nm, 30 min) of **7** rapidly produced lactone **4** and ketene **5**, but no absorptions assigned to ketone **6** and ozone grew at all. The photolabile intermediate **7**, which was a precursor of **4** and **5**, should be reasonably identified as the corresponding dioxirane.[10] The photochemical conversion of dioxirane to ester in matrices has been well established.[1,2]

The reaction of bicyclo[6.3.0]undeca-2,4,6,8,11-pentaen-10-ylidene (**1**) with O_2 is summarized in Scheme I. Though this scheme is apparently consistent with that of the reaction between cyclopentadienylidene and O_2,[1,11] there are some important differences in the properties of the intermediates. The transition of cyclopentadienone oxide occurs at 420 nm,[1c] while the maximum of the $\pi \rightarrow \pi^*$ transition of **3** is recorded at 582 nm. This considerable red shift is explained in terms of not only the extension of the conjugated π-system, but the π-electron-donating ability of the bicyclo[6.3.0]undecapentaenyl skeleton owing to the contribution of the stable bicyclic 10π cation, as shown in the canonical structure **3a**. This finding is in accord with CNDO/S predictions, where the $\pi \rightarrow \pi^*$ transition of tropone oxide was calculated to occur at 546 nm.[4] In the IR spectrum of **3**, the O–O stretching vibration is found at 931 cm^{-1}, which is in the range of the O–O stretchings reported for other carbonyl oxides.[1,2] This result is also in line with the prediction that the O–O bond lengths are little affected by the substitution of π-donating ring system.[4]

No simple explanation for the photochemical stability of **3** can be offered at the present time.[12] If the zwitterionic structure **3a** contributes largely to the electronic structure of **3**, this species is expected to be highly nucleophilic and to react as a 1,3-dipole. Experiments to reveal the reactivity of **3** are planned in our laboratories.

(10) The IR data of **7** are as follows. The relative intensities and ^{18}O isotopic shifts in cm^{-1} are designated in parentheses. **7**: 1537 (w, 1), 1399 (w, 4), 1386 (w, 18), 1343 (s, 9), 1327 (m, 9), 1135 (w, 4), 915 (w, 1), 874 (m, 2), 700 (m, 0).

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Synthesis and Reactions of Ester-Substituted Fulvenes. A New Route to $\Delta^{9(12)}$-Capnellene

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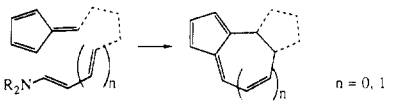
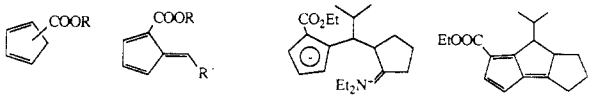
Summary: The condensation of cyclopentadienecarboxylic acid ester with aldehydes produces ester-substituted fulvenes regioselectively. The products undergo both intermolecular and intramolecular [6 + 2] cycloadditions to give the synthetically useful linearly fused tricyclopentanoids. A formal synthesis of $\Delta^{9(12)}$-capnellene is reported.

We previously reported the use of intermolecular and intramolecular cycloadditions of dienamines[2] and enamines[3] to fulvenes. The latter is a useful method for the synthesis of tricyclopentanoids, as shown below.



One drawback to this method is that the fulvene ring is always derived from cyclopentadiene. Consequently, three of the positions of the ring are unsubstituted in the product, so that the elaboration of these tricyclic intermediates into natural products presents difficulties which hinder the generality of this approach. One apparent solution to this is the use of a substituted cyclopentadiene as a starting material. Among the cyclopentadienes, cyclopentadienecarboxylic ester from cracking of Thiele's ester is cheap and easily available.[4] However, the regioselectivity of condensation of a substituted cyclopentadiene with an aldehyde is a potential complication. Ficini and co-workers reported earlier the reaction of ynamines with methyl cyclopentadienecarboxylate.[5] Two regioisomeric aminofulvenes were obtained in a 6:1 ratio. We have found that it is possible to prepare fulvenes from aldehydes regioselectively with the ester substituent at C-2 of the fulvene. These new types of fulvenes undergo cycloadditions regioselectively to give synthetically useful tricyclopentanoids. From one of these, a formal synthesis of $\Delta^{9(12)}$-capnellene was achieved.

When ester **2** was treated with isobutyraldehyde in THF at −30 °C in the presence of aqueous methylamine and a buffer solution consisting of methylamine and acetic acid (pH 8–9), fulvene **3** was obtained in 60% yield after chromatography on silica gel. These reaction conditions gave the fulvene in moderate yield, whereas use of strong bases or preformed cyclopentadienide gave only poor yields of product. Similarly, fulvenes **4** and **5** were prepared from pivalaldehyde in 40% and 55% yields, respectively.[6]



1 R = Me
2 R = Et

3 R = Et, R' = isopropyl
4 R = Me, R' = tert-butyl
5 R = Et, R' = tert-butyl

7

8

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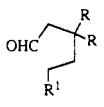
(5) Ficini, J.; Revial, G.; Jeannin, S. *Tetrahedron Lett.* **1981**, *22*, 2367.

0022-3263/90/1955-4504$02.50/0

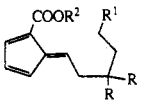
Only a single fulvene, resulting from the condensation of the aldehyde on the cyclopentadiene carbon α to the ester, is found in each case. The new fulvenes, **3–5**, are yellow liquids and were purified by chromatography on either alumina or silica gel. The structures of the fulvenes were confirmed by their ^{1}H NMR spectra. Due to the anisotropy of the ester carbonyl group, the exocyclic C-6 protons of the fulvenes resonate downfield as compared to the corresponding unsubstituted fulvenes. For example, the C-6 proton signal of **3** is centered at δ 7.33, while the corresponding signal of the unsubstituted fulvene is centered at δ 5.40. This establishes both the regioselectivity and stereoselectivity of the reaction. The ring protons of the fulvenes exhibit very similar ABX patterns in the ^{1}H NMR spectra. The peaks of hydrogens at C-3, C-4, and C-5 of fulvene **5** are centered at δ 7.30, 6.99, and 6.50, respectively. Therefore, the regioselectivity is the same as that reported by Ficini and co-workers, but higher. These regioselectivities may be the result of the thermodynamic control of the first step of the reaction, resulting from chelation in the intermediate. Similar regioselectivity is observed in the reactions of formylcyclopentadiene with ethoxydipropylcyclopropenyl cation[7] and from the electrophilic reactions of 6-donor-substituted fulvenes.[8]

These fulvenes were found to undergo ready cycloadditions to enamines. Intermolecular cycloaddition of the fulvene **3** with 1-(*N*,*N*-diethylamino)cyclopentene, **6**, was effected by slow addition of a solution of the enamine in ether to a dilute ethereal solution of the fulvene at 0 °C. Nucleophilic addition of **6** to the electrophilic 6-position of the fulvene, **3**, and cyclization of the resulting zwitterionic intermediate, **7**, with loss of diethylamine resulted in the formation of the tricyclic fulvene, **8**, which could be easily purified by chromatography on silica gel. The product was obtained in 56% yield. No attempt was made to determine the stereochemistry of this compound.[6]

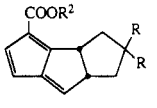
The formation of **8** demonstrates a new way to prepare the tricyclopentanoid skeleton, substituted on the unsaturated ring. To extend the scope of this cyclization, intramolecular versions of these enamine cycloadditions were also investigated.



9 R = H, R^1 = $CH(OMe)_2$
13 R = Me, R^1 = $\underline{CHO(CH_2)_3O}$



10 R = H, R^1 = $CH(OMe)_2$, R^2 = Me
11 R = H, R^1 = CHO, R^2 = Me
14 R = Me, R^1 = $\underline{CHO(CH_2)_3O}$, R^2 = Et

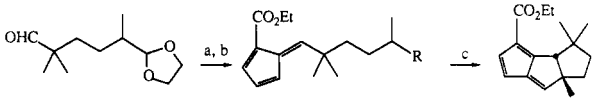


12 R = H, R^2 = Me
15 R = Me, R^2 = Et

The condensation of ketal aldehyde **9** with ester **1** afforded fulvene ester **10** in 55% yield. Hydrolysis of **10** with dilute acid and subsequent treatment of the aldehyde **11** with 1.1 equiv of *N*-methylaniline in anhydrous ether at room temperature in the presence of 4-Å molecular sieves provided the tricyclic ester **12** (25% overall in two steps). The conditions here are similar to those described recently for intramolecular Michael reactions of enamines.[9] This strategy of the construction of tricyclic ring also works when there are alkyl groups on the side chain of aldehyde **11**. For instance, **13**[10] reacted with **2** in the presence of *N*-methylaniline in THF to give fulvene, **14**, in 63% isolated yield. The aldehyde was then deprotected using diluted hydrochloric acid in THF and directly cyclized into the tricyclic fulvene **15** (24%), using 4-Å molecular sieves and *N*-methylaniline as the catalyst.

To demonstrate the use of this method in the construction of natural tricyclopentanoids, a formal synthesis of $\Delta^{9(12)}$-capnellene was performed. Molecular model inspection shows that the formation of the unproductive trans intermediate, which caused the low yields in the final steps to **12** and **15**, could be depressed in the presence of an alkyl group on the α-position of the open chain aldehyde. Therefore a higher yield of cyclization was expected in this case.

Aldehyde **16**, which was synthesized from 2-methylbutyrolactone in five steps, was condensed with **2** to form fulvene **17** in 58% yield. The hydrolysis of **17** with dilute



16 **17** R = $\underline{CHO(CH_2)_2O}$ **18** R = CHO **20**

(a) **2**, THF, 40% aqueous methylamine, HOAc, 58%; (b) HCl, THF; (c) *N*-methylaniline, 4-Å molecular sieves

hydrochloric acid (0.12 N) for 50 h afforded a mixture of two aldehydes, **18** and the partially cyclized aldehyde **19**, in a 1:1 ratio. When the mixture was treated, without separation, with *N*-methylaniline, **18** cyclized into **20**, but **19** remained unchanged because of the weakness of the base used. The latter, however, could be cyclized with basic alumina in DME in 84% yield. The overall yield of **20** from **17** is 52%. When **17** was hydrolyzed with more concentrated acid (10% HCl), **19** was obtained in 89% yield together with 2% of **18**. The behavior of **19** in cyclization indicates that the aldehyde group is cis to the cyclopentadiene ring.

Hydrogenation of **20** in the presence of Pd–C (10%) catalyst showed very low stereoselectivity; four saturated esters were formed. Although there have been reports that PtO_2 or Pt–C catalyzed reductions gave the thermodynamically most stable hydrogenated isomer,[11] the reduction of **20** under these conditions gave only the products having hydrogen added on the less hindered side, as indicated by the subsequent conversions of the products to the known saturated ketone. Attempted reduction of **20** using a large excess of sodium in HMPA[12] gave only starting material after the workup. Birch reduction with lithium in ammonia at −78 °C afforded **21**, with only one double bond reduced. The reduction with magnesium in methanol,[13] however, was very effective; **22** was formed in 64% yield without the presence of isomeric impurities.

(6) All new compounds were characterized by ^{1}H NMR, IR, and high-resolution mass spectroscopy. Some NMR ($CDCl_3$) data follow. **3**: δ 7.63 (d, 1 H, J = 10 Hz), 7.48 (1 H), 6.92 (1 H), 6.57 (1 H), these three groups of peaks are an ABX pattern, 4.34 (q, 2 H, J = 7 Hz), 3.42–2.78 (m, 1 H), 1.37 (t, 3 H, J = 7 Hz), 1.21 (d, 3 H, J = 7 Hz). **4**: δ 7.81 (br s, 1 H), 7.32 (1 H), 7.02 (1 H), 6.52 (1 H), these three groups of peaks are an ABX pattern, 3.80 (s, 3 H), 1.35 (s, 9 H). **5**: δ 7.80 (br s, 1 H), 7.30 (1 H), 6.99 (1 H), 6.50 (1 H), these three groups of peaks are an ABX pattern, 4.25 (q, 2 H, J = 7 Hz), 1.33 (t, 3 H, J = 7 Hz), 1.31 (s, 9 H). **8**: δ 6.77 (d, 2 H, J = 6 Hz), 5.99 (d, 2 H, J = 6 Hz), 4.27 (q, 2 H, J = 7 Hz), 2.80–0.83 (br m, with peaks at 1.35 (t, J = 7 Hz), 0.98 (d, J = 7 Hz), and 0.96 (d, J = 7 Hz) due to diastereomers, 18 H).

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(10) Compound **13** was prepared from commercially available ethyl 2-cyano-3-methylbut-2-enoate in four steps; see supplementary material.

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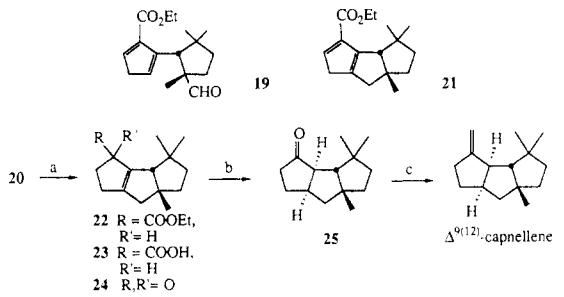

(a) (1) Mg, MeOH, rt, 64%; (2) 10% NaOH, 60 °C, 100%; (3) LDA, -78 °C, THF, HMPA; (4) O_2, rt; H_3O^+; (5) $Pb(OAc)_4$, 57%, three steps overall; (b) (1) Li, NH_3; (2) PDC, CH_2Cl_2, 62% overall; (c) $CH_2{=}PPh_3$

Acid **23**, formed by hydrolysis of **22**, was treated with LDA followed by oxygen to give a hydroxy acid, which was cleaved by lead tetraacetate to form the unsaturated ketone **24**. The ketone was then reduced with lithium in ammonia, and the product was oxidized with PDC in methylene chloride to give saturated ketone **25**. This has spectra identical with those of the ketone obtained earlier by Little and co-workers.[14] The reaction of **25** with a Wittig reagent to give $\Delta^{9(12)}$-capnellene has been reported.[14]

In summary, the ester-substituted fulvenes formed from the condensation of cyclopentadienecarboxylates can be use to construct linearly fused tricyclopentanoids by intermolecular[15] or intramolecular reactions with the double bonds of enamines or enols.

Acknowledgment. We are grateful to the National Institutes of Health for financial support of this research. We thank Professor T. Hudlicky for helpful suggestions and Professor R. D. Little for providing the spectra of compound **25**.

Supplementary Material Available: Schemes for the preparation of the reaction intermediates and NMR spectra of the compounds reported in this paper (37 pages). Ordering information is given on any current masthead page.

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(15) see also Wu, T.-C.; Houk, K. N. *J. Am. Chem. Soc.* **1983**, *105*, 5308.

Stereoselective Synthesis of 3-Amino 1,2-Diols via Intermolecular Pinacol Cross-Coupling of α-[(Alkoxycarbonyl)amino] Aldehydes with Aliphatic Aldehydes. Short Asymmetric Syntheses of Two 2,3,6-Trideoxy-3-amino Sugars

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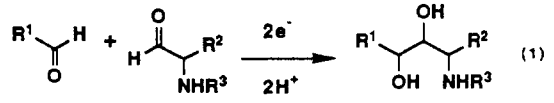
Summary: *syn,syn*-3-Amino 1,2-diols are prepared via a pinacol cross coupling reaction between *N*-Cbz- or *N*-Boc-α-amino aldehydes and aliphatic aldehydes. Application of this methodology to the syntheses of two amino sugars starting from *N*-Cbz-L-aspartic acid are described.

Amino sugars containing the 3-amino 1,2-diol subunit are important constituents of a variety of antibiotics.[1] Consequently, there has been a long-standing interest in the synthesis of such compounds. The majority of synthetic efforts in this area have focused on manipulation of naturally occurring carbohydrates.[1] However, in the last decade numerous acyclic synthetic approaches to these sugars have appeared.[2] One potentially versatile synthesis of the 3-amino 1,2-diol unit would involve the reductive coupling of an α-amino aldehyde with another aldehyde (an intermolecular pinacol cross-coupling reaction) (eq 1).



(1)

Noteworthy features of this reaction would be the construction of the diol group in a single carbon–carbon bond forming reaction starting from readily available and optically active starting materials. We have recently reported the first efficient and stereoselective method for coupling two different, yet electronically similar aldehydes, employing the easily prepared vanadium(II) reagent, $[V_2Cl_3(THF)_6]_2[Zn_2Cl_6]$ (**1**).[3] Successful pinacol cross-coupling generally requires slow addition of a chelating aldehyde to a mixture of **1** and a nonchelating aldehyde, followed by an aqueous workup. α-[(Alkoxycarbonyl)amino] aldehydes[2c] seemed likely candidates for this reaction. Herein, we report a new route to 3-amino 1,2-diols employing such aldehydes and apply this method to the syntheses of two amino sugars starting from *N*-Cbz-L-aspartic acid.

Slow addition (ca. 1 h) of *N*-Cbz- or *N*-Boc-α-amino aldehydes to a mixture of **1** and an aliphatic aldehyde in dichloromethane leads to the stereoselective and high yield synthesis of *N*-Cbz- or *N*-Boc-*syn,syn*-3-amino 1,2-diols (Table I).[4] The major isomer (*syn,syn*) is that expected from chelation control.[5,6] The α-[(alkoxycarbonyl)amino]

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(2) For reviews that contain discussions concerning the acyclic synthesis of amino sugars, see: (a) McGarvey, G. J.; Kimura, M.; Oh, T.; Williams, J. M. *J. Carbohydr. Chem.* **1984**, *3*, 125. (b) Hauser, F. M.; Ellenberger, S. R. *Chem. Rev.* **1986**, *86*, 35. (c) Jurczak, J.; Golebiowski, A. *Chem. Rev.* **1989**, *89*, 149.

(3) Freudenberger, J. H.; Konradi, A. W.; Pedersen, S. F. *J. Am. Chem. Soc.* **1989**, *111*, 8014.

(4) Determining the ratio of diastereomers obtained from these reactions by ^1H and ^{13}C NMR spectroscopy is complicated by the presence of rotamers resulting from the (alkoxycarbonyl)amino group. See the supplementary material for further details. The *syn,syn* stereochemistry was established via an X-ray structural analysis of the hydroxyoxazolidinone obtained from reacting **2** with 1 equiv of sodium hydride in tetrahydrofuran.

(5) For reviews of chelation-controlled addition reactions, see: (a) Reetz, M. T. *Organotitanium Reagents in Organic Synthesis*; Springer Verlag: Berlin, 1986. (b) Reetz, M. T. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 556. See ref 2c for specific examples of chelation-controlled reactions of *N*-protected α-amino aldehydes.

0022-3263/90/1955-4506$02.50/0