetate in hexanes. The solvent was removed under reduced pressure to afford 239 mg (quantitative) of the crude product as an off-white crystalline solid. ^{1}H NMR analysis of the reaction mixture revealed 3-(3β-hydroxy-5-cholesten-3α-yl)-2-phenylacetic acid lactones (**22** and **23**) was 68% of the reaction mixture as a mixture of diastereomers. Column chromatography on silica gel (eluent: 5% ethyl acetate in hexanes) afforded 149 mg (63%) of 3-(3β-hydroxy-5-cholesten-3αyl)-2-phenylacetic acid lactones (**22** and **23**) as a crystalline white solid, the diastereomer ratio of which was determined by ^{1}H NMR (600 MHz) to be 22:78. Isolation of analytical samples of β-lactones **22** and **23** was achieved by (silica gel loading ratio 100:1, eluent: 1−2% ethyl acetate in hexanes) to afford each as a white solid film.

3-(3β-Hydroxy-5-cholesten-3α-yl)-2*S*-phenylacetic acid lactone (22): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37−7.30 (comp, 3H), 7.16 (dd, *J* = 8.0, 1.7 Hz, 2H), 5.63−5.59 (m, 1H), 4.46 (s, 1H, α-H β-lactone), 3.05 (dddd, *J* = 13.3, 2.6, 2.6, 2.4 Hz, 1H, C4−H_{ax}), 2.15 (dd, *J* = 13.3, 2.8 Hz, 1H, C4−H_{eq}), 2.12−2.04 (m, 1H), 1.98 (ddd, *J* = 18.5, 13.9, 4.7 Hz, 1H, C2−H_{ax}), 1.96−1.91 (m, 1H), 1.88−1.80 (m, 1H), 1.80−1.74 (m, 1H, C2−H_{eq}), 1.70−0.95 (comp, 19H), 1.01 (s, 3H), 0.89 (d, *J* = 6.6 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 3H), 0.73 (ddd, *J* = 16.0, 12.2, 4.7 Hz, 1H), 0.66 (s, 3H), 0.40 (ddd, *J* = 18.3, 14.0, 4.3 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.7, 138.7, 130.9, 129.5, 128.6, 128.2, 124.2, 83.8, 63.6, 56.6, 56.2, 50.4, 44.6, 42.3, 39.5, 36.2, 35.7, 35.2, 32.1, 31.9, 29.7, 28.2, 28.0, 27.9, 24.3, 23.8, 22.8, 22.6, 21.0, 19.2, 18.7, 11.8; IR ($CDCl_3$) 1816 (C═O) cm^{-1}; HRMS (FAB$^+$) calcd for $C_{35}H_{51}O_2$ 503.3889, found 503.3889 (M^{+1}).

3-(3β-Hydroxy-5-cholesten-3α-yl)-2*R*-phenylacetic acid lactone (23): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33−7.25 (comp, 3H), 7.15 (dd, *J* = 8.3, 1.5 Hz, 2H), 4.48 (s, 1H, α-H β-lactone), 4.13−4.09 (m, 1H), 2.66 (dddd, *J* = 13.8, 2.9, 2.8, 2.5 Hz, 1H, C4−H_{ax}), 2.30 (dddd, *J* = 17.1, 14.2, 3.9, 1.0 Hz, 1H, C2−H_{ax}), 2.15 (dd, *J* = 13.8, 2.8 Hz, 1H, C4−H_{eq}), 2.07−1.99 (comp, 2H), 1.96 (dddd, *J* = 12.9, 3.3, 3.2, 3.2 Hz, 1H, C2−H_{eq}), 1.85−1.76 (m, 1H), 1.70−1.63 (m, 1H), 1.56−1.05 (comp, 18H), 1.04−0.85 (comp, 3H), 0.99 (s, 3H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.87 (d, *J* = 6.7 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 3H), 0.81 (ddd, *J* = 16.6, 11.9, 5.2 Hz, 1H), 0.64 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.6, 135.7, 130.8, 129.6, 128.1, 128.0, 124.0, 82.8, 63.8, 56.6, 56.2, 50.2, 42.3, 39.7, 39.5, 38.1, 36.4, 36.2, 36.1, 35.7, 33.8, 31.9, 31.7, 28.2, 28.0, 24.2, 23.8, 22.8, 22.5, 21.1, 19.2, 18.7, 11.8; IR ($CDCl_3$) 1817 (C═O) cm^{-1}; HRMS (FAB$^+$) calcd for $C_{35}H_{51}O_2$ 503.3889, found 503.3889 (M^{+1}).

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supply of Rh_2(*S*-DOSP)$_4$. Professor M. Anthony McKervey suggested to us the value of investigations of insertion reactions with steroidal systems.

Supporting Information Available: The methodology used for stereochemical assignments of C−H insertion products and $^1H/^{13}C$ spectra for **9**, **10**, **13a**, **14a**, **15a**, **13b**, **14b**, **15b**, **17**, **18**, **22**, and **23**. This material is available free of charge via the Internet at http://pubs.acs.org.

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