1 H, J = 6.2, 15.0 Hz), 3.37-3.80 (m, 1 H), 4.78 (d, 1 H, J = 5.3 Hz), 7.19-7.38 (m, 4 H). Selective irradation of the signal at δ 3.37-3.80 collapsed the doublet at δ 4.78 to a singlet. ^{13}C NMR ($CDCl_3$) 39.3, 55.0, 75.3, 125.1, 125.4, 127.0, 128.4 ppm.

The *cis*-*O*,*N*-diacetate of **39** was prepared according to the procedure of Wenkert and co-workers:[30] mp 117-120 °C (benzene-hexanes) (lit.[30] mp 118-120 °C); ^{1}H NMR ($CDCl_3$) δ 2.01 (s, 3 H), 2.05 (s, 3 H), 2.72-3.50 (m, 2 H), 4.66-5.04 (m, 1 H), 6.00 (d, 1 H, J = 6.0 Hz), 7.07-7.49 (m, 4 H); ^{13}C NMR ($CDCl_3$) 21.1, 23.2, 36.9, 51.6, 76.3, 124.9, 126.7, 127.3, 129.7, 139.2, 141.7, 169.8, 169.9 ppm.

Epimerization Studies of *trans*-2-Amino-1-indanol (40). A solution of **40** (70 mg, 0.5 mmol) in aqueous 2.3 N $HClO_4$ (14%, 4 mL) was heated to reflux (1 h). The reaction was then basified with aqueous 6 N NH_4OH and the solution extracted with methylene chloride (3 × 20 mL). The organic layers were dried (K_2CO_3), concentrated in vacuo, and then analyzed directly by ^{13}C NMR. Comparison of the peak intensities of comparable carbon atoms indicated that both *cis*- and *trans*-2-amino-1-indanol (**39** and **40**, respectively) were present in an approximate ratio of 1:2.2.

Repetition of this reaction both at 0 °C (1 h) and at room temperature (30 min) did not lead to the formation of the cis-adduct **39** (TLC analysis).

Epimerization Studies of *cis*-2-Amino-1-indanol (39). The preceding reaction was repeated with a solution of **39** (70 mg, 0.5 mmol) in aqueous 2.3 N $HClO_4$ (14%, 4 mL). ^{13}C NMR analysis of the reaction after reflux (1 h) and workup indicated the presence of *cis*- and *trans*-2-amino-1-indanol (**39** and **40**, respectively) in a ratio of 1.4:1.

Repetition of this reaction both at 0 °C (1 h) and at room temperature (30 min) did not lead to the formation of the trans-adduct **40** (TLC analysis).

Kinetic Study of Ring Opening of 4 with $HClO_4$. A solution of **4** (310 mg, 3.13 mmol) in 14% $HClO_4$ in D_2O (2.3 N, 3.13 mL) was transferred to a 10-mm NMR tube. Acetonitrile (0.1 mL) was added as an internal standard and then the tube sealed with a torch. The NMR tube was then immersed in an oil bath and maintained at 85 ± 1 °C. At periodic intervals, the tube was removed and the ^{13}C NMR spectrum recorded. The reaction was monitored for 3 h. The rate of ring opening was determined by comparing the peak heights of comparable carbon signals in the starting material and product.

Kinetic Study of Ring Opening of 5 with $HClO_4$. With use of the procedure described for **4**, the rate of ring opening of **5** (370 mg, 3.27 mmol) was determined in 14% $HClO_4$ in D_2O (2.3 N, 3.27 mL) at 85 ± 1 °C. The reaction was monitored for 3 h.

Kinetic Study of Ring Opening of 6 with $HClO_4$. An ice-cold aqueous solution of 2.3 N $HClO_4$ (14%, 8 mL) was added to cold **6** (1.00 g, 7.6 mmol). The solution was stirred at 0 °C. The reaction was monitored for 40 min. At periodic intervals aliquots (2 mL) were removed and quenched with ice-cold dilute aqueous NH_4OH. The basic aqueous solution was then extracted with methylene chloride (3 × 15 mL), and the combined organic layers were dried (K_2CO_3), filtered, and evaporated to dryness. The residue was directly analyzed by ^{13}C NMR. The rate of ring opening was determined by comparing the peak heights of comparable carbon signals in the starting material and products.

Measurement of pK_a of *trans*-6-Azabicyclo[3.1.0]hexan-2-ol (4). A dilute (2.5×10^{-4} M) aqueous solution of **4** was made up with CO_2-free distilled water. The titrations were performed automatically with standardized aqueous 0.1 N HCl. The cell was thermostated at 25 ± 0.2 °C Each titration was continued beyond the end pont. The pK_a value was determined by standard graphical methods with the average value for three measurements reported.

Acknowledgment. We thank the National Institutes of Health (Grant No. CA29756) and the Robert A. Welch Foundation for their generous support of this research.

Registry No. **4**, 86288-25-7; **5**, 86288-26-8; **6**, 26536-31-2; **6** (*N*-phenylcarbamoyl derivative), 50673-02-4; **7**, 86333-90-6; **9**, 3212-60-0; **10**, 86307-64-4; **11**, 86307-65-5; **12** (isomer 1), 86288-27-9; **12** (isomer 2), 86333-91-7; **13** (isomer 1), 86333-92-8; **13** (isomer 2), 86333-93-9; **14**, 86288-28-0; **15**, 86333-94-0; **16**, 29782-88-5; **17** (isomer 1), 86288-29-1; **17** (isomer 2), 86333-95-1; **18** (isomer 1), 86288-30-4; **18** (isomer 2), 86333-96-2; **19** (isomer 1), 86288-31-5; **19** (isomer 2), 86333-97-3; **20**, 930-30-3; **21**, 40459-88-9; **22**, 86288-32-6; **23** (isomer 1), 86288-33-7; **23** (isomer 2), 86333-98-4; **24** (isomer 1), 86288-34-8; **24** (isomer 2), 86333-99-5; **25** (isomer 1), 86288-35-9; **25** (isomer 2), 86334-00-1; **26** (isomer 1), 86288-36-0; **26** (isomer 2), 86334-01-2; **27**, 95-13-6; **28**, 86288-37-1; **29**, 86288-38-2; **30**, 86288-39-3; **31**, 86288-40-6; **32**, 86288-41-7; **33**, 86288-42-8; **34**, 86288-43-9; **38**, 86288-44-0; **39**, 23337-80-6; **40**, 13575-72-9.

9,10-*syn*-Podocarpane Diterpenoids. An Approach to the Tricyclic Skeleton by Diels-Alder Cycloaddition. Related Crystal Structure Determination and Theoretical Aspects

Fulvia Orsini and Francesca Pelizzoni*

Centro di Studio per le Sostanze Organiche Naturali del CNR, Istituto di Chimica Organica della Facoltà di Scienze della Università, 20133 Milano, Italy

Demetrio Pitea

Istituto di Chimica Fisica, Università di Milano, 20133 Milano, Italy

Ezio Abbondanti and Angelo Mugnoli

Istituto di Chimica Fisica della Università di Genova Palazzo delle Scienze, 16132 Genova, Italy

Received November 15, 1982

The cycloaddition of 2-carbomethoxy-1,4-benzoquinone with vinylcyclohexene is reported. The configuration at C-9 has been determined by X-ray diffraction on compound **5**, whose structure is strictly related to that of the adduct **3**, which is a useful intermediate for the total synthesis of 9,10-*syn*-podocarpane diterpenoids. It is shown that a complete PMO treatment can account for the regio- and stereochemical outcome of the reaction.

We report herein the use of the Diels-Alder reaction in a short stereospecific approach to the total synthesis of the 9,10-*syn*-podocarpane diterpenoids, a class of rather unusual natural compounds of biological interest. Many examples have been reported, such as Annonalide in *Annona coriacea*,[1] Momilactones in *Oriza sativa*,[2] Icacina and re-

0022-3263/83/1948-2866$01.50/0

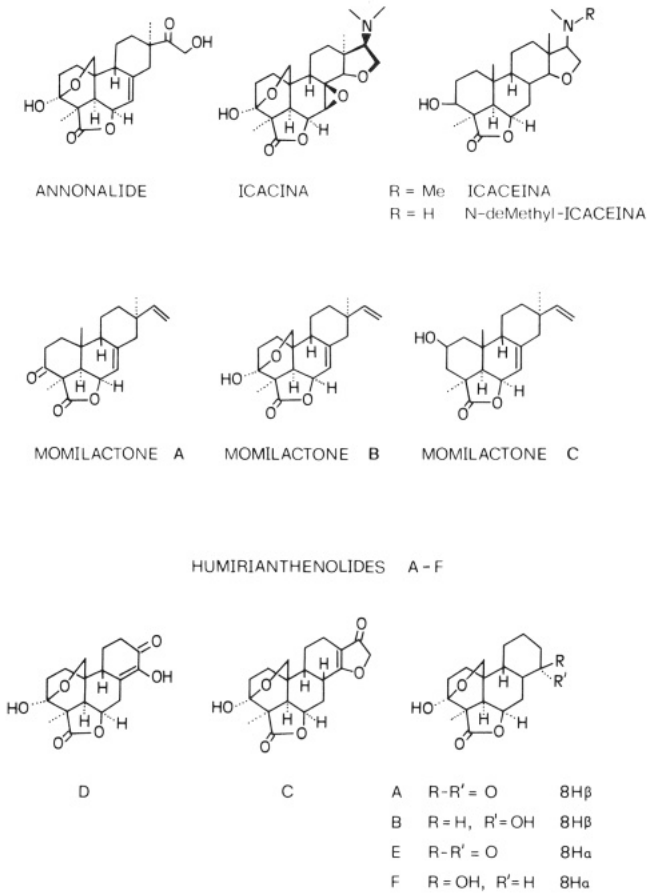
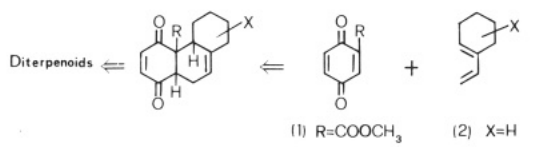


Figure 1. 9,10-*syn*-Podocarpane diterpenoids.

Scheme I



lated alkaloids in *Icacina guestfeldtii*,[3] and Humirianthenolides in *Humirianthera rupestris*[4] (Figure 1).

A retrosynthetic analysis suggested that the tricyclic skeleton of 9,10-*syn*-podocarpane compounds could be built up by coupling of an appropriately functionalized vinyl cyclohexene with quinones to give Diels–Alder adducts. These adducts should contain the required skeletal features and those functionalities which could be modified later in order to obtain the desired diterpenoids (Scheme I).

This approach to hydrophenanthrenes could seem "conceptually obvious"; however, a main question had to be answered: would the cycloaddition follow the "endo" rule, *this being essential to obtain the required 9,10-syn arrangement*? This rule appears to be a useful guide in many additions, but it is not always obeyed.[5] In similar reported condensations (in that, for example, between the 2-carbomethoxy-1,4-benzoquinone and 1-acetoxy-1-vinylcyclohexene)[6] the stereochemical outcome of the reaction was assumed on the basis of analogies and not verified in this sense. Our second aim was to fit in the regiochemical outcome of the reaction which was experimentally determined with perturbational calculations. To clarify these points we have investigated the cycloaddition of the quinone **1** with the vinylcyclohexene **2** from an experimental and theoretical point of view.

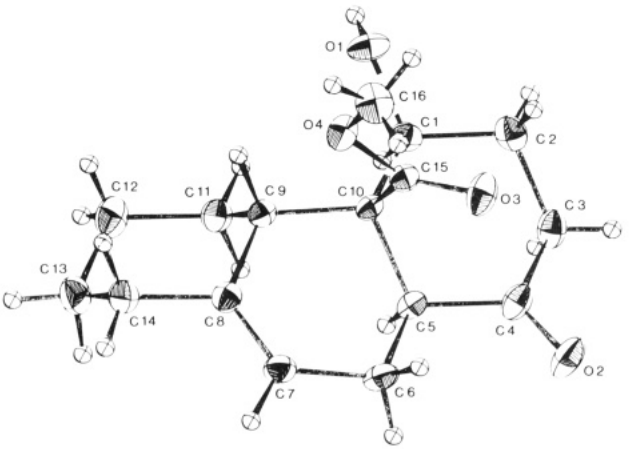
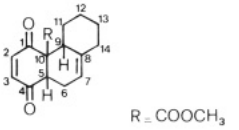


Figure 2. Thermal ellipsoid plot of the compound **5** at the 0.30 probability level. Hydrogen atoms, treated as isotropic, are on an arbitrary scale.

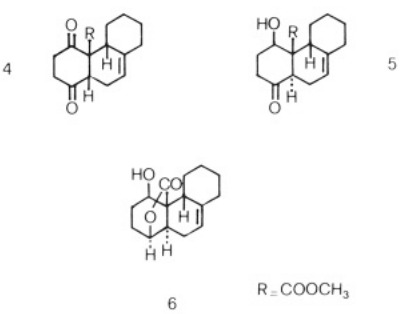
Results and Discussion

2-Carbomethoxy-1,4-benzoquinone (**1**) reacts with 1-vinylcyclohexene (**2**) to give the adduct **3**. Its spectro-



3

scopic properties, reported in the Experimental Section, settle all the structural features but the relative configuration at C-9, which has been determined by X-ray diffraction. To obtain a suitable material for the crystal structure determination, we reduced the adduct **3** with zinc dust in acetic acid to the dione **4** which was reduced to the ketol **5** with $NaBH_4$ with concomitant inversion of the configuration at C-5. The lactone **6** was obtained as a byproduct. The results of the crystal structure determination of compound **5**[7] do confirm the regio- and stereoselectivity of the Diels–Alder reaction and establish the stereochemistry around atoms C-5, C-9, and C-10 (see Figure 2). Whereas in rings A and C the torsion angles



(1) Orsini, F.; Pelizzoni, F.; McPhail, A. T.; Onan, K. D.; Wenkert, E. *Tetrahedron Lett.* **1977**, 1085 and references quoted therein.
(2) Kato, T.; Aizawa, H.; Tsunakawa, M.; Sasaki, N.; Kitahara, G.; Takahashi, N. *J. Chem. Soc., Perkin Trans. 1* **1977**, 250.
(3) On'okoko, P.; Vanhaelen, M. *Phytochemistry* **1980**, *19*, 303 and references quoted therein.
(4) Roque, N. F.; Zoghbi, G. B.; Gottlieb, H. E. *Phytochemistry* **1981**, *20*, 1669.
(5) Carruthers, W. "Some Modern Methods of Organic Synthesis", 2nd ed.; Cambridge University Press: New York, 1978.
(6) Ansell, M. F.; Culling, G. C. *J. Chem. Soc.* **1961**, 2908.
(7) A preliminary account was reported by: Mugnoli, A.; Moretto, A.; Orsini, F.; Pelizzoni, F. 12th International Congress of Crystallography, Ottawa, Aug 1981.

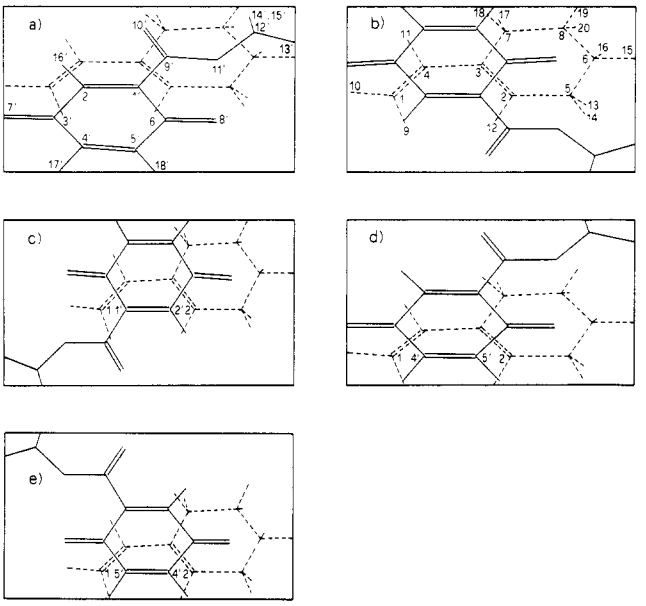


Figure 3. Transition-state models as projections on the *xy* plane: (a) A-exo, (b) A-endo, (c) B-endo, (d) C-endo, (e) D-endo.

reflect the typical chair conformation, the puckering of ring B is limited by the presence of the C(7)–C(8) double bond. The internal strain of the molecule is noticed by some large $C(sp^3)$–$C(sp^3)$ bond lengths along the rings. An intermolecular hydrogen bond is observed between O(1) and O(2) in $x, y, z - 1$ at a distance of 2.88 Å and with an angle O(1)–H···O(2) of 175°. Other nonbonding distances are in the normal range with respect to the sum of relevant van der Waals radii.

The four regioisomers A–D which are a priori possible for the Diels–Alder adduct are shown in Figure 3. In the framework of the FMO approximation, the regioselectivity is governed by the interaction of the most nucleophilic terminus, i.e., that with the larger terminal HOMO coefficient, of the diene **2** with the site of the largest LUMO coefficient of the quinone **1**.[8,9] The most nucleophilic terminus of the diene is C(2):[10] the preferred interaction should be that between atoms 2 and 2′, and the unique or prevalent product should be the adduct B. On consideration of the squares of the coefficients,[8] the order of regioselectivity B > A > C > D is predicted. According to these qualitative previsions, the values of E_η calculated for the HOMO(2)–LUMO(1) interaction in the symmetric approach (Table I in the supplementary material) indicate both that the B adduct is preferred and that the order is A > C > D.

As these regioselectivities are not in agreement with the experimental findings, the complete intermolecular orbital treatment of Salem and Devaquet[11] has been applied. This theory was originally developed by considering the intermolecular overlap of the π molecular orbitals of the two addends. Therefore, in a strict sense, it seems applicable only to geometrical situations in which the molecular

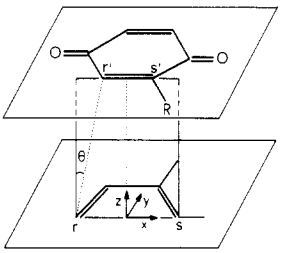


Figure 4. Geometry of the symmetric approach of the reactants.

planes of the diene and dienophile skeletons are parallel. Here, the molecules were considered to interact in a four-center approach with the molecular planes of diene and dienophile skeletons parallel to each other (Figure 4). Both symmetric and asymmetric configurations were studied.

The analysis of the most important terms in the E_{mix} addend for the symmetric reaction path (Table II in the supplementary material) justifies the failure of the FMO approximation in the present case. Particularly, the strongest of all interactions is the LUMO(2)–IHOMO(1) interaction, i.e., that between a vacant MO of **2** and an occupied MO of **1**. When the denominator of the E_{mix} term was corrected to compensate for the proximity of the molecules,[12,13] the HOMO(2)–LUMO(1) term becomes the more important one, but its relative weight is not greater than 40%; moreover, the LUMO(2)–IHOMO(1) interaction is still more important than the LUMO(2)–HOMO(1) one. The analysis also shows that the $E_\eta(j,k')$ contributions are larger than $E_\eta(k,j')$, but the two terms are of the same order of magnitude.

The complete results for the symmetric approach (Table III in the supplementary material) show that the formation of the adduct A is slightly preferred at any distance both if only the E_{mix} addend or the $E_{over} = E_{mix} + E_{rep}$ addend is considered. When the polar term is added to distinguish between endo and exo structures, the gap is reduced. At short distances, where the reaction is "overlap" controlled, the A-endo approach seems to be favored. With increasing distance, the reaction becomes "charge" controlled, and the B-endo approach prevails. These results confirm that the formation of the adducts C and D can be neglected.

The effect of asymmetric approaches is shown in Figure 5. It can be seen that the endo structures are more stable than the corresponding exo ones at all distances, so the exo approaches can be neglected too. With decreasing distance, there is an inversion in the relative stability of B-endo and A-endo structures, the zone of inversion being located between $4.0 > R_{rr'} > 3.5$ Å. The point of inversion corresponds approximately to the symmetric configuration.

In conclusion, the complete PMO treatment indicates that the formation of the A-endo adduct is the result of a concerted, slightly asymmetric mechanism, the reaction "zone" being located in the 3.5–4.0-Å range of distances.

The reliability of this range was tested through the effect of physical interactions (E_{nb}): the results obtained for symmetric configurations indicate that the orientation leading to the A-endo is favored at $R > 3.4$ Å where $(E_{nb})_{B\text{-endo}} - (E_{nb})_{A\text{-endo}} \simeq 2.5$ kJ mol^{-1}. Therefore, the "reaction" at a distance of about 3.5 Å could be assumed as a reference zero for the activation energy; correspondingly, the distance separating the addends in the "real"

(8) (a) Salem, L. *J. Am. Chem. Soc.* **1968**, *90*, 542, 553. (b) Devaquet, A.; Salem, L. *Ibid.* **1969**, *91*, 3793. (c) Devaquet, A. *Mol. Phys.* **1970**, *20*, 233.

(9) Fleming, I. "Frontier Orbitals and Organic Chemical Reactions"; Wiley: London, 1976.

(10) Rozeboom, M. L.; Tegmo-Larsson, I. M.; Houk, K. N. *J. Org. Chem.* **1981**, *46*, 2338.

(11) The polarization of the HOMO(2) gives coefficient magnitudes in the order $C_2 > C_1$ which is similar to that expected for a 3-substituted diene. On the contrary, the polarization of the LUMO(2) is typical for the LUMO of a 2-substituted diene. Details are reported in Table IV (supplementary material). For the numbering of the atoms see Figure 3.

(12) Fukui, K. "Theory of Orientation and Stereoselection"; Springer-Verlag: West Berlin, 1975.

(13) (a) Houk, K. N. *Acc. Chem. Res.* **1975**, *8*, 361. (b) Houk, K. N. In Marchand, A. P.; Lehr, R. E. "Pericyclic Reactions"; Academic Press: New York, 1977; Vol. 2.

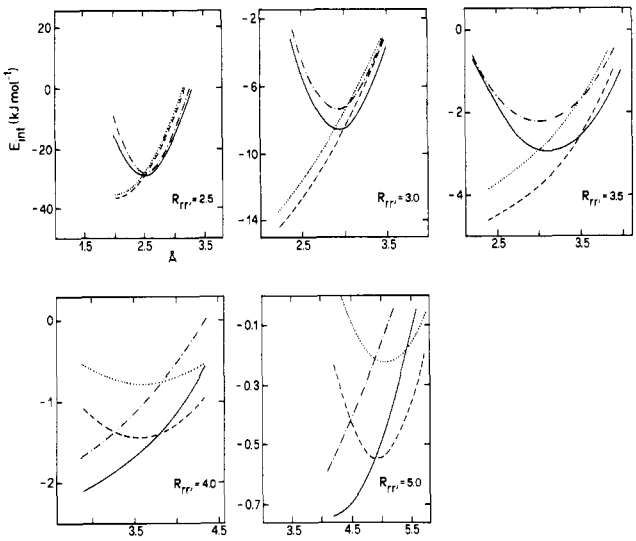


Figure 5. Sections of the total perturbation energy surfaces at constant $R_{rr'}$ values for the adducts A-endo (—), A-exo (-·-), B-endo (---), and B-exo (···).

transition state should be somewhat lower.

In conclusion, the Diels–Alder addition of quinone **1** with diene **2** yields a convenient intermediate for the synthesis of the title compounds.

Experimental Section

IR spectra were recorded with a Perkin-Elmer 681 spectrophotometer, ^{13}C NMR spectra with a Varian XL-100 spectrometer, ^1H NMR spectra of the compounds **4–6** with a Varian XL-100 spectrometer, and ^1H NMR spectrum of the compound **3** with a Brucker WH-270 spectrometer. Chemical shifts are given in δ units and coupling constants in hertz. Mass spectra were recorded with a Varian Mat 112 instrument and UV spectra with a Perkin-Elmer 551 spectrophotometer. All ethereal solvents were dried by them refluxing over $LiAlH_4$ and distilling them from it immediately before use. Dimethylformamide was stirred overnight over 4A molecular sieves and distilled under nitrogen at 20 mmHg (48 °C). Isopropyl alcohol was distilled from sodium wires. Gentisic acid (from Aldrich) was esterified with methanol–HCl to afford 2-carbomethoxy-1,4-benzoquinone in 80% yield. 1-Vinylcyclohexane-1-ol (synthetized from vinyl magnesium bromide and cyclohexanone) was transformed into 1-vinylcyclohexene via pyrolysis of its *N*-p-toluenesulfonylcarbamate.[14] Flash chromatographies were performed according to the procedure developed by Still and co-workers.[15]

Preparation of Silver Oxide. A 12-g sample of $AgNO_3$ was dissolved, with stirring, in 120 mL of distilled water. Concentrated NaOH was then added until the reaction mixture was basic. The precipitated silver oxide was filtered from the aqueous solution and then washed extensively with several portions of distilled water, with acetone, and finally with diethyl ether. It was then dried for several hours under vacuum (85% yields).

Diels–Alder Reaction of 1-Vinylcyclohexene with 2-Carbomethoxy-1,4-benzoquinone. A 5-mmol sample of 2-carbomethoxy-1,4-benzoquinone and 5 mmol of vinylcyclohexene were suspended in 10 mL of benzene–ether (3:1), cooled at 0 °C, and vigorously stirred. Silver oxide (10 mmol) was added at once, and the mixture was stirred for an additional 0.5 h at 0 °C and then filtered through a Celite layer which was subsequently washed three times with ether. Removal of the solvent at reduced pressure afforded 1.4 g of crude material. Crystallization from *n*-propanol afforded 1.255 g (92% yield) of the adduct **3**: mp 78–80 °C; IR ($CHCl_3$) 1750, 1705, 1685, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) 6.78 and 6.6 (AB system, 2 H, $J_{2,3}$ = 10, hydrogens at C-2 and C-3), 5.22 (br d, 1 H, $J_{7,6\beta}$ = 5, $J_{7,6\alpha}$ = 2, hydrogen at C-7), 3.77 (s, 3 H, $COOCH_3$), 3.7 (dd, 1 H, $J_{5\beta,6\alpha}$ = 7, $J_{5\beta,6\beta}$ = 2, hydrogen at C-5), 2.97 (br d, 1 H, $J_{9\beta,11\alpha}$ = 12, $J_{9\beta,11\beta}$ = 3, hydrogen at C-9), 2.64 (ddd, 1 H, $J_{6\alpha,6\beta}$ = 18, $J_{6\beta,7}$ = 5, $J_{6\beta,5}$ = 2, β hydrogen at C-6), 1.89 (br dd, 1 H, $J_{6\alpha,6\beta}$ = 18, $J_{6\alpha,5\beta}$ = 7, $J_{6\alpha,7}$ = 2, α hydrogen at C-6); ^{13}C NMR ($CDCl_3$) 197.5 (s, C-1 or C-4), 196.9 (s, C-1 or C-4), 170.0 (s, $COOCH_3$), 141.1 (d, C-2 or C-3), 139.5 (d, C-2 or C-3), 139.0 (s, C-8), 114.8 (d, C-7), 63.6 (s, C-10), 53.1 (q, $COOCH_3$), 47.1 (d, C-5), 42.1 (d, C-9), 36.5 (t), 33.4 (t), 28.4 (t), 27.4 (t), 20.5 (t); mass spectrum, *m/z* 274 (M^+), 242, 215, 214, 197, 187, 186, 173 UV λ_{max} 205 nm (ϵ 8200), 226 (11 000). Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61. Found: C, 70.41; H, 7.01.

Zinc Reduction of 3. To a stirred solution of 0.600 g of **3** in 5 mL of glacial acetic acid was added 0.960 g of zinc dust in small portions. The reaction mixture was allowed to stir at room temperature for 15 min. The mixture was poured in 1 mL of ice–water. The zinc was removed by filtration, and the filtrate was washed with chloroform. The aqueous layer was extracted four times with chloroform, and the combined chloroform extracts were washed with 10% sodium bicarbonate and dried over sodium sulfate. Removal of the solvent gave 0.586 g (96.6% yield) of a colorless solid. Recrystallization from diisopropyl ether–ethyl acetate afforded 0.485 g (80%) of a colorless crystalline **4**: mp 120–122 °C; IR ($CHCl_3$) 1750, 1715 cm^{-1}; ^1H NMR ($CDCl_3$) 5.3 (m, 1 H, vinylic hydrogen at C-7), 3.8 (s, 3 H, $COOCH_3$), 3.7 (dd, 1 H, $J_{5\beta,6\beta}$ = 2, $J_{5\beta,6\alpha}$ = 7, hydrogen at C-5), mass spectrum, *m/z* 276 (M^+), 244, 226, 216, 202, 199, 188, 174. Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.54; H, 7.24. Found: C, 69.81; H, 7.07.

Preparation of the Ketol 5. A stirred solution of 0.132 g (3.5 mmol) of sodium borohydride in 4.4 mL of dry dimethylformamide was cooled to −20 °C in a nitrogen atmosphere. A solution of 2.424 g (8.78 mmol) of **4** in 9 mL of dry dimethylformamide was dropped in over a few minutes. The reaction mixture was left at 0 °C for 24 h, acidified with HCl, and extracted three times with ethyl acetate. The combined organic extracts were washed with water and dried over sodium sulfate, and the solvent was removed at reduced pressure. The crude material (2.1 g) was chromatographed over silica gel and eluted with ethyl acetate–hexane (1:1). The ketol **5** was obtained in 55% yield as a colorless solid which was crystallized from *n*-propanol–diisopropyl ether: mp 155 °C; IR ($CHCl_3$) 1715 cm^{-1}; ^1H NMR ($CDCl_3$) 5.3 (m, 1 H, hydrogen at C-7), 4.2 (dd, 1 H, $J_{1\alpha,2\beta}$ = 12, $J_{1\alpha,2\alpha}$ = 5, hydrogen at C-1), 3.7 (s, 3 H, $COOCH_3$), 2.94 (ddd, 1 H, $J_{9\beta,11\alpha}$ = 12, $J_{9\beta,11\beta}$ = 3, $J_{9,7}$ = 1, hydrogen at C-9), 2.32 (dd, 1 H, $J_{5\alpha,6\beta}$ = 11, $J_{5\alpha,6\alpha}$ = 6, hydrogen at C-5); mass spectrum, *m/z* 278 (M^+), 260, 246, 228. Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.10; H, 8.01. Found: C, 68.93; H, 8.25. By elution with ethyl acetate–hexane (6:4) was obtained the lactone **6**: 12% yield; mp 184–186 °C (ethyl acetate–diisopropyl ether); IR ($CHCl_3$) 3300, 1770 cm^{-1}; ^1H NMR ($CDCl_3$) 5.25 (m, 1 H, hydrogen at C-7), 4.24 (m, 1 H, main *J* = 4, hydrogen at C-4), 3.88 (dd, 1 H, $J_{1\alpha,2\beta}$ = 10, $J_{1\alpha,2\alpha}$ = 6, hydrogen at C-1); mass spectrum, *m/z* 248 (M^+), 230, 185, 176, 159, 145, 143. Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.58; H, 8.06. Found: C, 72.26; H, 7.82.

The reduction of the diketone **4** was also performed in dry isopropyl alcohol in the presence of sodium borohydride for 5 h at 0 °C. The ketol **5** was obtained in 63% yield.

Crystallographic Study of Compound 5. A prismatic crystal (0.20 × 0.26 × 0.31 mm) after preliminary examination by means of Weissenberg photographs was centered on a Philips PW 1100 four-circle diffractometer equipped with a graphite monochromator. Thirty reflections measured with Mo Kα radiation were used in least-squares refinement of the lattice parameters, resulting in a = 9.021 (1) Å, b = 20.909 (2) Å, c = 7.544 (1) Å, β = 93.15 (1)°, monoclinic space group $P2_1/n$, d_{obsd} = 1.303 (by flotation in a dilute K_2HgI_4 solution), and d_{calcd} = 1.301 g cm^{-3} for Z = 4 ($C_{16}H_{22}O_4$, mol wt 278.35).

Intensities were collected with Mo Kα radiation (λ = 0.710 69 Å) in the ω-scan mode (scan width 1.20°, scan speed 0.040° s^{-1}, ϑ range from 2.5° to 27.5°). Two check reflections were monitored periodically to test crystal decomposition or movement. Lorentz and polarization factors were applied; absorption effects were neglected (μ = 0.54 cm^{-1} for Mo Kα radiation). A total of 3251 independent reflections were measured, of which 1516 having $F \geq 2\sigma(F)$ were considered as observed.

Structure Solution and Refinement. The structure was solved by direct methods by using the SHELX 76[16] system of

(14) Roach, L. C.; Daly, W. H. *Chem. Commun.* **1970**, 606.
(15) Still, C. W.; Kahn, M.; Metra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(16) Sheldrick, G. M. "SHELX 76, A program for Crystal Structure Determination"; University of Cambridge: England, 1976.

programs. The E map with the highest parachor value allowed location of the nonhydrogen atoms; all the hydrogen atoms were recognized subsequently via difference electron density syntheses during the refinement. This was performed by isotropic and then anisotropic full-matrix least-squares procedures on carbon and oxygen atoms, with a total number of 181 parameters; the contributions of the hydrogen atoms were included in the structure factor calculations with a thermal factor equal to the U (equivalent) value of the bonded atom. In the final cycle all shifts were less than 0.07σ; the discrepancy index over the 1516 observed reflections converged to $R = 0.051$. A final difference map showed no significant features, the electron density values ranging between +0.22 and −0.24 e Å^{-3}.

Theoretical Calculations. Within the framework of second-order perturbation theory and with the assumption that different atoms of the first molecule do not interact at the same time with the same atom of the second one, i.e., considering only two-center interactions, the treatment of Salem and Devaquet[8] leads to three components of the interacton energy (E_{int}) between two conjugated molecules in their ground states. The equations for the closed-shell repulsion term (E_{rep}) and the attractive term (E_{mix}), both of which depend on the overlap between interacting orbitals ($E_{over} = E_{rep} + E_{mix}$), are those reported in ref 8a (eq 15). The equation for the polar term (E_{pol}), representing electrostatic interactions between net charges on the atoms, is eq 31c in ref 8c. For the sake of simplicity, the E_{mix} addend of eq 15 in ref 8a has been simbolyzed as follows: $E_{mix} = [E_\eta(j,k') + E_S(j,k')] + [E_\eta(k,j') + E_S(k,j')]$.

Nonbonded interactions between all pairs of atoms s and s' of the two addends were treated by using a Lennard-Jones "6-12" potential function.[17] The values of the parameters were the same as those given in Table IV of ref 15.

Resonance integrals $\eta_{rr'}$ were assumed to be proportional to the overlap integral $S_{rr'}$, and the proportionality parameter K was evaluated through the following: (i) the Mulliken approximation[18] where $K = (\beta_r + \beta_{r'})/2$, with $\beta_C = -21$ eV and $\beta_O = -31$ eV; (ii) the Wolfsberg-Helmholtz approximation,[19] where $K = k(H_{rr} + H_{r'r'})$ with $H(2pC) = -11.4$ eV, $H(2pO) = -14.8$ eV, and $k = 1.75/2$. At large distances (5 Å) between the two centers, the variations of η_{CC} and η_{CO} with the distance as calculated by method i are a little more negative than when calculated by method ii, the difference increasing as the distance diminishes. As preliminary calculations have shown that the E_{mix} value is not significantly influenced by the used appoximation, that of Wolfsberg-Helmholz was used.

Overlap integrals were calculated by standard formulas.[20] The deviations of the overlapping orbitals from the alignment required for pure σ overlapping were taken into account by use of the correction $S_{rr'} = S_{rr'}(\sigma,\sigma)\cos^2\theta + S_{rr'}(\pi,\pi)\sin^2\theta$ where the integrals $S_{rr'}(\sigma,\sigma)$ and $S_{rr'}(\pi,\pi)$ were calculated by the standard formulas, and θ is the angle between the line joining atoms r and r' and the axis of the $2p\pi$ orbitals centered on r and r' (Figure 4).

The molecular geometries of 2-carbomethoxy-1,4-benzoquinone (**1**) and 1-vinylcyclohexene (**2**) were optimized by both molecular mechanics (force filed method) and quantum mechanical (MNDO method) calculations. Details will be reported in separate papers.[21,22] For the coplanar conformations shown in Figure 3 calculations by both MNDO and ab initio methods were carried out: similar results were obtained both for the ordering of π orbitals and the coefficients magnitudes. For the parent 1,4-benzoquinone as well as for compounds **1** and **2**, the experimental values of the first ionization potential and electron affinity, when available, are in generally good agreement with values calculated by MNDO method: so, the π orbital energies, coefficients, and net charges obtained by these calculations were used here.

Acknowledgment. We thank Dr. W. Porzio, CNR-ICM, Milan, for the collection of intensities with the PW 1100 diffractometer and Prof. K. N. Houk for helpful discussion. Financial support from the Italian CNR is gratefully acknowledged (Progetto Finalizzato per la Chimica Fine e Secondaria and Grant No. CT81.01684.03).

Registry No. **1**, 3958-79-0; **2**, 2622-21-1; **3**, 86309-53-7; **4**, 86309-54-8; **5**, 86309-55-9; **6**, 86309-56-0.

Supplementary Material Available: Tables listing the results of PMO calculations (Table I–III), energies and coefficients of the MNDO MO's of compounds **1** and **2** (Table IV), final coordinates and their estimated standard deviations for heavier atoms (Table V), coordinates for hydrogen atoms (Table VI), thermal parameters with their estimated standard deviations (Table VII), bond distances, bond angles, and selected torsion angles with their estimated standard deviations (Tables VIII–X) for product **5** (10 pages). Ordering information is given on any current masthead page.

(17) Scott, R. A.; Scheraga, H. A. *J. Chem. Phys.* **1966**, *45*, 2091.
(18) Mulliken, R. S. *J. Phys. Chem.* **1952**, *56*, 295.
(19) Wolfsberg, M.; Helmholz, L. *J. Chem. Phys.* **1952**, *20*, 837.
(20) Mulliken, R. S.; Rieke, C. A.; Orloff, D.; Orloff, H. *J. Chem. Phys.* **1949**, *17*, 1248.
(21) Pitea, D.; Moro, G. *J. Mol. Struct.*, in press.
(22) Pitea, D.; Moro, G.; Tantardini, G. F.; Todeschini, R. *J. Mol. Struct.*, in press.

Stereocontrolled Palladium(II)-Mediated Coupling of Furanoid Glycals with a Pyrimidinylmercuric Salt. Facile C-Nucleoside Syntheses

Uli Hacksell and G. Doyle Daves, Jr.*

Department of Chemistry, Lehigh University, Bethlehem, Pennsylvania 18015

Received January 7, 1983

Reactions of new, chiral furanoid glycals with (1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)mercuric acetate in the presence of a stoichiometric quantity of $Pd(OAc)_2$ resulted in regio- and stereospecific formation of α or β C-nucleosides. Results obtained demonstrate that preselection of the direction of attack by the organopalladium reagent on the cyclic enol ether double bond can be accomplished by adjustment of the relative steric bulks of the C_3 and C_4 substituents of trans-substituted furanoid glycals. With cis-substituted glycals, the attack occurs on the unsubstituted face of the ring.

Ongoing studies of the regio- and stereochemistry of palladium-mediated carbon–carbon bond forming reactions of cyclic enol ethers (glycals)[1,2] directed toward the development of a general synthesis of C-nucleosides[3,4] have

0022-3263/83/1948-2870$01.50/0