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# Bicyclo[3.1.0]hexanes from sugar-derived diazo compounds and iodonium ylides. Diastereocontrol and synthetic applications

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**Abstract**—The CuI and $Rh_2(OAc)_4$ catalyzed decomposition of ethyl 2-diazo-4,5-isopropylidenedioxy-3-oxo-6-heptenoate results in intramolecular cyclopropanation products with opposite diastereoselectivity. In contrast, decomposition of the respective iodonium ylide can proceed without catalysts to give the cyclopropanation products with diastereoselectivity unchangeable by the presence of CuI and $Rh_2(OAc)_4$, revealing thus, that in this particular case the reaction is an electrophilic addition of the iodonium center to the double bond. The synthetic importance of these reactions has been demonstrated by preparing a number of precursors of cyclopentyl, cyclopropyl and bicyclo[3.1.0]hexyl antiviral carbocyclic nucleosides. 

## 1. Introduction

Carbocyclic nucleosides have been widely studied as potential antiviral and antitumor agents,[1] and among them, those with cyclopentyl, cyclopropyl or bicyclo[3.1.0]hexyl sugar parts, such as aristeromycin (**1**),[2] nucleoside A-5021 (**2**)[3] and the nitrobenzylthioinosine analog of neplanocin C **3**,[4] exhibiting significant antiviral activity, have attracted considerable attention (Fig. 1). It is most likely that the sugar moiety of these and related nucleosides could be prepared from hydroxylated bicyclo[3.1.0]hexane derivatives **4** with the proper absolute configuration, as common precursors. Nucleophilic opening of the cyclopropane ring would lead to hydroxylated cyclopentanoids and therefore to cyclopentyl nucleosides, whereas reduction of the ketone and ester groups would give products, with the bicyclo[3.1.0]hexane skeleton retained, which are precursors of **3** and related nucleosides. Finally, glycolic cleavage of the cyclopentane ring would result in precursors of cyclopropyl nucleosides, such as **2**. Furthermore, compounds of the general structure **4** are potential precursors of several classes of natural products and synthetic analogs (prostanoids, cyclitols, aminocyclitols). It is, consequently, highly desirable to synthesize bicyclo[3.1.0]hexanes **4**, in enantiomerically pure form and the intramolecular cyclopropanation of sugar derived chiral diazo compounds and iodonium ylides is an attractive approach.

Although there is little doubt about the mechanism of the metal-catalyzed decomposition of diazo compounds, which proceeds most probably via a metallo-carbenoid intermediate,[5] the mechanism of metal-initiated iodonium ylide decomposition towards cyclopanation products is a field of controversy. Moriarty et al.[6] who first investigated such CuCl-catalyzed intramolecular cyclopropanations of iodonium ylides, have suggested a stepwise electrophilic addition of the iodonium center to the double bond, followed by reductive elimination of iodobenzene to afford the cyclopropane ring. Recently, however, Müller et al.[7] observed a substantial degree of asymmetric induction in Cu-catalyzed intramolecular cyclopropanations of some iodonium ylides, which is consistent with a carbenoid mechanism.

In this paper,[8] we describe the diastereoselectivity of the metal-catalyzed intramolecular cyclopropanations of some chiral sugar derived unsaturated diazo compounds and iodonium ylides. Furthermore, we have demonstrated their synthetic potential by using the cyclopropanation products to prepare the sugar part of some cyclopentyl, cyclopropyl and bicyclo[3.1.0]hexyl carbocyclic nucleosides.

## 2. Results and discussion

Treatment of iodide **5** (Scheme 1), easily accessible from D-ribose in two steps,[9] with activated Zn in ethanol afforded pentenal **6** in 95% yield.[10] Because of the partial epimerization to *epi*-**6** (Fig. 2), upon standing or in the chromatography column, this aldehyde was directly converted to the ketoester **7** (76% yield), by slow addition of a

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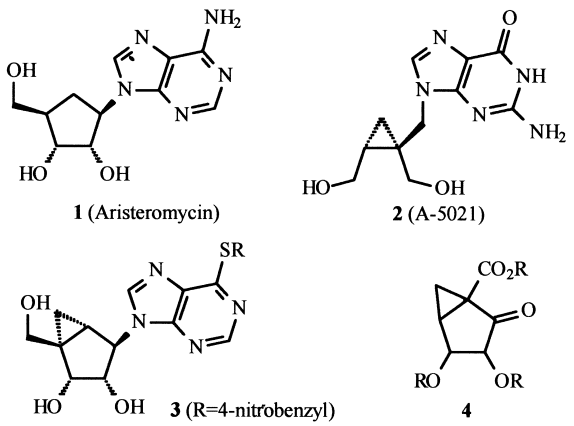


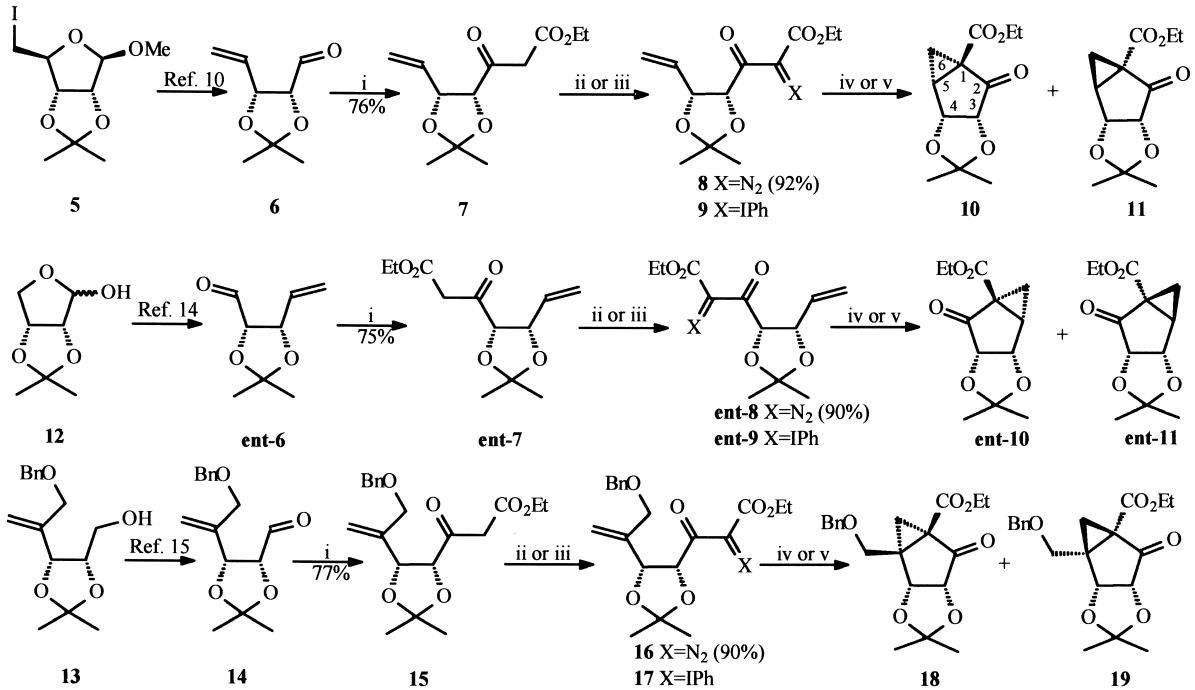

**Figure 1.**

methylene chloride solution of **6** to ethyl diazoacetate[11] at 0°C, in the presence of dry $SnCl_2$. These reaction conditions should be strictly applied, since the presence of moisture and elevated temperatures dramatically decrease the yield of **7**, leading to the formation of a mixture of the two epoxides **20** as main products, the stereochemistry of which was not completely assigned; *epi*-**7** was also isolated (Fig. 2). Under the above mentioned reaction conditions, the epimerization of **7** was totally suppressed, whereas the epoxides **20** were the normal side-products (yield ~10%).

Compound **7** was then converted to the diazo compound **8** (92%) and the respective iodonium ylide **9**, by standard procedures.[12,13] The ylide, found to be unstable on attempted isolation, was further used without characterization. Refluxing of **8** in toluene with a 5% molar ratio of CuI for 3 h, gave a mixture of the cyclopropanation products **10** and **11**, which were easily separated chromatographically (81%, **10/11**=4.5:1 diastereoisomeric ratio). However, when $Rh_2(OAc)_4$ was employed as a catalyst, diazo compound **8** was decomposed in 1.5 h to the same cyclopropanation products, but with opposite diastereoselectivity (74%, **10/11**=1:3 diastereoisomeric ratio). Iodonium ylide **9**, in turn, was decomposed within 30 min, in methylene chloride solution at 20°C, under an argon atmosphere, to give again **10** and **11**, in moderate yield and a slight preference of **11** (45% from **7**, **10/11**=1:1.5 diastereoisomeric ratio). Surprisingly, both CuI and $Rh_2(OAc)_4$ gave the same yield and diastereoselectivity, and we also found that this reaction proceeds smoothly even without the presence of any catalyst to give similar results.

It is worth mentioning that the enantiomers *ent*-**10** and *ent*-**11** were prepared by the same reaction sequence, starting from aldehyde *ent*-**6**, which is readily available from the naturally abundant D-arabinose, via the protected D-erythrose[14] (Scheme 1), obviously with the same diastereoselection outcome. From a synthetic point of view, it is interesting that all isomers **10**, *ent*-**10**, **11** and *ent*-**11** could be selectively built by starting from the proper pentenal **6** or *ent*-**6**, preparing the right intermediate diazo compound or iodonium ylide and choosing the appropriate catalyst.

Applying an analogous pathway, diazo compound **16** was synthesized from **13**, which in turn was prepared from L-ribulose according to the literature,[15] by Swern oxidation and addition of the resulting unsaturated aldehyde **14** to ethyl diazoacetate, as discussed above to give the ketoester **15** in 76% yield (68% overall). Further treatment




**Scheme 1.** *Reagents and conditions*: (i) $N_2CHCO_2Et$, $SnCl_2$, $CH_2Cl_2$, 0°C, 2 h. (ii) $TsN_3$, $Et_3N$, EtOH, 20°C, 12 h. (iii) $PhI(OAc)_2$, KOH (4 equiv.), EtOH, −5°C, 30 min. (iv) CuI, toluene, reflux, 3 h for diazo compounds or CuI, $CH_2Cl_2$, 20°C, $N_2$, 30 min for iodonium ylides (for iodonium ylides see also text). (v) $Rh_2(OAc)_2$, toluene, reflux, 1.5 h for diazo compounds or $Rh_2(OAc)_2$, $CH_2Cl_2$, 20°C, $N_2$, 30 min for iodonium ylides (for yields see text).

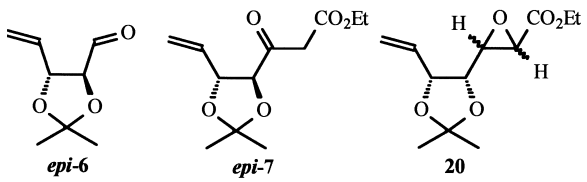



**Figure 2.**

of **15** with $TsN_3$ and $Et_3N$ afforded **16** (90%). Unfortunately, we failed to prepare the iodonium ylide **17**, following the known methods,[15] possibly because the enolate generated from **15** is sterically hindered, not allowing the approach of the $PhI(OAc)_2$ species and compound **15** was quantitatively epimerized to 4-*epi*-**15**. Decomposition of **16** by $Rh_2(OAc)_4$ in refluxing toluene for 2.5 h, afforded compound **19** exclusively in 58% isolated yield, while the use of CuI or CuCl as catalysts favored the formation of **18** (**18/19**=2:1 and 1.7:1 diastereoisomeric ratios, respectively) in moderate isolated yields (28 and 43%, respectively). The bulkier $Cu(OSO_2CF_3)$ also catalyzed the same reaction (54% yield), favoring slightly the formation of **19** (diastereoisomeric ratio 1:1.6). No reaction was observed when CuI was used as a catalyst and the mixture was refluxed in lower boiling point solvents (e.g. THF, methylene chloride).

The configurations of the newly formed stereocenters in **10**, *ent*-**10**, **11**, *ent*-**11**, **18**, **19** were deduced from the $^1H$ NMR coupling constants and the observed NOE enhancements. It has been demonstrated[16] that the bicyclo[3.1.0]-hexane system adopts boat-like conformations, with such $H_4-C_4-C_5-H_5$ dihedral angles (Scheme 1), which result in $J_{4,5}\sim0$ and $\sim4$ Hz, when the 4-H and 5-H have a *trans*- or *cis*-disposition, respectively. In compound **10**, the 4-H signal appeared at $\delta$ 5.04 as a ddd with $J_{3,4}$=8.0 Hz, $J_{4,5}$=5.5 Hz and $J_{4,6exo}$=1.1 Hz, whereas in compound **11** the 4-H resonance appeared at $\delta$ 4.30 as a dd with $J_{3,4}$=4.9 Hz and $J_{4,6exo}$=1.6 Hz, data which match perfectly with the assigned structures. Furthermore, the strong signal enhancement of both 3-H and 5-H protons, when irradiating the 4-H signal, unequivocally confirms the configuration proposed.

The structure discrimination of compounds **18** and **19** was based on NOE experiments, since the 5-H is lacking and the coupling constants could not be useful. For compound **18**, the 3-H and 4-H signals appeared at $\delta$ 4.42 (d, $J_{3,4}$=8.2 Hz) and 5.17 (dd, $J_{3,4}$=8.2 Hz and $J_{4,6exo}$=1.6 Hz), respectively, while the 6-$H_{endo}$ and 6-$H_{exo}$ protons resonanced at $\delta$ 1.87 (d, $J_{gem}$=5.5 Hz) and 2.10 (dd, $J_{gem}$=5.5 Hz and $J_{4,6exo}$=1.6 Hz), respectively. Similarly, in compound **19**, the 3-H and 4-H signals appeared at $\delta$ 4.81 (d, $J_{3,4}$=5.0 Hz) and 4.34 (dd, $J_{3,4}$=5.0 Hz and $J_{4,6exo}$=1.6 Hz), respectively, while the 6-$H_{endo}$ and 6-$H_{exo}$ protons resonanced at $\delta$ 1.36 (d, $J_{gem}$=6.0 Hz) and 2.20 (dd, $J_{gem}$=6.0 Hz and $J_{4,6exo}$=1.6 Hz), respectively. Whereas no appreciable enhancement to the signals of 6-$H_{endo}$ or 6-$H_{exo}$ protons appeared when irradiating the 3-H or 4-H signals in compound **18**, a strong signal enhancement of the 6$_{endo}$-H in compound **19** ($\delta$ 1.29) was observed upon saturation of both 3-H or 4-H protons, revealing thus indirectly the configuration of the newly formed stereocenters in compounds **18** and **19**.

The variation of diastereoselectivities observed should originate in the different reaction mechanisms followed by diazo compounds and iodonium ylides, under the applied conditions: the metal-catalyzed decomposition of diazo compounds proceeds most probably via a metallo-carbenoid intermediate,[5] whereas the iodonium ylide decomposition is, in our particular case, a stepwise electrophilic addition of the iodonium center to the double bond, as proposed by Moriarty,[6] with possible formation of intermediates like **I-1** or **I-2** (Fig. 3). Further reductive elimination of iodobenzene affords the cyclopropane ring. Since the decomposition reaction of iodonium ylide is independent of the catalyst used (or not), being completed at the same time (within 30 min) and giving the same results, regarding yields and diastereoselectivity, it is apparent that the metal is not coordinated with these intermediates. Furthermore, **I-1** leading to the formation of **10**, looks less favored compared to **I-2**, because of the stronger interactions of the bulkier iodophenyl group with one methyl of the acetonide group in **I-1** than the respective ones of the ethoxycarbonyl group in **I-2**.

Comparing the results reported by Moriarty[6] and Müller[7] with our present observations, it can be suggested that the intramolecular cyclopropanations of iodonium ylides do not follow a single and unified mechanism. Depending upon the reaction conditions (solvent, temperature, catalyst) and the nature of the substrate a stepwise electrophilic addition of the iodonium center to the double bond or the formation of metallo-carbenoid intermediate can occur. It seems possible, that in our particular case the *cis*-geometry of the dioxolane ring might be crucial, placing both the double bond and the iodonium center in close proximity, and thus favoring the stepwise mechanism.

Regarding the decomposition of diazo compounds, it is generally accepted that the metallo-carbenoids intermediately formed preserve their structural integrity during the addition to the double bond.[5] Thus, in the $Rh_2(OAc)_4$ catalyzed cyclopropanation of **8** the transition state **TS-1** (R=H) leading to the formation of **10**, is destabilized by the interactions of the bulk Rh(II) species with the acetonide group, compared to those of the ethoxycarbonyl group in **TS-2** (R=H). When CuI was the catalyst, the interactions of the ethoxycarbonyl group in **TS-2** (R=H) with the acetonide

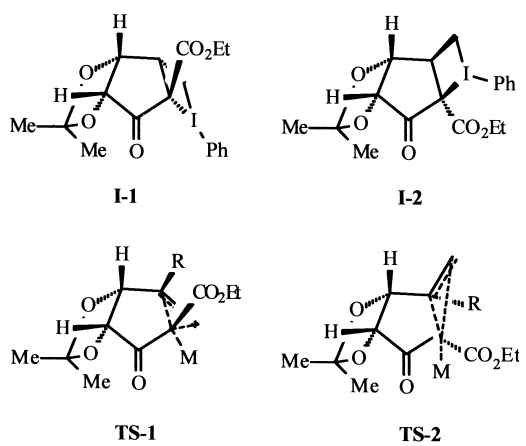



**Figure 3.**

group predominate over those of the smaller atom of Cu with the acetonide. The **TS-1** is further destabilized when R=$CH_2OBn$, as in the case of decomposition of **16**, by an additional repulsion between the R and the $CO_2Et$ groups. It is also possible that the Lewis acidic copper coordinates to one of the acetonide oxygens, thus directing the stereochemistry through **TS-1**. This pathway would not be open to the coordinatively saturated rhodium carbenoid.

The hydroxylated bicyclo[3.1.0]hexane derivatives prepared could serve as excellent precursors of carbocyclic nucleosides. To demonstrate this possibility, compounds **10**, **11** and **19** were further subjected to a number of synthetic transformations.

The reduction of **10** with $NaBH_4$ or $LiAlH_4$ was highly stereoselective, affording compounds **21** and **22**, respectively, as the sole products, in good yields (Fig. 4). Similarly, the protected tetrol **23** was stereoselectively prepared by reduction of **11** with $LiAlH_4$. Compound **21** was also reduced to **22** upon treatment with $LiAlH_4$ in high yield. The configuration of the newly formed C-2 center was easily deduced in all cases by NOE experiments and the coupling constant between the 2-H and 3-H protons. For example, the 2-H proton of compound **21** appeared at $\delta$ 5.00 as a doublet with $J_{2,3}$=6.8 Hz, a coupling constant, which indicates a *cis*-disposition of the 2-H and 3-H protons, taking into account the boat-like conformation of the bicyclo[3.1.0]hexane system. In addition, irradiation of the 2-H proton caused a significant enhancement of the 3-H signal, leaving little doubt about the configuration of the C-2 center.

The importance of these tetrols becomes evident when comparing the structure of nucleoside **3** (Fig. 1) with that of *ent*-**22** (accessible from *ent*-**10**), which has the correct configuration to be transformed into **3**, apparently making our method convenient for the synthesis of this type of nucleoside.

Attempted decarboxylations of compounds **10**, **11** and **19** with preservation of the cyclopropane ring were less successful. Thus, prolonged heating of **11** with DMSO/$H_2O$/NaCl[17] at 160°C gave the desired ketone **24** (Fig. 4), but only in 18% yield. On the contrary, compound **10**, under the same reaction conditions, underwent a further cyclopropane ring cleavage to give the cyclopentanone **25**, also in low yield (23%), whereas conventional hydrolysis of **19** with NaOH in THF/$H_2O$ afforded again low yields (25%) of the acid **26**.

In contrast, treatment of the cyclopropanation products **10**, **11** and **19** with PhSH in *t*-BuOK/*t*-BuOH, led to cyclopropane ring cleavage and formation of the β-keto esters **27**–**29**, respectively, in high yields (Scheme 2). Subsequent decarboxylation of these β-keto esters afforded good overall yields of cyclopentanoids **30**–**32**, direct precursors of cyclopentane nucleosides, as the thiophenyl group can be easily transformed to a hydroxyl group via a Pummerer oxidation.[18] It is interesting to note that while β-keto esters **28** and **29**, exist exclusively as enols, compound **27** is a keto/enol mixture (~2:3 ratio), apparently because the ethoxycarbonyl group in the keto form of **28**

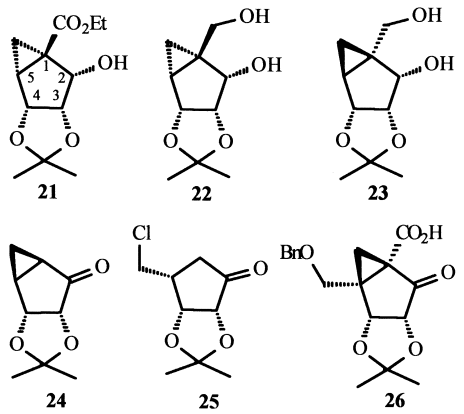
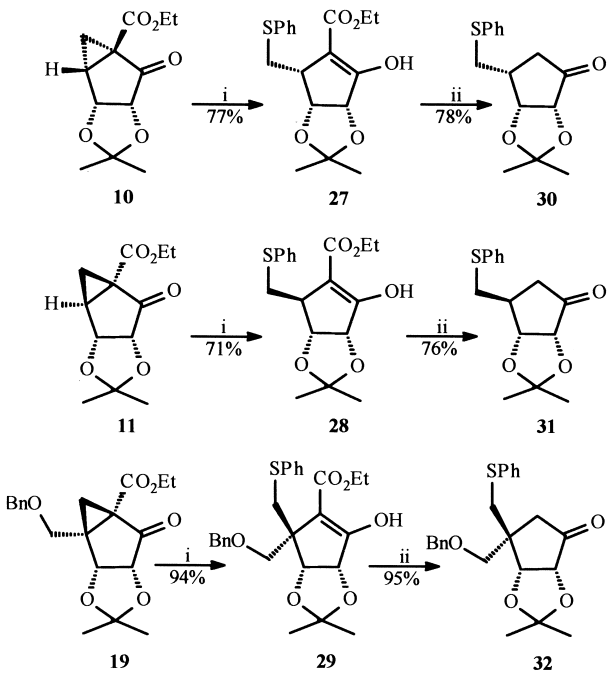



**Figure 4.**

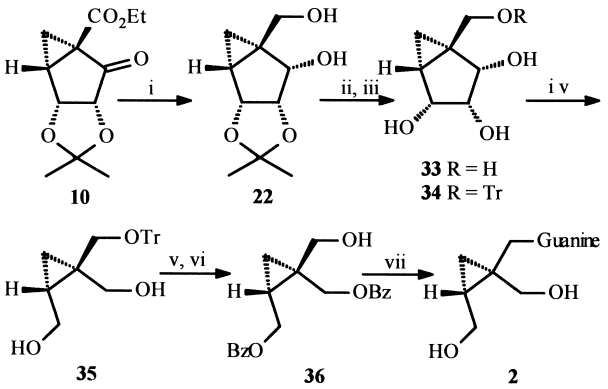
and **29** is more sterically hindered than that of **27**. In the last case, this group adopting a *trans*-disposition to the all-*cis* other substituents minimizes the steric interactions.

Cyclopropane nucleoside A-5021 (**2**)—recently reported by Tsuji et al.[3]—and related nucleosides as well, could also be accessible, using cyclopropanation products **10**, *ent*-**10**, **11** and *ent*-**11** as intermediates. Derivative **2**, along with some 5-substituted uracil analogs,[9] exhibits extraordinary activity against HSV-1 and VZV, being superior and more selective than acyclovir. It becomes evident when comparing the structure of **2**, **10**, *ent*-**10**, **11** and *ent*-**11**, that the configuration of the two chiral centers of the cyclopropane ring of **2** matches to those of **10** or *ent*-**11**. Thus, the sugar moiety of **2** could be prepared by conventional reduction, deprotection and glycolic cleavage reactions.

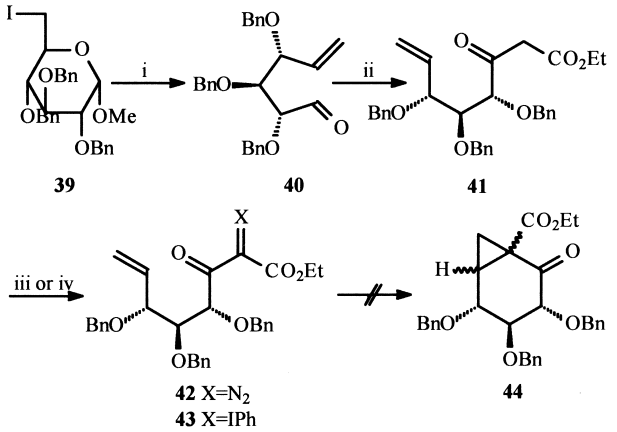
Acetonide removal from the partially protected tetrol **22**—reduction product of **10** with $LiAlH_4$—followed by tritylation of the primary hydroxyl group (Scheme 3) afforded **34**.




**Scheme 2.** *Reagents and conditions*: (i) PhSH, *t*-BuOK, *t*-BuOH, 20°C, 3–12 h. (ii) DMSO, $H_2O$, NaCl, 160°C, 5 h.




**Scheme 3.** *Reagents and conditions*: (i) $LiAlH_4$, $Et_2O$, −10°C, 30 min, 80%. (ii) HCl, $H_2O$, THF, 20°C, 30 min. (iii) TrCl, DMAP, $Et_3N$, DMF, 20°C, 24 h, 65% from **22**. (iv) $NaIO_4$, THF, $H_2O$, 45 min then $NaBH_4$, MeOH, 30 min (twice), 55% overall. (v) BzCl, pyridine, 0°C, 1 h. (vi) $HCO_2H$, $Et_2O$, 20°C, 20 min, 60% from **35**. (vii) Ref. 3a.




**Scheme 4.** *Reagents and conditions*: (i) Zn, EtOH, reflux, 2 h. (ii) $N_2CHCO_2Et$, 0°C, 10 min, 65% from **39**. (iii) $TsN_3$, $Et_3N$, EtOH, 20°C, 10 h, 84%. (iv) $PhI(OAc)_2$, KOH (4 equiv.), EtOH, −5°C, 30 min.

Further glycolic cleavage required prolonged stirring with an excess of $NaIO_4$, to afford low yields of **35** upon $NaBH_4$ reduction, the mixture of polyols **37** and **38** being the main products (Fig. 5). Evidently, the initially formed hydroxy-bis-aldehydes exist predominantly as lactols, a structure favored by the *cis*-disposition of these groups relative to the cyclopropane ring, thus resisting the action of $NaIO_4$.

To overcome this problem, **34** was subjected to two consecutive glycolic cleavage/$NaBH_4$ reduction treatments, to afford the desired compound **35**, in good overall yield. Conventional benzoylation of the two free hydroxyl groups and detritylation gave the known compound **36**, which can be readily converted to the nucleoside A-5021 (**2**), according to the literature.[3a]

In an attempt to extend the cyclopropanation methodology into the synthesis of hydroxylated bicyclo[4.1.0]heptanes, such as **44** (Scheme 4), the keto ester **41** was prepared by addition of ethyl diazocetate to the chiral hexenal **40**, easily accessible from D-glucose.[19] Iodide **39** was converted to **40** when treated with activated zinc in refluxing ethanol, and was further used, without purification. To our surprise, ethyl diazocetate added smoothly to **40** to give **41** in 65% yield, without the presence of an $SnCl_2$ catalyst. It is possible that the hexenal **40** was contaminated by $Zn^{2+}$ salts from the previous reductive elimination step, which catalyzed the reaction.

The keto ester was then easily converted to the respective diazo compound **42** and iodonium ylide **43**. As in the case of **9** and *ent*-**9** (Scheme 1), the ylide **43**, being unstable, was prepared in situ and used in the next step without purification. However, all attempts for catalytic decomposition of **42** and **43** yielded a complex mixture of products, where bicyclo[4.1.0]heptanes, like **44**, were not possible to be detected.

Although bicyclo[4.1.0]heptanes have been previously prepared by intramolecular cyclopropanation of metallocarbenoid intermediates,[5] the tendency of the latter to form five-membered rings might lead either to C–H insertion reactions or to intermediate oxonium ylides by addition of one oxygen of the benzyloxy groups to the carbenoid carbon, which further decompose to several unidentified products.

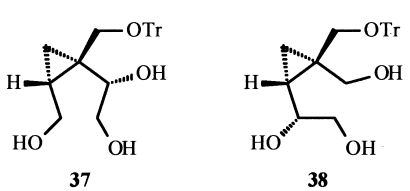



**Figure 5.**

## 3. Conclusion

In short, the diastereoselectivity of the metal-catalyzed intramolecular cyclopropanations of *erythro*-2-diazo-4,5-isopropylidenedioxy-3-oxo-6-heptenoate strongly depends on the catalyst used. The *endo* product predominates when CuI catalyzes the reaction, whereas $Rh_2(OAc)_4$ as a catalyst favors the formation of the *exo* adduct. However, the diastereoselectivity of the cyclopropanation of the respective iodonium ylides is independent of the catalyst used and proceeds with similar results, even without the presence of any catalyst. Our results are in accordance with the mechanism suggested by Moriarty et al.[6] which involves a stepwise electrophilic addition of the iodonium center to the double bond, followed by reductive elimination of iodobenzene to afford the cyclopropane ring. The synthetic potential of these reactions was also demonstrated by preparing precursors of carbocyclic nucleosides and by developing a new synthesis of enantiopure antiviral cyclopropane nucleoside A-5021.

## 4. Experimental

### 4.1. General

All reagents are commercially available and were used without further purification. Solvents were dried by standard methods. The progress of the reactions was checked by thin layer chromatography (TLC) on Merck silica gel $60F_{254}$ glass plates (0.25 mm). The spots were visualized by heat

staining with anisaldehyde in ethanol/sulfuric acid. Column chromatography was performed with Merck silica gel 60 (0.063–0.200 mm). Optical rotations were determined at room temperature on an A. Krüss P3000 Automatic Digital Polarimeter. Melting points were determined on a Kofler hot-stage microscope and are uncorrected. Infrared spectra were recorded on a Perkin–Elmer 297 spectrophotometer. The $^1$H and $^{13}$C NMR spectra were recorded at 300 and 75 MHz, respectively, on a Bruker 300 AM spectrometer, with tetramethylsilane (TMS) as internal standard. Mass spectra were recorded under electron-impact (EI) conditions at 70 eV on a VG TS-250 spectrometer and microanalyses were performed on a Perkin–Elmer 2400-II Element analyzer. High-resolution mass spectra (HRMS) were obtained on a VG ZAB-ZSE mass spectrometer under fast-atom bombardment (FAB) conditions with nitrobenzyl alcohol (NBA) as the matrix or on an IONSPEC FTMS spectrometer (matrix-assisted laser-desorption ionization, MALDI) with 2,5-dihydroxybenzoic acid (DHB) as matrix.

### 4.2. General procedure for the synthesis of keto-esters 7, *ent*-7 and 15

To a solution of aldehyde **6**, *ent*-**6** or **14** (prepared from the appropriate precursor **5**, **12** or **13** (10 mmol) according to the literature procedure)[10,14,15] in $CH_2Cl_2$ (35 mL), anhydrous $SnCl_2$ (190 mg, 1.0 mmol) was added. The resulting mixture was cooled to 0°C and $N_2CHCO_2Et$ (1.14 g, 10 mmol) was added dropwise during a period of 1 h under argon atmosphere and the mixture was stirred for another 1 h at the same temperature. $H_2O$ (60 mL) was then added, the organic layer was separated and the aqueous layer was extracted with $CH_2Cl_2$ (3×60 mL). The combined organic layers were dried over $Na_2SO_4$, the solvent was removed on a rotary evaporator and the residue was chromatographed on a column of silica gel with hexane/ethyl acetate as the eluent to give keto esters **7**, *ent*-**7** or **15** as pale yellow liquids.

**4.2.1. Ethyl (4*R*,5*R*)-4,5-isopropylenedioxy-3-oxo-6-heptenoate (7).** This compound was obtained in 76% yield (72% from **5**). $[\alpha]_D^{27}$=+45.6 (*c* 1.6, $CHCl_3$); IR (neat) 1740, 1720, 1650 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.26 (t, *J*=7.3 Hz, 3H), 1.40 (s, 3H), 1.57 (enol) and 1.62 (keto) (s and s, total 3H), 3.35 (keto) and 5.47 (enol) (d, *J*=16.5 Hz and s, total 1H), 3.60 (keto) and 11.94 (enol) (d, *J*=16.5 Hz and s, total 1H), 4.17 (q, *J*=7.3 Hz, 2H), 4.61 (keto) and 4.68 (enol) (d, *J*=8.1 Hz and d, *J*=7.3 Hz, total 1H), 4.79 (enol) and 4.88 (keto) (dd as t, *J*=7.3 Hz and dd as t, *J*=8.1 Hz, total 1H), 5.30 (m, 2H), 5.70 (m, 1H), (from integration keto/enol ~5:1); $^{13}$C NMR ($CDCl_3$) (keto form) $\delta$ 13.7, 24.3, 26.3, 47.2, 60.8, 78.3, 82.5, 110.5, 118.7, 131.5, 166.5, 202.1 and (enol form) $\delta$ 13.8, 24.6, 26.7, 59.9, 77.1, 79.0, 89.3, 109.6, 118.7, 132.5, 172.2, 173.0; MS *m*/*z* (%) 242 ($M^+$, 46), 227 (26), 185 (100), 167 (19), 127 (79), 59 (63); HRMS (*m*/*z*) calcd for $C_{12}H_{18}O_5$ 242.1154 ($M^+$), found 242.1150.

**4.2.2. Ethyl (4*S*,5*S*)-4,5-isopropylenedioxy-3-oxo-6-heptenoate (*ent*-7).** This compound was obtained in 75% yield (69% from **12**). $[\alpha]_D^{27}$=−45.3 (*c* 1.6, $CHCl_3$) with spectra identical to those of **7**.

**4.2.3. Ethyl (4*R*,5*R*)-6-[(benzyloxy)methyl]-4,5-isopropylenedioxy-3-oxo-6-heptenoate (15).** This compound was obtained in 76% yield (68% from **13**). $[\alpha]_D^{27}$=~0.0 (*c* 0.3, $CHCl_3$); IR (neat) 1730, 1710, 1640 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.24 (keto) and 1.31 (enol) (t, *J*=7.0 Hz and t, *J*=7.0 Hz, total 3H), 1.41 (keto) and 1.51 (enol) (s and s, total 3H), 1.61 (enol) and 1.67 (keto) (s and s, total 3H), 3.30 (keto) and 5.52 (enol) (d, *J*=16.0 Hz and s, total 1H), 3.62 (keto) and 11.88 (enol) (d, *J*=16.0 Hz and s, total 1H), 3.94 (keto) and 4.02 (enol) (d, *J*=12.7 Hz and d, *J*=13.1 Hz, total 1H), 4.03 (keto) and 4.07 (enol) (d, *J*=12.7 Hz and d, *J*=13.1 Hz, total 1H), 4.15 (keto) and 4.27 (enol) (q, *J*=7.0 Hz and q, *J*=7.0 Hz, total 2H), 4.45 (d, *J*=12.0 Hz, 1H), 4.53 (d, *J*=12.0 Hz, 1H), 4.60 (keto) and 4.65 (enol) (d, *J*=8.0 Hz and d, *J*=5.8 Hz, total 1H), 4.91 (enol) and 4.99 (keto) (d, *J*=5.8 Hz and d, *J*=8.0 Hz, total 1H), 5.29 (s, 1H), 5.44 (s, 1H), 7.34 (br s, 5H), (from integration keto/enol ~9:1); $^{13}$C NMR ($CDCl_3$) (keto form) $\delta$ 13.9, 24.4, 26.2, 47.3, 61.0, 70.8, 72.2, 77.1, 82.5, 110.2, 114.8, 127.6, 127.7, 128.3, 137.8, 139.7, 166.9, 202.7 and (enol form) $\delta$ 14.0, 25.1, 26.3, 60.1, 70.9, 72.1, 76.8, 77.4, 109.2, 114.9, 127.4, 127.5, 128.2, 138.0, 139.9, 140.0, 172.1, 174.1; MS *m*/*z* (%) 362 ($M^+$, 71), 306 (31), 288 (32), 241 (43), 187 (100), 115 (93). Anal. calcd for $C_{20}H_{26}O_6$: C, 66.28; H, 7.23. Found: C, 66.07; H, 6.96.

### 4.3. General procedure for the synthesis of diazo compounds 8, *ent*-8 and 16

To a solution of keto ester **7**, *ent*-**7** or **15** (10 mmol), in absolute ethanol (60 mL) tosyl azide (2.366 g, 12 mmol) and $Et_3N$ (13 mL) were added and the mixture was stirred at room temperature for 12 h. The volatiles were then removed on a rotary evaporator and the residue was chromatographed on a column of silica gel with hexane/ethyl acetate as the eluent to give diazo compounds **8**, *ent*-**8** or **16** as colorless liquids.

**4.3.1. Ethyl (4*R*,5*R*)-2-diazo-4,5-isopropylenedioxy-3-oxo-6-heptenoate (8).** This compound was obtained in 92% yield. $[\alpha]_D^{27}$=+55.7 (*c* 1.6, $CHCl_3$); IR (neat) 2130, 1705, 1610 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.30 (t, *J*=7.1 Hz, 3H), 1.43 (s, 3H), 1.65 (s, 3H), 4.28 (q, *J*=7.1 Hz, 2H), 4.98 (dd as t, *J*=7.7 Hz, 1H), 5.22 (d, *J*=10.5 Hz, 1H), 5.37 (d, *J*=16.5 Hz, 1H), 5.61 (d, *J*=7.7 Hz, 1H), 5.69 (ddd, *J*=16.5, 10.5, 7.7 Hz, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 14.3, 25.3, 26.7, 61.6, 78.8, 80.3, 110.6, 119.5, 132.6, 161.0, 188.0 (*C*=$N_2$ not appeared); MS *m*/*z* (%) 268 ($M^+$, 100), 253 (46), 211 (99), 127 (87); HRMS (*m*/*z*) calcd for $C_{12}H_{16}N_2O_5$ 268.1059 ($M^+$), found 268.1021.

**4.3.2. Ethyl (4*S*,5*S*)-2-diazo-4,5-isopropylenedioxy-3-oxo-6-heptenoate (*ent*-8).** This compound was obtained in 90% yield. $[\alpha]_D^{27}$=−55.7 (*c* 1.6, $CHCl_3$) with spectra identical to those of **8**.

**4.3.3. Ethyl (4*R*,5*R*)-2-diazo-6-[(benzyloxy)methyl]-4,5-isopropylenedioxy-3-oxo-6-heptenoate (16).** This compound was obtained in 90% yield. $[\alpha]_D^{27}$=−36.3 (*c* 1.8, $CHCl_3$); IR (neat) 2120, 1700, 1650 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.29 (t, *J*=7.1 Hz, 3H), 1.41 (s, 3H), 1.63 (s, 3H), 3.91 (d, *J*=13.8 Hz, 1H), 3.99 (d, *J*=13.8 Hz, 1H), 4.24 (q, *J*=7.1 Hz, 2H), 4.47 (s, 2H), 5.11 (d, *J*=8.0 Hz, 1H),

5.25 (s, 1H), 5.34 (s, 1H), 5.67 (d, $J$=8.0 Hz, 1H), 7.3 (br s, 5H); $^{13}$C NMR ($CDCl_3$) $\delta$ 14.3, 24.7, 26.0, 61.6, 69.3, 72.4, 79.1, 80.0, 110.0, 115.3, 127.5 (two overlapping peaks), 128.3, 138.3, 141.3, 161.0, 187.7 ($C$=$N_2$ not appeared); MS $m/z$ (%) 388 ($M^+$, 100), 361 (10), 314 (15), 281 (31), 195 (100), 127 (74), 91 (62); HRMS ($m/z$) calcd for $C_{20}H_{24}N_2O_6$ 388.1634 ($M^+$), found 388.1641.

### 4.4. Decomposition of diazo compounds 8 and *ent*-8

*Method A*. To a well stirred solution of the diazo compound **8** or *ent*-**8** (536 mg, 2 mmol) in toluene (20 mL) was added CuI (20 mg) and the resultant mixture was refluxed for 3 h. Evaporation of the solvent and subsequent column chromatography on silica gel with hexane/ethyl acetate as the eluent gave **10** or *ent*-**10** at first (317 mg, 66%), followed by the diastereoisomer **11** or *ent*-**11** (72 mg, 15%) as colorless oils.

*Method B*. To a well stirred solution of the diazo compound **8** or *ent*-**8** (536 mg, 2 mmol) in toluene (25 mL) was added $Rh_2(OAc)_4$ (10 mg) and the resultant mixture was refluxed for 1.5 h. Evaporation of the solvent and subsequent column chromatography on silica gel with hexane/ethyl acetate as the eluent gave **10** or *ent*-**10** at first (90 mg, 19%), followed by the diastereoisomer **11** or *ent*-**11** (265 mg, 55%).

**4.4.1. Ethyl (1*R*,3*R*,4*R*,5*R*)-3,4-isopropylenedioxy-2-oxobicyclo[3.1.0]hexane-1-carboxylate (10).** $[\alpha]_D^{27}$=−87.0 ($c$ 1.0, $CHCl_3$); IR (neat) 1755, 1725 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.28 (t, $J$=7.1 Hz, 3H), 1.31 (s, 3H), 1.51 (s, 3H), 1.81 (dd, $J$=5.2, 5.0 Hz, 1H, 6-H$_{endo}$), 2.10 (ddd, $J$=8.2, 5.0, 1.1 Hz, 1H, 6-H$_{exo}$), 2.76 (ddd, $J$=8.2, 5.5, 5.2 Hz, 1H, 5-H), 4.21 (q, $J$=7.1 Hz, 2H), 4.37 (d, $J$=8.0 Hz, 1H, 3-H), 5.04 (ddd, $J$=8.0, 5.5, 1.1 Hz, 1H, 4-H); $^{13}$C NMR ($CDCl_3$) $\delta$ 14.0, 20.5, 24.2, 25.6, 32.8, 41.7, 61.6, 73.5, 80.4, 114.8, 166.8, 199.5; MS $m/z$ (%) 240 ($M^+$, 100), 225 (21), 211 (23), 195 (22), 183 (22), 166 (14), 136 (55) 108 (58); HRMS ($m/z$) calcd for $C_{12}H_{17}O_5$ 241.1076 ($M^+$+H), found 241.1081.

**4.4.2. Ethyl (1*S*,3*R*,4*R*,5*S*)-3,4-isopropylenedioxy-2-oxobicyclo[3.1.0]hexane-1-carboxylate (11).** $[\alpha]_D^{27}$=−76.3 ($c$ 1.0, $CHCl_3$); IR (neat) 1750, 1715 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.29 (t, $J$=7.0 Hz, 3H), 1.29 (t, $J$=5.5 Hz, 1H, 6-H$_{endo}$), 1.37 (s, 3H), 1.44 (s, 3H), 2.12 (ddd, $J$=8.5, 5.5, 1.6 Hz, 1H, 6-H$_{exo}$), 2.87 (dd, $J$=8.5, 5.5 Hz, 1H, 5-H), 4.23 (q, $J$=7.0 Hz, 2H), 4.30 (dd, $J$=4.9, 1.6 Hz, 1H, 4-H), 4.73 (d, $J$=4.9 Hz, 1H, 3-H); $^{13}$C NMR ($CDCl_3$) $\delta$ 13.9, 20.3, 25.5, 27.3, 35.4, 36.0, 61.4, 75.3, 79.2, 113.2, 166.9, 202.0; MS $m/z$ (%) 240 ($M^+$, 100), 225 (41), 211 (6), 195 (7), 182 (25), 165 (11), 136 (39) 108 (32); HRMS ($m/z$) calcd for $C_{12}H_{17}O_5$ 241.1076 ($M^+$+H), found 241.1094.

**4.4.3. Ethyl (1*S*,3*S*,4*S*,5*S*)-3,4-isopropylenedioxy-2-oxobicyclo[3.1.0]hexane-1-carboxylate (*ent*-10).** $[\alpha]_D^{27}$=+84.5 ($c$ 0.2, $CHCl_3$).

**4.4.4. Ethyl (1*R*,3*S*,4*S*,5*R*)-3,4-isopropylenedioxy-2-oxobicyclo[3.1.0]hexane-1-carboxylate (*ent*-11).** $[\alpha]_D^{27}$=+78.7 ($c$ 1.0, $CHCl_3$).

### 4.5. Decomposition of diazo compound 16

*Method A*. To a well stirred solution of the diazo compound **16** (194 mg, 0.5 mmol) in toluene (5 mL) was added CuI (6 mg) and the resultant mixture was refluxed for 5 h. Evaporation of the solvent and subsequent column chromatography on silica gel with hexane/ethyl acetate as the eluent gave first **18** (33 mg, 18.5%), followed by the diastereoisomer **19** (17 mg, 9.5%), as colorless oils.

*Method B*. To a well stirred solution of the diazo compound **16** (194 mg, 0.5 mmol) in toluene (5 mL) was added CuCl (50 mg) and the resultant mixture was refluxed for 2 h. Evaporation of the solvent and subsequent column chromatography on silica gel with hexane/ethyl acetate as the eluent gave first **18** (48 mg, 27%), followed by the diastereoisomer **19** (29 mg, 16%).

*Method C*. To a well stirred solution of the diazo compound **16** (194 mg, 0.5 mmol) in toluene (5 mL) was added $Rh_2(OAc)_4$ (3 mg) and the resultant mixture was refluxed for 2.5 h. Evaporation of the solvent and subsequent column chromatography on silica gel with hexane/ethyl acetate as the eluent gave **19** (104 mg, 58%).

*Method D*. To a well stirred solution of the diazo compound **16** (194 mg, 0.5 mmol) in toluene (5 mL) was added $Cu(OSO_2CF_3)$ (0.5 mL of a 10% solution in $CH_3CN$) and the resultant mixture was refluxed for 5 h. Evaporation of the solvent and subsequent column chromatography on silica gel with hexane/ethyl acetate as the eluent gave first **18** (37 mg, 21%), followed by the diastereoisomer **19** (60 mg, 33%).

**4.5.1. Ethyl (1*R*,3*R*,4*R*,5*R*)-5-[(benzyloxy)methyl]-3,4-isopropylenedioxy-2-oxobicyclo[3.1.0]hexane-1-carboxylate (18).** $[\alpha]_D^{27}$=−42.1 ($c$ 1.0, $CHCl_3$); IR (neat) 1750, 1710 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.23 (t, $J$=7.1 Hz, 3H), 1.32 (s, 3H), 1.51 (s, 3H), 1.87 (d, $J$=5.5 Hz, 1H, 6-H$_{endo}$), 2.10 (dd, $J$=5.5, 1.6 Hz, 1H, 6-H$_{exo}$), 3.47 (d, $J$=10.5 Hz, 1H), 4.00 (d, $J$=10.5 Hz, 1H), 4.17 (two dq as m, 2H), 4.42 (d, $J$=8.2 Hz, 1H, 3-H), 4.45 (d, $J$=11.5 Hz, 1H), 4.51 (d, $J$=11.5 Hz, 1H), 5.17 (dd, $J$=8.2, 1.6 Hz, 1H, 4-H), 7.3 (br s, 5H); $^{13}$C NMR ($CDCl_3$) $\delta$ 14.0, 22.5, 24.2, 25.7, 44.8, 45.7, 61.8, 68.1, 73.3, 75.6, 80.0, 114.8, 127.6, 127.8, 128.4, 137.6, 165.7, 205.8; MS $m/z$ (%) 360 ($M^+$, 14), 303 (9), 239 (23), 211 (31), 196 (41), 181 (31), 165 (24), 137 (22) 92 (100), 91 (73). Anal. calcd for $C_{20}H_{24}O_6$: C, 66.65; H, 6.71. Found: C, 66.74; H, 6.62.

**4.5.2. Ethyl (1*S*,3*R*,4*R*,5*S*)-5-[(benzyloxy)methyl]-3,4-isopropylenediooxy-2-oxobicyclo[3.1.0]hexane-1-carboxylate (19).** $[\alpha]_D^{27}$=−27.2 ($c$ 0.7, $CHCl_3$); IR (neat) 1740, 1710 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.21 (t, $J$=7.0 Hz, 3H), 1.36 (d, $J$=6.0 Hz, 1H), 1.40 (s, 3H), 1.43 (s, 3H), 2.20 (d, $J$=6.0 Hz, 1H), 3.52 (d, $J$=10.0 Hz, 1H), 4.13 (d, $J$=10.0 Hz, 1H), 4.16 (q, $J$=7.0 Hz, 2H), 4.34 (dd, $J$=5.0, 1.6 Hz, 1H, 4-H), 4.55 (d, $J$=12.0 Hz, 1H), 4.60 (d, $J$=12.0 Hz, 1H), 4.81 (d, $J$=5.0 Hz, 1H, 3-H), 7.3 (br s, 5H); $^{13}$C NMR ($CDCl_3$) $\delta$ 13.9, 22.5, 26.0, 27.6, 41.8, 44.1, 61.7, 66.4, 73.3, 76.5, 79.0, 113.6, 127.5, 127.7, 128.3, 137.8, 165.8, 203.1; MS $m/z$ (%) 360 ($M^+$, 74), 345 (17), 315 (22), 303 (74), 285 (56), 254 (91), 239 (83), 211 (41),

195 (82), 181 (74), 165 (34), 139 (52), 92 (100), 91 (75). Anal. calcd for $C_{20}H_{24}O_6$: C, 66.65; H, 6.71. Found: C, 66.34; H, 6.62.

### 4.6. General procedure for the preparation and decomposition of iodonium ylides 9 and *ent*-9

To a cold stirred solution of keto ester **7** or *ent*-**7** (242 mg, 1 mmol) in EtOH (5 mL) was added at −5°C a solution of KOH (224 mg, 4 mmol) in EtOH (5 mL) followed by addition at the same temperature of a solution of $PhI(OAc)_2$ (322 mg, 1 mmol) in EtOH (10 mL). The mixture was kept at −5°C for 30 min, then poured into $H_2O$ (20 mL), extracted with $CH_2Cl_2$ (2×50 mL) and the organic layer was dried over $Na_2SO_4$. The solution was concentrated to 10 mL and stirred at room temperature either with CuI (10 mg) or $Rh_2(OAc)_4$ (5 mg) or without any catalyst for 30 min under argon atmosphere. Evaporation of the solvent and subsequent column chromatography on silica gel with hexane/ethyl acetate as the eluent gave in all cases first **10** or *ent*-**10** (43 mg, 18%), followed by **11** or *ent*-**11** (65 mg, 27%).

**4.6.1. Ethyl (1*R*,2*S*,3*R*,4*R*,5*R*)-2-hydroxy-3,4-isopropylenedioxybicyclo[3.1.0]hexane-1-carboxylate (21).** To a solution of **10** (480 mg, 2 mmol) in absolute EtOH (30 mL) was added $NaBH_4$ (114 mg, 3 mmol) and the mixture was stirred at 0°C for 1 h. The volume of the mixture was reduced to ~10 mL, $H_2O$ (20 mL) was added and then extracted with $CH_2Cl_2$ (3×20 mL). The organic layer was dried over $Na_2SO_4$, the solvent was removed on a rotary evaporator and the residue was chromatographed on silica gel with hexane/ethyl acetate as the eluent to give **21** as colorless oil (329 mg, 68%). $[\alpha]_D^{27}=-43.9$ (*c* 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1.26 (t, *J*=7.1 Hz, 3H), 1.30 (s, 3H), 1.52 (m, 2H, 6-H), 1.56 (s, 3H), 2.10 (ddd, *J*=8.8, 5.4, 4.9 Hz, 1H, 5-H), 2.5 (br s, 1H, OH), 4.16 (two dq as m, 2H), 4.60 (dd as t, *J*=6.8 Hz, 1H, 3-H), 4.87 (dd, *J*=6.8, 5.4 Hz, 1H, 4-H), 5.00 (d, *J*=6.8 Hz, 1H, 2-H); $^{13}$C NMR ($CDCl_3$) $\delta$ 14.2, 15.8, 24.6, 26.0, 32.5, 40.8, 61.0, 70.1, 79.2, 79.6, 113.0, 171.9; HRMS (*m*/*z*) calcd for $C_{12}H_{18}NaO_5$ 265.1046 ($M^+$+Na), found 245.1054.

**4.6.2. (1*S*,2*S*,3*R*,4*R*,5*R*)-1-(Hydroxymethyl)-3,4-isopropylenedioxybicyclo[3.1.0]hexane-2,3,4-triol (22).** *From* **10**. To a solution of **10** (480 mg, 2 mmol) in dry THF (30 mL) was added $LiAlH_4$ (198 mg, 5.2 mmol) and the mixture was stirred at −10°C for 30 min. A few drops of $H_2O$ were added and the solids were filtered off and washed with MeOH (3×20 mL). The solvent was evaporated and the residue was chromatographed on silica gel with ethyl acetate as the eluent to give **22** as colorless oil (320 mg, 80%). $[\alpha]_D^{27}=-7.2$ (*c* 1.0, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 0.66 (dd, *J*=7.8, 4.5 Hz, 1H, 6-$H_a$), 1.20 (dd, *J*=5.9, 4.5 Hz, 1H, 6-$H_b$), 1.30 (s, 3H), 1.55 (s, 3H), 1.62 (ddd, *J*=7.8, 5.9, 4.0 Hz, 1H, 5-H), 3.05 (br s, 2H, two OH), 3.45 (d, *J*=11.7 Hz, 1H), 3.79 (d, *J*=11.7 Hz, 1H), 4.55 (dd as t, *J*=6.8 Hz, 1H, 3-H), 4.61 (d, *J*=6.8 Hz, 1H, 2-H), 4.88 (dd, *J*=6.8, 4.0 Hz, 1H, 4-H); $^{13}$C NMR ($CDCl_3$) $\delta$ 10.9, 24.5, 25.9, 26.1, 41.1, 65.1, 72.0, 79.2, 80.0, 112.3; HRMS (*m*/*z*) calcd for $C_{10}H_{16}NaO_4$ 223.0941 ($M^+$+Na), found 223.0935.

*From* **21**. To a solution of **21** (121 mg, 0.5 mmol) in dry THF (10 mL) was added $LiAlH_4$ (38 mg, 1 mmol) and the mixture was stirred at −10°C for 30 min. A few drops of $H_2O$ were added and the solids were filtered off and washed with MeOH (3×10 mL). The solvent was evaporated and the residue was chromatographed on silica gel with ethyl acetate as the eluent to give **22** as colorless oil (38 mg, 76%).

**4.6.3. (1*R*,2*S*,3*R*,4*R*,5*S*)-1-(Hydroxymethyl)-3,4-isopropylenedioxybicyclo[3.1.0]hexane-2,3,4-triol (23).** To a solution of **11** (240 mg, 1 mmol) in dry THF (15 mL) was added $LiAlH_4$ (99 mg, 2.6 mmol) and the mixture was stirred at −10°C for 30 min. A few drops of $H_2O$ were added and the solids were filtered off and washed with MeOH (3×20 mL). The solvent was evaporated and the residue was chromatographed on silica gel with ethyl acetate as the eluent to give **23** as colorless oil (82 mg, 82%). $[\alpha]_D^{27}=-5.1$ (*c* 0.5, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ −0.01 (dd, *J*=6.1, 4.3 Hz, 1H), 0.67 (dd, *J*=8.6, 6.1 Hz, 1H), 1.36 (s, 3H), 1.53 (s, 3H), 1.80 (dd, *J*=8.6, 4.3 Hz, 1H), 2.91 (br s, 2H), 3.53 (d, *J*=11.9 Hz, 1H), 4.00 (d, *J*=11.9 Hz, 1H), 4.07 (d, *J*=5.8 Hz, 1H), 4.28 (dd, *J*=5.8, 5.4 Hz, 1H), 4.64 (d, *J*=5.4 Hz, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 11.6, 24.5, 25.3, 26.0, 35.9, 64.7, 72.0, 80.4, 82.5, 112.8; HRMS (*m*/*z*) calcd for $C_{10}H_{16}NaO_4$ 223.0941 ($M^+$+Na), found 223.0939.

**4.6.4. (1*R*,3*R*,4*R*,5*S*)-3,4-Isopropylenedioxy-bicyclo-[3.1.0]hexan-2-one (24).** To a solution of **11** (240 mg, 1 mmol) in DMSO (10 mL) were added NaCl (73 mg, 1.25 mmol) and $H_2O$ (2 drops) and the mixture was refluxed for 5 h. $H_2O$ (50 mL) was added and the mixture was extracted with $CH_2Cl_2$ (3×50 mL). The organic layer was dried over $Na_2SO_4$, the solvent was removed on a rotary evaporator and the residue was chromatographed on silica gel with hexane/ethyl acetate as the eluent to give **24** as white crystals (30 mg, 18%). Mp 70–71°C (from $Et_2O$/hexane); $[\alpha]_D^{27}=-254.8$ (*c* 0.05, $CHCl_3$); IR (nujol) 1725 $cm^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 0.92 (m, 1H, 6-$H_a$), 1.36 (s, 3H), 1.37 (m, 1H, 6-$H_b$), 1.45 (s, 3H), 2.04 (ddd, *J*=9.0, 4.7, 4.3 Hz, 1H, 5-H), 2.43 (ddd, *J*=8.7, 4.7, 4.0 Hz, 1H, 1-H), 4.24 (dd, *J*=4.8, 1.8 Hz, 1H, 4-H), 4.79 (d, *J*=4.8 Hz, 1H, 3-H); $^{13}$C NMR ($CDCl_3$) $\delta$ 12.3, 25.5, 25.6, 25.9, 27.3, 77.3, 77.7, 113.1, 209.3; MS *m*/*z* (%) 168 ($M^+$, 22), 153 (60), 110 (63), 82 (100), 59 (17). Anal. calcd for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 64.38; H, 7.33.

**4.6.5. (2*R*,3*R*,4*R*)-4-(Chloromethyl)-2,3-isopropylenedioxycyclopentanone (25).** To a solution of **10** (240 mg, 1 mmol) in DMSO (10 mL) were added NaCl (73 mg, 1.25 mmol) and $H_2O$ (2 drops) and the mixture was refluxed for 5 h. $H_2O$ (50 mL) was added and the mixture was extracted with $CH_2Cl_2$ (3×50 mL). The organic layer was dried over $Na_2SO_4$, the solvent was removed on a rotary evaporator and the residue was chromatographed on silica gel with hexane/ethyl acetate as the eluent to give **25** as a white foam (47 mg, 23%). $[\alpha]_D^{27}=-186.0$ (*c* 0.05, $CHCl_3$); IR (nujol) 1740 $cm^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.38 (s, 3H), 1.42 (s, 3H), 2.35 (dd, *J*=18.2, 12.2 Hz, 1H), 2.47 (dd, *J*=18.2, 7.7 Hz, 1H), 2.62 (m, 1H), 3.69 (dd, *J*=10.7, 6.9 Hz, 1H), 3.82 (dd, *J*=10.7, 8.2 Hz, 1H), 4.29 (d, *J*=4.8 Hz, 1H), 4.85 (dd, *J*=4.8, 4.3 Hz, 1H); $^{13}$C NMR

($CDCl_3$) $\delta$ 25.1, 26.6, 38.0, 38.5, 43.5, 77.1, 80.4, 112.8, 212.1; MS *m/z* (%) 206 ($M^+$+2, 18), 204 ($M^+$, 55), 169 (22), 149 (27), 147 (80), 132 (15), 130 (45), 51 (100). Anal. calcd for $C_9H_{13}ClO_3$: C, 52.82; H, 6.40. Found: C, 53.01; H, 6.32.

**4.6.6. (1*S*,3*R*,4*R*,5*S*)-5-[(Benzyloxy)methyl]-3,4-isopropylenedioxy-2-oxobicyclo[3.1.0]hexane-1-carboxylic acid (26).** A mixture of **19** (180 mg, 0.5 mmol) in THF (15 mL) and aqueous 0.1N NaOH (15 mL) was refluxed for 4 h and then carefully neutralized with dilute aqueous HCl. $H_2O$ (50 mL) was added and the mixture was extracted with $CH_2Cl_2$ (3×50 mL). The organic layer was dried over $Na_2SO_4$, the solvent was removed on a rotary evaporator and the residue was chromatographed on silica gel with hexane/ethyl acetate as the eluent to give **24** as a white foam (41.5 mg, 25%). $[\alpha]_D^{27}$=+119.4 (*c* 0.07, $CHCl_3$); IR ($CHCl_3$) 1740, 1700 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.40 (s, 3H), 1.42 (s, 3H), 1.87 (d, *J*=5.2 Hz, 1H, 6-$H_a$), 2.43 (dd, *J*=5.2, 1.6 Hz, 1H, 6-$H_b$), 3.98 (d, *J*=10.2 Hz, 1H), 4.15 (d, *J*=10.2 Hz, 1H), 4.48 (dd, *J*=5.0, 1.6 Hz, 1H, 4-H), 4.62 (s, 2H), 4.94 (d, *J*=5.0 Hz, 1H, 3-H), 7.35 (br s, 5H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 25.7, 27.3, 29.3, 39.1, 48.6, 65.5, 73.7, 76.2, 77.9, 114.5, 127.7, 127.8, 128.4, 137.9, 166.7, 202.2; HRMS (*m/z*) calcd for $C_{18}H_{20}NaO_6$ 355.1152 ($M^+$+Na), found 355.1153.

### 4.7. General procedure for the synthesis of compounds 27–29

To a solution of compound **10**, **11** or **19**, (1 mmol) in *t*-BuOH (12 mL) were added *t*-BuOK (134 mg, 1.2 mmol), and PhSH (121 mg, 1.1 mmol) and the mixture was stirred at room temperature for 7 h (compound **10**) or 3 h (compound **11**) or 12 h (compound **19**). The solution was quenched with dilute aqueous HCl. $H_2O$ (50 mL) was added and the mixture was extracted with $CH_2Cl_2$ (3×50 mL). The organic layer was dried over $Na_2SO_4$, the solvent was removed on a rotary evaporator and the residue was chromatographed on silica gel with hexane/ethyl acetate as the eluent to give **27**, **28** or **29**.

**4.7.1. Ethyl (3*R*,4*R*,5*R*)-3,4-isopropylenedioxy-2-oxo-5-[(phenylthio)methyl]cyclopentanecarboxylate (27).** This compound was obtained in 77% yield as white crystals. Mp 57–59°C (from $Et_2O$/hexane); $[\alpha]_D^{27}$=+33.9 (*c* 0.8, $CHCl_3$); IR (nujol) 1760, 1715 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.28 (keto) and 1.35 (enol) (t, *J*=7.5 Hz and t, *J*=7.5 Hz, total 3H), 1.34 (keto) and 1.40 (enol) (s and s, total 3H), 1.42 (keto) and 1.46 (enol) (s and s, total 3H), 2.89–3.20 (keto/enol) and 10.32 (enol) (m and br s, total 3H), 3.43 (keto) and 3.71 (enol) (d; *J*=12.0 Hz and d, *J*=13.0 Hz, total 1H), 4.22 (keto) and 4.25 (enol) (q, *J*=7.5 Hz, and q, *J*=7.5 Hz, total 2H), 4.30 (keto) and 4.92 (enol) (d, *J*=4.0 Hz and d, *J*=6.0 Hz, total 1H, 3-H), 4.81 (enol) and 4.87 (keto) (dd as t, *J*=6.0 Hz and dd as t, *J*=4.0 Hz, total 1H, 4-H), 7.35 (m, 5H) (from integration keto/enol ~2:3); $^{13}C$ NMR ($CDCl_3$) (keto/enol form) 14.1, 14.15, 24.8, 25.7, 26.7, 27.2, 30.6, 33.1, 38.9, 42.1, 55.8, 60.8, 61.9, 75.6, 76.4, 79.9, 80.3, 102.3, 112.0, 112.9, 125.4, 126.4, 128.2, 128.8, 129.0, 129.3, 135.4, 137.2, 167.8, 169.9, 171.4, 205.5; MS *m/z* (%) 350 ($M^+$, 31), 335 (8), 292 (41), 274 (14), 241 (19), 227 (36), 186 (61), 141 (72), 123 (58), 81 (100). Anal. calcd for $C_{18}H_{22}O_5S$: C, 61.70; H, 6.33. Found: C, 61.90; H, 6.35.

**4.7.2. Ethyl (3*R*,4*R*,5*S*)-3,4-isopropylenedioxy-2-oxo-5-[(phenylthio)methyl]cyclopentanecarboxylate (28).** This compound was obtained in 71% yield as a colorless oil. $[\alpha]_D^{27}$=+19.5 (*c* 0.6, $CHCl_3$); IR (neat) 1710, 1660 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.28 (t, *J*=7.1 Hz, 3H), 1.36 (s, 3H), 1.42 (s, 3H), 2.97 (dd, *J*=12.0, 7.4 Hz, 1H), 3.25 (dd, *J*=7.4, 2.3 Hz, 1H), 3.35 (dd, *J*=12.0, 2.3 Hz, 1H), 4.13 (q, *J*=7.1 Hz, 2H), 4.52 (d, *J*=5.8 Hz, 1H), 5.11 (d, *J*=5.8 Hz, 1H), 7.18 (d, *J*=7.5 Hz, 1H), 7.26 (t, *J*=7.5 Hz, 2H), 7.35 (d, *J*=7.5 Hz, 2H), 10.06 (br s, 1H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 14.1, 25.4, 27.2, 36.8, 45.5, 60.5, 80.3, 80.7, 102.2, 111.3, 126.3, 128.8, 129.7, 136.0, 168.8, 171.2; MS *m/z* (%) 350 ($M^+$, 14), 349 (40), 334 (23), 292 (29), 275 (17), 229 (56), 181 (61), 140 (83), 125 (100), 108 (96). Anal. calcd for $C_{18}H_{22}O_5S$: C, 61.70; H, 6.33. Found: C, 61.84; H, 6.44.

**4.7.3. Ethyl (2*R*,3*R*,4*R*)-2-[(benzyloxy)methyl]-3,4-isopropylenedioxy-5-oxo-2-[(phenylthio)methyl]-cyclopentanecarboxylate (29).** This compound was obtained in 94% yield as a colorless oil. $[\alpha]_D^{27}$=+37.6 (*c* 1.0, $CHCl_3$); IR (neat) 1705, 1655 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.12 (t, *J*=7.0 Hz, 3H), 1.38 (s, 3H), 1.40 (s, 3H), 3.41 (d, *J*=13.6 Hz, 1H), 3.54 (d, *J*=13.6 Hz, 1H), 3.67 (d, *J*=8.6 Hz, 1H), 3.83 (d, *J*=8.6 Hz, 1H), 4.13 (q, *J*=7.1 Hz, 2H), 4.51 (d, *J*=5.8 Hz, 1H), 4.57 (d, *J*=12.5 Hz, 1H), 4.59 (d, *J*=12.5 Hz, 1H), 5.27 (d, *J*=5.8 Hz, 1H), 7.3 (m, 10H), 10.40 (br s, 1H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 13.9, 25.9, 27.3, 41.1, 53.4, 60.3, 71.0, 73.3, 80.8, 81.7, 102.1, 111.4, 126.5, 127.4, 127.7, 128.2, 128.7, 130.6, 136.5, 138.6, 168.7, 173.0; MS *m/z* (%) 470 ($M^+$, 5), 469 (17), 423 (7), 347 (43), 275 (86), 249 (68), 123 (100), 91 (37). Anal. calcd for $C_{26}H_{30}O_6S$: C, 66.36; H, 6.23. Found: C, 66.26; H, 6.45.

### 4.8. General procedure for the synthesis of compounds 30–32

To a solution of compound **29**, **28** or **29**, (0.25 mmol) in DMSO (5 mL) were added NaCl (20 mg, 0.5 mmol) and $H_2O$ (1 drop) and the mixture was refluxed for 5 h. $H_2O$ (50 mL) was added and the mixture was extracted with $CH_2Cl_2$ (3×50 mL). The organic layer was dried over $Na_2SO_4$, the solvent was removed on a rotary evaporator and the residue was chromatographed on silica gel with hexane/ethyl acetate as the eluent to give **30**, **31** or **32**.

**4.8.1. (2*R*,3*R*,4*R*)-2,3-Isopropylenedioxy-4-[(phenyl-sulfanyl)methyl]cyclopentanone (30).** This compound was obtained in 78% yield as white crystals. Mp 84–85°C (from hexane); $[\alpha]_D^{27}$=+19.5 (*c* 0.6, $CHCl_3$); IR (nujol) 1730 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.34 (s, 3H), 1.41 (s, 3H), 2.34–2.47 (m, 3H), 3.12 (dd, *J*=13.0, 6.0 Hz, 1H), 3.29 (dd, *J*=13.0, 6.5 Hz, 1H), 4.20 (d, *J*=4.8 Hz, 1H), 4.79 (dd, *J*=4.8, 4.2 Hz, 1H), 7.23 (d, *J*=7.0 Hz, 1H), 7.31 (dd as t, *J*=8.0, 7.0 Hz, 2H), 7.39 (d, *J*=8.0 Hz, 2H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 25.1, 26.8, 34.3, 35.3, 39.1, 78.2, 80.3, 112.5, 126.5, 129.0, 129.9, 135.6, 212.9; MS *m/z* (%) 278 ($M^+$, 24), 203 (10), 141 (18), 123 (100), 110 (52). Anal. calcd for $C_{15}H_{18}O_3S$: C, 64.72; H, 6.52. Found: C, 64.53; H, 6.40.

**4.8.2. (2*R*,3*R*,4*S*)-2,3-Isopropylenedioxy-4-[(phenyl-sulfanyl)methyl]cyclopentanone (31).** This compound was obtained in 76% yield as a colorless oil. $[\alpha]_D^{27}=-117.0$ (*c* 0.3, $CHCl_3$); IR (nujol) 1745 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.33 (s, 3H), 1.42 (s, 3H), 2.27 (d, *J*=18.0 Hz, 1H), 2.67 (m, 1H), 2.79 (dd, *J*=18.0, 8.7 Hz, 1H), 2.91 (dd, *J*=13.3, 6.3 Hz, 1H), 3.01 (dd, *J*=13.3, 6.8 Hz, 1H), 4.32 (d, *J*=5.0 Hz, 1H), 4.67 (d, *J*=5.0 Hz, 1H), 7.3 (m, 5H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 24.8, 26.8, 37.0, 38.0, 39.5, 78.3, 81.1, 112.2, 127.0, 129.2, 130.3, 134.9, 212.9; MS *m*/*z* (%) 278 ($M^+$, 100), 263 (15), 141 (77), 123 (93), 110 (99). Anal. calcd for $C_{15}H_{18}O_3S$: C, 64.72; H, 6.52. Found: C, 64.64; H, 6.58.

**4.8.3. (2*R*,3*R*,4*R*)-4-[(Benzyloxy)methyl]-2,3-isopropylenedioxy-4-[(phenylsulfanyl)methyl]-cyclopentanone (32).** This compound was obtained in 76% yield as a colorless oil. $[\alpha]_D^{27}=-53.0$ (*c* 0.2, $CHCl_3$); IR (nujol) 1745 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.31 (s, 3H), 1.39 (s, 3H), 2.31 (d, *J*=18.7 Hz, 1H), 2.42 (d, *J*=18.7 Hz, 1H), 3.14 (d, *J*=13.5 Hz, 1H), 3.21 (d, *J*=13.5 Hz, 1H), 3.59 (d, *J*=9.1 Hz, 1H), 3.75 (d, *J*=9.1 Hz, 1H), 4.41 (d, *J*=5.2 Hz, 1H), 4.47 (s, 2H), 4.58 (d, *J*=5.2 Hz, 1H), 7.3 (m, 10H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 24.8, 26.7, 40.4, 42.8, 45.3, 71.6, 73.3, 79.5, 81.2, 112.2, 126.7, 127.5, 127.6, 128.3, 129.1, 129.8, 136.2, 138.2, 212.1; HRMS (*m*/*z*) calcd for $C_{23}H_{26}NaO_4S$ 421.1444 ($M^+$+Na), found 421.1434.

**4.8.4. (1*S*,2*S*,3*R*,4*R*,5*R*)-1-[(Trityloxy)methyl]bicyclo-[3.1.0]hexane-2,3,4-triol (34).** To a solution of compound **22** (200 mg, 1 mmol) in THF (5 mL) was added aqueous 1N HCl (5 mL) and the mixture was stirred at room temperature for 15 min. The volatiles were then carefully evaporated off on a rotary evaporator to afford pure tetrol **33** [$^1H$ NMR ($D_2O$) $\delta$ 0.48 (dd as t, *J*=6.6 Hz, 1H), 1.32 (dd as t, *J*=4.6 Hz, 1H), 1.58 (m, 1H), 3.27 (d, *J*=11.7 Hz, 1H), 3.91 (dd, *J*=6.4, 5.4 Hz, 1H), 3.92 (d, *J*=11.7 Hz, 1H), 4.33 (dd, *J*=6.6, 5.4 Hz, 1H), 4.45 (d, *J*=6.4 Hz, 1H); $^{13}C$ NMR ($D_2O$) $\delta$ 9.7, 26.7, 34.7, 64.1, 69.8, 71.4, 72.0] was dissolved in dry DMF (10 mL). Dry $Et_3N$ (202 mg, 2 mmol), catalytic DMAP (25 mg) and trityl chloride (306 mg, 1.1 mmol) were then added to this solution and the resultant mixture was stirred at room temperature for 24 h under argon atmosphere. The volatiles were then removed under reduced pressure and the residue was chromatographed on silica gel with $CH_2Cl_2$/MeOH 40:1 as the eluent to give **34** as a colorless syrup (261 mg, 65%). $[\alpha]_D^{27}=-19.5$ (*c* 0.8, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 0.39 (dd, *J*=8.2, 5.2 Hz, 1H), 1.35 (dd, *J*=5.2, 4.2 Hz, 1H), 1.54 (ddd, *J*=8.2, 5.4, 4.2 Hz, 1H), 1.6 (br, 3H), 3.14 (d, *J*=9.8 Hz, 1H), 3.25 (d, *J*=9.8 Hz, 1H), 3.96 (dd as t, *J*=5.4 Hz, 1H), 4.38 (dd, *J*=5.9, 5.4 Hz, 1H), 4.48 (d, *J*=5.9 Hz, 1H), 7.27 (m, 9H), 7.43 (m, 6H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 9.9, 28.1, 34.2, 66.6, 69.8, 71.7, 73.8, 86.7, 127.1, 127.9, 128.6, 143.9; HRMS (*m*/*z*) calcd for $C_{26}H_{26}NaO_4$ 425.1723 ($M^+$+Na), found 425.1716.

**4.8.5. {(1*R*,2*R*)-2-(Hydroxymethyl)-2-[(trityloxy)-methyl]cyclopropyl}methanol (35).** To a solution of compound **34** (201 mg, 0.5 mmol) in THF/$H_2O$ 1:1 (20 mL) was added at 0°C, $NaIO_4$ (610 mg, 2.85 mmol), the mixture was stirred at this temperature for 45 min and then allowed to warm at room temperature. The resultant mixture was then extracted with $CH_2Cl_2$ (3×50 mL), the organic layer was dried over $Na_2SO_4$, the solvent was evaporated off on a rotary evaporator and the residue was dissolved in dry EtOH (30 mL). $NaBH_4$ (57 mg, 1.5 mmol) was then added to this solution and the mixture was stirred at room temperature for 30 min under argon atmosphere. The solvent was then removed on a rotary evaporator and the residue was treated again with $NaIO_4$ and $NaBH_4$ according to the procedures described above. Compound **35** was obtained as a colorless oil (103 mg, 55% overall) by chromatographing the final residue on silica gel with $CH_2Cl_2$/ethyl acetate as the eluent. $[\alpha]_D^{27}=-27.7$ (*c* 0.5, $CHCl_3$); $^1H$ NMR ($CDCl_3$) $\delta$ 0.35 (dd as t, *J*=5.4 Hz, 1H), 0.56 (dd, *J*=8.3, 5.4 Hz, 1H), 1.25 (br s, 1H), 1.30 (m, 1H), 1.65 (br, 1H), 3.02 (d, *J*=9.8 Hz, 1H), 3.19 (d, *J*=9.8 Hz, 1H), 3.28 (d, *J*=11.7 Hz, 1H), 3.32 (dd, *J*=12.2, 5.4 Hz, 1H), 4.05 (dd, *J*=12.2, 5.4 Hz, 1H), 4.15 (d, *J*=11.7 Hz, 1H), 7.30 (m, 9H), 7.46 (m, 6H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 13.7, 24.8, 26.7, 63.6, 65.7, 70.9, 87.0, 127.2, 128.0, 128.6, 143.6; HRMS (*m*/*z*) calcd for $C_{25}H_{26}NaO_3$ 397.1774 ($M^+$+Na), found 397.1774.

**4.9. [(1*S*,2*R*)-2-[(Benzoyloxy)methyl]-1-(hydroxy-methyl)cyclopropyl]methyl benzoate (36)**

Benzoyl chloride (56 mg, 0.4 mmol) was added to a solution of **35** (75 mg, 0.2 mmol) in dry pyridine (10 mL) at 0°C and the mixture was stirred at the same temperature for 1 h. Saturated aqueous $NH_4Cl$ was then added and the mixture was extracted with $CH_2Cl_2$ (3×50 mL). The solvent was removed, the residue was dissolved in $HCO_2H/Et_2O$ 3:2 (20 mL) and the resultant mixture was stirred at 0°C for 30 min. The mixture was diluted with $H_2O$ (20 mL) and $Et_2O$ (20 mL), then neutralized by adding saturated $Na_2CO_3$ and extracted with $CH_2Cl_2$ (3×50 mL). The organic layer was washed with $H_2O$ and dried over $Na_2SO_4$ to give after evaporating the solvent and chromatographing the final residue on silica gel with hexane/ethyl acetate as the eluent, compound **35** as a colorless oil (41 mg, 60% overall) with NMR data identical to those reported in the literature.[3a] $[\alpha]_D^{27}=-5.5$ (*c* 0.2, $CHCl_3$).

**4.9.1. Ethyl (4*R*,5*S*,6*R*)-4,5,6-tribenzyloxy-3-oxo-7-octenoate (41).** To a solution of **39** (574 mg, 1 mmol) in 95% EtOH (10 mL) activated Zn (654 mg, 10 mmol) was added and the mixture was refluxed with vigorous stirring under argon atmosphere until complete disappearance of **39** (~2 h). The mixture was cooled to room temperature, the solids were filtered off and the solvent was evaporated to give pure aldehyde **40**. Ethyl diazoacetate (130 mg, 1.1 mmol) was added dropwise to this compound at 0°C with vigorous stirring under argon atmosphere. After 10 min at the same temperature the mixture was chromatographed on a column of silica gel with hexane/ethyl acetate as the eluent, to give compound **41** as a colorless oil (328 mg, 65% overall). $[\alpha]_D^{27}=+12.7$ (*c* 1.0, $CHCl_3$); IR (neat) 1740, 1715, 1640 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) of the keto form $\delta$ 1.20 (t, *J*=6.9 Hz, 3H), 3.49 (d, *J*=16.4 Hz, 1H), 3.65 (d, *J*=16.4 Hz, 1H), 3.79 (dd, *J*=5.8, 3.8 Hz, 1H), 4.09 (q, *J*=6.9 Hz, 2H), 4.11 (m, 1H), 4.17–5.01 (m, 7H), 5.29 (m, 2H), 5.78 (m, 1H), 7.34 (br s, 15H); distinguishable peak for the enol form $\delta$ 11.93 (s), (from integration keto/enol ~20:1); $^{13}C$ NMR ($CDCl_3$) of the keto form $\delta$ 14.1, 46.9,

61.1, 71.0, 73.4, 74.7, 80.6, 82.7, 85.3, 119.6, 127.6, 127.8, 127.9, 128.0, 128.1 (two peaks), 128.3, 128.4, 128.5, 134.8, 137.2, 137.7, 138.0, 167.8, 204.0; MS *m/z* (%) 502 ($M^+$, 9), 431 (5), 395 (22), 357 (9), 266 (13), 249 (21), 197 (24), 181 (59), 105 (66), 91 (100), 77 (39), 65 (23). Anal. calcd for $C_{31}H_{34}O_6$: C, 74.08; H, 6.82. Found: C, 74.31; H, 6.72.

**4.9.2. Ethyl (4*R*,5*S*,6*R*)-2-diazo-4,5,6-tribenzyloxy-3-oxo-7-octenoate (42).** To a solution of keto ester **41** (502 mg, 1 mmol) in absolute ethanol (6 mL), tosyl azide (260 mg, 1.3 mmol) and $Et_3N$ (1.3 mL) were added and the mixture was stirred at room temperature for 10 h. The volatiles were then removed on a rotary evaporator and the residue was chromatographed on a column of silica gel with hexane/ethyl acetate as the eluent to give diazo compound **42** as a colorless oil (445 mg, 84%). $[\alpha]_D^{27}=+27.7$ (*c* 1.0, $CHCl_3$); IR (neat) 2125, 1700, 1665 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.18 (t, *J*=7.2 Hz, 3H), 3.91 (dd, *J*=7.8, 2.5 Hz, 1H), 4.07 (q, *J*=7.2 Hz, 1H), 4.10–4.75 (m, 8H), 5.15 (m, 2H), 5.74 (m, 1H), 7.34 (br s, 15H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 14.3, 61.3, 70.9, 73.1, 74.3, 78.9, 82.8, 83.2, 119.7, 127.4, 127.7, 127.8 (two overlapping peaks), 128.0, 128.2, 128.3 (two overlapping peaks), 129.2, 134.7, 137.2, 138.2, 138.5, 160.8, 188.9 (*C*=$N_2$ not appeared); MS *m/z* (%) 500 ($M^+-N_2$, 25), 439 (44), 393 (75), 339 (51), 337 (29), 303 (44), 271 (40), 195 (32), 181 (100), 147 (66), 105 (31), 92 (83), 91 (63), 77 (28), 65 (55), 51 (6), 39 (21). Anal. calcd for $C_{31}H_{32}N_2O_6$: C, 70.44; H, 6.10, N, 5.30. Found: C, 70.49; H, 6.23; N, 5.15.

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