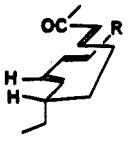
Antibiotic X-14547A: Total Synthesis of the Right-Hand Half†

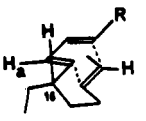
Summary: A nine-step, stereoselective synthesis of **3**, the right-hand half of antibiotic X-14547A (**1**), is described. The key step of this synthesis is the Lewis acid catalyzed intramolecular Diels–Alder reaction of **4** which establishes the relative stereochemistry of the perhydroindene nucleus of **1**.

Sir: X-14547A (**1**), isolated from *Streptomyces antibioticus* NRRL8167 by Westley et al. in 1978,[1] is an unusual ionophore antibiotic of the polyether class.[2] X-14547A is active against gram-positive bacteria, is useful as a growth promotant for ruminants, and has antitumor activity.[1,3] X-14547A is structurally unique among this class of natural products. It is the first ionophore reported to possess a 1,3-butadiene moiety, it is only the second member of this class to possess a pyrrole ring,[4] and it is only the second natural product known to possess a trans-fused hexahydroindene ring system.[5] We report herein a short, stereoselective synthesis of **3**, the right-hand half of **1**.[6]

Our strategy for the synthesis of **1** is outlined in Scheme I. A key feature of this plan is the recognition that the four stereocenters of the cyclohexenyl ring of **3** might be introduced by the endo intramolecular Diels–Alder reaction of **4**.[7] Examination of molecular models of the two diastereomeric endo transition states available to **4** suggested that transition state A, leading to **3**, should be



A

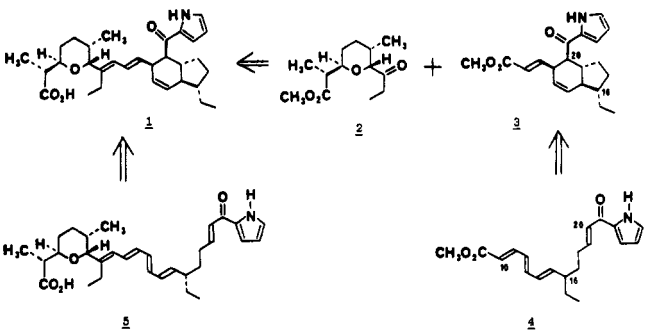


B

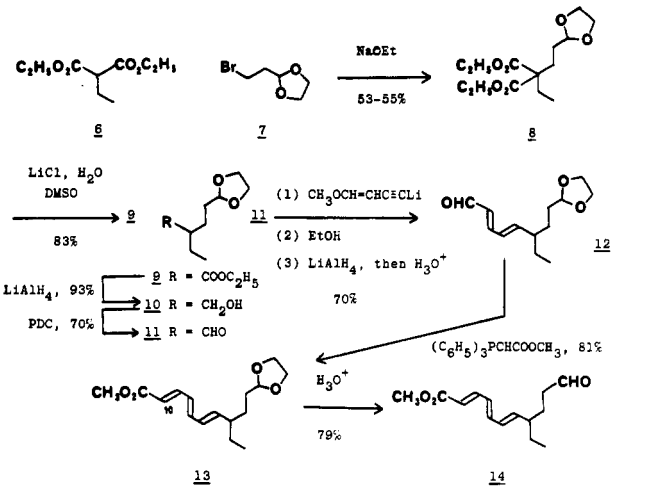
preferred over B, leading to the enantiomer of the ethyl epimer of **3**, as a consequence of a destabilizing steric interaction between H_a and the C-16 ethyl group in transition state B. It was expected that differentiation of transition states A and B would be more pronounced than was observed in our total synthesis of dendrobine,[7a-c] since an ethyl group is more bulky than a protected hydroxyl group. Although the details of the biosynthesis of **1** are unknown, we speculate that an intramolecular Diels–Alder reaction of a triene such as **5** may be involved in this process.[8]

Aldehyde **14**, the penultimate precursor of **3**, was synthesized by the route outlined in Scheme II. Condensation of diethyl ethylmalonate (**6**) with bromide **7**[9] (NaOEt, EtOH, reflux, 13 h) afforded 53–55% of **8**[10a,c] (plus 13–15%

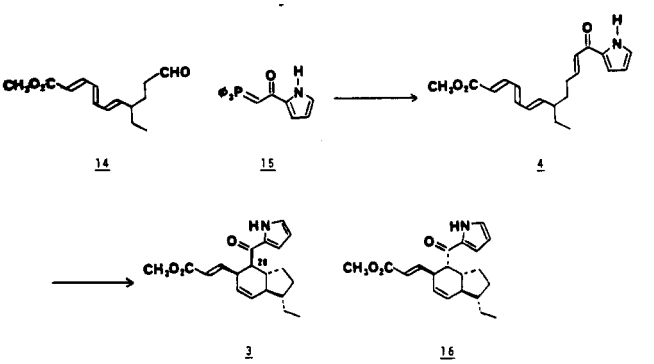
Scheme I



Scheme II



Scheme III



† This work was described in part at the 2nd Chemical Congress of the North American Continent, Las Vegas, 1980, Abstract No. ORGN 304.

(1) (a) Westley, J. W.; Evans, R. H., Jr.; Liu, C.-M.; Hermann, T.; Blount, J. F. *J. Am. Chem. Soc.* **1978**, *100*, 6784. (b) Liu, C.-M.; Hermann, T. E.; Liu, M.; Bull, D. N.; Palleroni, N. J.; Prosser, B. L. T.; Westley, J. W.; Miller, P. A. *J. Antibiot.* **1979**, *32*, 95. (c) Westley, J. W.; Evans, R. H., Jr.; Sello, L. H.; Troupe, N.; Liu, C.-M.; Blount, J. F. *Ibid.* **1979**, *32*, 100. (d) Westley, J. W.; Liu, C.-M. U.S. Patent 4 100 171, 1978.

(2) (a) Westley, J. W. *Adv. Appl. Microbiol.* **1977**, *22*, 177. (b) Pressman, B. C. *Annu. Rev. Biochem.* **1976**, *45*, 501.

(3) Westley, J. W., personal communication.

(4) A-23187 also contains an acylpyrrole: Chaney, M. O.; Demarco, P. V.; Jones, N. D.; Occolowitz, J. L. *J. Am. Chem. Soc.* **1974**, *96*, 1932.

(5) Ircinianin contains a trans-fused hexahydroindene ring system; the biosynthesis is thought to involve an intramolecular Diels-Alder reaction: Hofheinz, W.; Schönholzer, P. *Helv. Chim. Acta* **1977**, *60*, 1367.

(6) Syntheses of a number of ionophore antibiotics have been reported in recent years. (a) Lasalocid A: Nakata, T.; Schmid, G.; Vranesic, B.; Okigawa, M.; Smith-Palmer, T.; Kishi, Y. *J. Am. Chem. Soc.* **1978**, *100*, 2933; Nakata, T.; Kishi, Y. *Tetrahedron Lett.* **1978**, 2745; Ireland, R. E.; Thaisrivongs, S.; Wilcox, C. S. *J. Am. Chem. Soc.* **1980**, *102*, 1155; Ireland, R. E.; McGarvey, G. J.; Anderson, R. C.; Badoud, R.; Fitzsimmons, B.; Thaisrivongs, S. *Ibid.* **1980**, *102*, 6178. (b) Monesin: Schmid, G.; Fukuyama, T.; Akasaka, K.; Kishi, Y. *J. Am. Chem. Soc.* **1979**, *101*, 259; Fukuyama, T.; Wang, C.-L. J.; Kishi, Y. *Ibid.* **1979**, *101*, 260; Fukuyama, T.; Akasaka, K.; Karanewsky, D. S.; Wang, C. L. J.; Schmid, G.; Kishi, Y. *Ibid.* **1979**, *101*, 262; Collum, D. B.; McDonald, J. H., III; Still, W. C. *Ibid.* **1980**, *102*, 2117, 2118, 2120. (c) A23187: Evans, D. A.; Sacks, C. E.; Kleschick, W. A.; Taber, T. R. *Ibid.* **1979**, *101*, 6789; Grieco, P. A.; Williams, E.; Tanaka, H.; Gilman, S. *J. Org. Chem.* **1980**, *45*, 3537.

(7) Stereochemical studies of the intramolecular Diels–Alder reactions of methyl deca-2(*E*),7(*E*),9(*E*)-trienoates: (a) Roush, W. R. *J. Am. Chem. Soc.* **1978**, *100*, 3599; (b) Roush, W. R. *J. Org. Chem.* **1979**, *44*, 4008; (c) Roush, W. R. *J. Am. Chem. Soc.* **1980**, *102*, 1390; (d) Roush, W. R.; Ko, A. I.; Gillis, H. R. *J. Org. Chem.* **1980**, *45*, 4264; (e) Roush, W. R.; Gillis, H. R. *Ibid.* **1980**, *45*, 4267; (f) Roush, W. R.; Gillis, H. R. *Ibid.* **1980**, *45*, 4283.

(8) Intramolecular Diels–Alder reactions have been postulated in the biosynthesis of a number of natural products. (a) Cyclopiperaceae alkaloids: Joshi, B. S.; Viswanathan, N.; Gawad, D. H.; Balakrishnan, V.; Philipsborn, W. v. *Helv. Chim. Acta* **1975**, *58*, 2295. (b) Ikarugamycin: Ito, S.; Hirata, Y. *Tetrahedron Lett.* **1972**, 2557. (c) For indole alkaloids and others, review: Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 10. (d) See also ref 5.

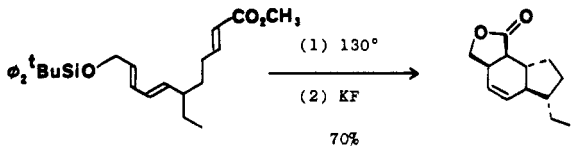
(9) Büchi, G.; Wüest, H. *J. Org. Chem.* **1969**, *34*, 1122.

0022-3263/81/1946-1509$01.25/0

of recovered **6** which was easily separated by distillation). Treatment of **8** with LiCl (2 equiv) and H_2O (1 equiv) in refluxing Me_2SO[11] afforded 83% of **9**.[10a,c] Reduction of **9** with $LiAlH_4$ afforded alcohol **10**[10a,c] (93–100%) which without purification was oxidized with pyridinium dichromate[12] (PDC, 1.5 equiv; CH_2Cl_2) to afford 67–70% of aldehyde **11**.[10a,c] Condensation of **11** with the lithium anion of 1-methoxybut-1-en-3-yne (BuLi, THF, −78 °C) at 0 °C with warming to room temperature over 3 h followed by sequential addition of EtOH (0.7 equiv), $LiAlH_4$ (1.5 equiv, 3 h, 23 °C), and then 1 N HCl (23 °C, 2–3 h) afforded[13] 70% of dienal **12**[10a,c] [UV (95% EtOH) 274 nm (log ε 4.42); semicarbazone,[10b] mp 129–131 °C] of approximate 90% isomeric purity. Condensation of **12** with [(carbomethoxy)methylene]triphenylphosphorane in benzene (reflux) afforded triene ester **13**[10a,c] in 81% yield (>90% isomerically pure), hydrolysis of which afforded the desired aldehyde **14**[10a,b] in 79% yield.[14]

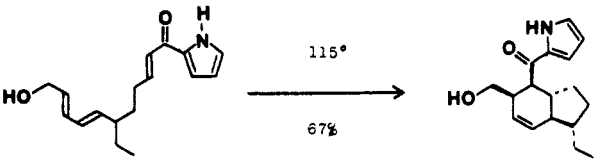
The stage was now set for olefination of **14** to **4** and for cyclization of **4** to **3** (Scheme III). Both transformations were accomplished in a single operation by refluxing an inhomogeneous[15b] mixture of **14** and phosphorane **15**[15] (1.5 equiv) in toluene (25 h). In this manner there was obtained 26% of **3**[16] (mp 143.5–144.5 °C), 35% of a mixture of **3** and two isomers tentatively assigned cis ring fusions[17] (ca. 70:20:10, respectively), and 5% of **16**,[10a,c,18] the acyl pyrrole epimer of **3**. Alternatively, treatment of **14** with **15** in CH_2Cl_2 (room temperature, 4 days) afforded 57% of **4**[19] together with 4% of **3** and 24% of recovered **14**. Cyclization of **4** in the presence of 0.95 equiv of $EtAlCl_2$[7e] (CH_2Cl_2, 0 °C with warming to room temperature over 1.5 h) proved to be highly selective, affording **3** (71% yield) contaminated by less than 5% of other stereoisomers.[20] Tetraene **4** is thus the most reactive precursor of the perhydroindene nucleus yet studied.[7]

The stereochemistry depicted for the cyclohexenyl ring of **3** was assigned on the basis of similarities of the NMR spectrum of **3**[16] to the NMR spectrum of **1**[1c] and also by analogy to the NMR spectra of other perhydroindene Diels–Alder adducts.[7] In particular, the ^1H resonance for H-20 of **3** [δ 3.45 (dd, J = 10.5, 6.1 Hz)] compares favorably to the corresponding signal for **1** [δ 3.40 (dd, J = 10.7, 6.6 Hz)]. The coupling constants for these signals are diagnostic of trans-fused, endo, Diels–Alder adducts deriving from all-trans triene precursors.[7] Stereochemistry at C-16 was assigned by analogy to the report by Nicolaou and Magolda that **18** is the major cycloadduct of **17**.[21] Using



17 18

simple modifications of the route summarized in Scheme II, we have synthesized triene **19**.[22] Cyclization of **19** (toluene, reflux, 17 h, 67%) afforded a mixture of isomers, among which **20**[23] was identified as the major product



19 20

(>75%) by comparison with the 250-MHz NMR spectrum of authentic **20** prepared from **18** by Nicolaou and Magolda.[21a] The stereochemistry assigned to **3** is therefore well-founded.

The facility and high stereoselectivity realized in the cyclization of **3** suggests that cyclization of **5** to **1** is conceivable under biological conditions. Further progress toward the total synthesis of **1** along the lines suggested in Scheme I will be reported in due course.

Acknowledgment is made to the National Institutes of Health (Grant No. GM 26782), to the Research Corp., and to the MIT Undergraduate Research Program for support of this research. The authors are grateful to Dr. J. W. Westley for a generous sample of X-14547A, to

(10) (a) All new compounds were fully characterized by NMR, IR, and mass spectroscopy. (b) This compound gave a satisfactory combustion analysis (±0.3%). (c) The elemental composition of this compound was verified by a precise mass measurement.

(11) Krapcho, A. P.; Weimaster, J. F.; Eldridge, J. M.; Jahngen, E. G. E., Jr.; Lovey, A. J.; Stephens, W. P. *J. Org. Chem.* **1978**, *43*, 138.

(12) Corey, E. J.; Schmidt, G. *Tetrahedron Lett.* **1979**, 399.

(13) Marshall, D.; Whiting, M. C. *J. Chem. Soc.* **1956**, 4081.

(14) Isomerically pure **13** was obtained in 67% yield by careful chromatography of the product obtained from the Wittig olefination of **12**. Hydrolysis of **13** so obtained afforded 79% of **14** along with 5% of the C(10)-C(11) cis double bond isomer. Since olefin isomerization occurred in this step, the olefin mixtures obtained in previous steps were not routinely separated.

(15) (a) Phosphorane **15** was prepared, starting from 2-(α-chloroacetyl)pyrrole (**21**) (Ermili, A.; Castro, A. J.; Westfall, P. A. *J. Org. Chem.* **1965**, *30*, 339) by standard procedures. Treatment of **21** with triphenylphosphine in refluxing C_6H_6 afforded the corresponding phosphonium salt, which was then dissolved in acidic (pH ~3) methanol. The solution was filtered, the pH was adjusted to ~13 with aqueous NaOH, and the precipitated **15** was isolated by filtration. This material was washed with methanol and ether and then dried in vacuo for at least 24 h prior to use (49% yield; mp 250 °C dec). (b) Ylide **15** is only slightly soluble in organic solvents such as toluene and CH_2Cl_2.

(16) Data for **3**: ^1H NMR (250 MHz, $CDCl_3$) δ 9.93 (br s, NH), 7.04, 6.90, 6.23 (3 m, 3 H, pyrrole CH), 6.82 (dd, J = 15.4, 8.1 Hz, 1 H), 6.03 (d, J = 9.6 Hz, 1 H), 5.58 (d, J = 15.8 Hz, 1 H), 5.39 (dt, J = 9.6, 3.6 Hz, 1 H), 3.61 (s, 3 H), 3.45 (dd, J = 10.7, 6.2 Hz, H-20), 3.39 (m, 1 H), 0.90 (t, J = 7.4 Hz, CH_3); ^{13}C NMR (62.8 MHz, $CDCl_3$, proton decoupled) δ_c 190.3, 166.7, 147.9, 132.1, 131.3, 127.0, 125.4, 121.7, 116.1, 110.6, 51.4, 51.3, 50.2, 43.5, 43.4, 40.6, 29.4, 27.1, 26.6, 12.4; IR (KBr) 3270, 1700, 1615, 1530 cm^{-1}; mass spectrum, m/e 327 (parent ion). Anal. Calcd for $C_{20}H_{25}NO_3$: C, 73.37; H, 7.70; N, 4.28. Found: C, 73.20; H, 7.94; N, 4.10.

(17) The NMR spectrum of this mixture contains two triplets centered at δ 2.78 (J = 11 Hz) and δ 2.75 (J = 11 Hz) which were assigned to H-20 of the cis fused isomers. Pure **3** was separated from this mixture by crystallization.

(18) Isomer **16** probably derives from the Z dienophile isomer of **4**, which is expected to be a minor product of the Wittig reaction. For stereochemical studies of the Diels–Alder reactions of activated (*Z,E,-E*)-deca-2,7,9-trienoates, see ref 7.

(19) Data for **4**: NMR (250 MHz, $CDCl_3$) δ 10.6 (br s, NH), 7.10, 6.97, 6.29 (3 m, 3 H, pyrrole CH), 7.32 (dd, J = 11.5, 15.1 Hz, H-11), 7.04 (dt, J = 15.4, 7.0 Hz, H-19), 6.73 (d, J = 15.4 Hz, H-20), 6.56 (dd, J = 10.3, 14.7 Hz, H-13), 6.25 (H-12, superimposed on pyrrole CH signal), 6.12 (dd, J = 10.5, 15.1 Hz, H-14), 5.88 (d, J = 15.1 Hz, H-10), 5.66 (dd, J = 9.2, 15.1 Hz, H-15), 3.74 (s, 3 H), 0.85 (t, J = 7.4 Hz, CH_3); IR (neat) 3250, 1710, 1650, 1610, 1595, 1540 cm^{-1}; UV (95% EtOH) λ_{max} 306 nm (log ε 4.67), 252 (sh, 4.1); mass spectrum, m/e 327 (parent ion).

(20) The 250-MHz ^1H NMR spectrum of **3** so obtained contains a trace (<5%) of another stereoisomer which we believe to be the ethyl epimer of **3** (a triplet, J = 7 Hz, centered at δ 0.84 is diagnostic of this isomer). The cis-fused isomers noted in the 115 °C cyclization (see ref 17) were not observed in this case.

(21) (a) Nicolaou, K. C.; Magolda, R. L.: details described at the 2nd Chemical Congress of the North American Continent, Las Vegas, Aug 1980, Abstract No. ORGN 156; *J. Org. Chem.*, preceding paper in this issue. The stereochemistry of **18** was confirmed by X-ray analysis. (b) Professor S. V. Ley, Imperial College, has informed us that his group has also prepared **18** by an intramolecular Diels–Alder reaction.

(22) Triene **19** was prepared from **12** by three steps: (i) $LiAlH_4$, Et_2O (95%); (ii) H_2O, HOAc, THF (4:1:5.7), reflux, 28 h (87%); (iii) condensation with **15** [2 equiv, CH_2Cl_2, 23 °C, 3 days, 32% yield (25% yield of aldehyde was recovered)].

(23) Data for **20**: NMR (250 MHz, $CDCl_3$) δ 10.0 (br s, NH), 7.09, 6.99, 6.29 (3 m, 3 H, pyrrole CH), 6.10 (br d, J = 10 Hz, 1 H), 5.59 (dt, J = 10.0, 2.6 Hz, 1 H), 3.59 (m, CH_2OH), 3.46 (dd, J = 11.4, 7.0 Hz, H-20), 2.70 (m, OH), 0.92 (t, J = 7.3 Hz, CH_3); IR (CH_2Cl_2) 3440, 3260, 1617 (br), 1540 cm^{-1}; mass spectrum, m/e 273 (parent ion).

Professor K. C. Nicolaou for a comparative NMR spectrum of **20**, to Professors K. C. Nicolaou and S. V. Ley for providing us with copies of their manuscripts prior to publication, and to Dr. Catherine Costello for high-resolution mass spectra.

Registry No. **3**, 76584-17-3; **3** (ethyl epimer), 76584-18-4; **3** (cis fusion isomer 1), 76584-31-1; **3** (cis fusion isomer 2), 76584-32-2; **4**, 76584-19-5; **4**, 76584-19-5; **4** (Z dienophile isomer), 76612-59-4; **6**, 133-13-1; **7**, 18742-02-4; **8**, 64298-16-4; **9**, 76584-20-8; **10**, 76584-21-9; **11**, 76584-22-0; **12**, 76584-23-1; **12** semicarbazone, 76584-24-2; **13**, 76584-25-3; **14**, 76584-26-4; **14** (C(10)–C(11) cis double bond isomer), 76584-27-5; **15**, 76584-28-6; **16**, 76584-29-7; **19**, 76584-30-0; **20**, 76566-85-3; **21**, 53391-62-1; $CH_3OCH{=}CHC{\equiv}CLi$, 76584-33-3; $(C_6H_5)_3PCHCOOCH_3$, 2605-67-6; triphenylphosphine, 603-35-0.

Supplementary Material Available: Full spectroscopic data for compounds **8**–**16** and **19** (3 pages). Ordering information is given on any current masthead page.

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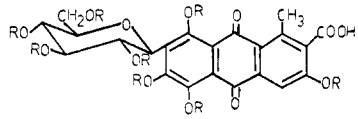
Received November 12, 1980

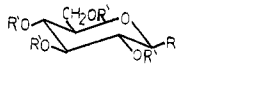
Assignment of the β Configuration to the *C*-Glycosyl Bond in Carminic Acid

Summary: Chemical evidence is given that carminic acid is 7β-*D*-glucopyranosyl-9,10-dihydro-3,5,6,8-tetrahydroxy-1-methyl-9,10-dioxo-2-anthracenecarboxylic acid.

Sir: Carminic acid (**1a**) is the main component of the cochineal food dye obtained from *Dactylopius coccus* feeding on *Opuntia* and *Nopalea* cacti.[1] The structure of the compound has long been established but the stereochemistry of the C-glycosyl bond has not yet been determined.[2] Commonly, the glycosidic bond is considered to be α, but the β configuration has also been reported.[3] The present paper is concerned with the conclusive proof that the *C*-glycosydic bond in (**1a**) has the β configuration.



1a, R = H
b, R = $COCH_3$



2a, R = CO_2H; R' = H
b, R = CH_2OH; R' = H
c, R = CO_2CH_3; R' = $COCH_3$

The ^{13}C NMR spectrum of **1a**[4] showed the resonance of six sp^3 carbons[5] at values comparable with those reported for the carbon atoms of the *C*-glycosyl fragment of flavanoid *C*-β-*D*-glycopyranosides.[6] The ^1H NMR spectrum of the acetate **1b**[7] showed one acetyl group at an unsuaully high-field position (δ 1.83), indicative of a 2′-acetate group of the *C*-β-*D*-glycopyranosyl fragment as in flavanoid *C*-β-*D*-glycopyranosides.[8] Inspection of the structure of **1a** suggested that a significant product to ascertain the β stereochemistry could be 2,6-anhydro-*D*-glycero-*D*-guloheptonic acid (**2a**), the homoacid of the carbohydrate moiety formally deriving from **1a** under suitable oxidation conditions. Reduction of this acid yields the meso compound 2,6-anhydro-*D*-glycero-*D*-guloheptitol (**2b**). Compound **1a** (in water, 0.1 M) was ozonized at 10 °C until the color changed from red to brownish yellow.[9] For esterification of the formed carboxylic acid, the dry residue obtained by evaporation of the solvent was refluxed in methanol. Gas chromatographic–mass spectral analysis of a trifluoroacetylated sample of the crude reaction residue revealed the presence of glucose in the mixture,[10] but no trace of arabinose was found.[9] Acetylation of the esterified residue, followed by column chromatography on silica gel G–Celite (1:1 v/v, eluted with benzene–diethyl ether, 9:1) afforded the tetramethyl tetraacetate ester **2c**: mp 145–146 °C; $[\alpha]^{22}_D$ +5° (*c* 5, $CHCl_3$); identical melting and mixture melting points and IR, ^1H NMR, ^{13}C NMR, and mass spectra with those obtained from an authentic sample prepared from **2a**.[11] Compound **2c** gave the known **2b**:[12] mp 204–205 °C; $[\alpha]^{20}_D$ 0 ± 0.1°. These results unequivocally prove the β configuration of the *C*-glycosyl bond of carminic acid, allowing definite assignment of the structure **1a** to the compound. The simple reaction sequence proposed here from **1a** appears to be a good approach to determine the stereochemistry of *C*-glycosyl bonds of natural aromatic *C*-glycosides.

Acknowledgment. The work was supported by Ministero della Pubblica Istruzione.

Registry No. **1a**, 1260-17-9; **1b**, 76173-05-2; **2a**, 57129-89-2; **2b**, 13964-83-5; **2c**, 76318-46-2.

Supplementary Material Available: Experimental details and ^{13}C NMR shifts of sugar carbons of carminic acid (**1a**) (2 pages). Ordering information is given on any current masthead page.

(1) Baranyovits, F. L. C. *Endeavour* **1978**, *2*, 85.
(2) For a review on the present state of knowledge on the chemistry of carminic acid see: Lloyd, A. G. *Food Chem.* **1980**, *5*, 91.
(3) Loon, J. W.; Chem, H. H.; Sim, S. K.; Plambeck, J. A. *Bioorg. Chem.* **1979**, *8*, 17.
(4) A commercial sample was used in this study without any purification (carminic acid from Merck, A.G., batch N. 9659763; a gift from Davide Campari S.p.A., Milano). The sample did not contain N, S, and halogens and had 0.23% ignition residue (principally Pb, Na, and Ca). The titer determined by alkalimetry was 90 ± 1% (triprotic). The field-desorption mass spectrum showed ions at *m/e* 492 and 514 (M^+ of the acid and of Na salt, respectively). The calculated ϵ_{max} value for **1a** was 8660 ± 90 at 494 nm (see: Marshall, P. N.; Horobin, R. V. *Stain Technol.* **1974**, *49*, 2). Most of the analyses were performed by Drs. S. Moretti and M. T. Joannisci of Davide Campari S.p.A., Milano.
(5) Two other signals at δ 48.5 (q, CH_3OH, crystallization solvent[3]) and 19.8 (q, aromatic CH_3), respectively, were present in this region of the spectrum (in dimethyl-d_6 sulfoxide).
(6) Chari, V. M.; Wagner, H.; Schilling, G.; Nesmelyi, A. *Symp. Pap.—IUPAC Int. Symp. Chem. Nat. Prod. 11th* **1978**, *2*, 279.
(7) Dimroth, O.; Kämmerer, H. *Chem. Ber.* **1920**, *53*, 471.
(8) Hillis, W. E.; Horn, D. H. S. *Aust. J. Chem.* **1965**, *18*, 531.
(9) Ali, M. A.; Haynes, L. J. *J. Chem. Soc.* **1959**, 1033.
(10) Ando, S.; Ariga, T.; Yamakawa, T. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1335. The main peak in the gas chromatograph was associated with a substance showing the same retention time and mass spectrum as the pertrifluoroacetate methyl ester of **2a**.
(11) Fuchs, E. F.; Lehmann, J. *Chem. Ber.* **1975**, *108*, 2254.
(12) Coxon, B.; Fletcher, H. G. *J. Am. Chem. Soc.* **1963**, *85*, 2637.

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Received August 5, 1980