$I > 3\sigma(I)$ were used in the full-matrix least-squares refinement after analytical absorption correction. Non-hydrogen atoms were refined in (x, y, z, U_{ij}) and hydrogen atoms in (x, y, z, U). At convergence R, R' were 0.039 and 0.047, reflection weights being $(\sigma^2(F_o) + 0.0005(F_o)^2)^{-1}$. Neutral atom scattering factors were used, those for the non-hydrogen atoms being corrected for anomalous dispersion ($f'f''$).[22] Computation was carried out by using the X-RAY 76 program system[23] implemented by S. R. Hall on a Perkin-Elmer 3240 computer.

Acknowledgment. We are grateful for assistance from the ANU Microanalytical Section and the RSC NMR Service.

Registry No. $[Os^{IV}(en\text{-}H)_2(en)]^{2+}$, 16923-53-8; $[Os^{IV}(en\text{-}H)(en)_2]^{3+}$, 83095-58-3; $[Os(en)_2(im)]^{2+}$, 83095-59-4; $[Os(en)_2(diim)]^{2+}$, 83095-60-7; $[Os(en)(diim)_2]^{2+}$, 83095-61-8; $[Os(en)_3]^{3+}$, 46138-85-6; $(NH_4)_2OsBr_6$, 24598-62-7.

Supplementary Material Available: Listing of structure factor amplitudes (observed and calculated) and thermal parameters (1 page). Ordering information is given on any current masthead page.

(22) "International Tables for X-ray Crystallography"; Ibers, J. A., Hamilton, W. C., Eds.; Kynoch Press: Birmingham, 1974; Vol. 4.
(23) "The X-RAY System—Version of March, 1976", Technical Report TR-446, Computer Science Center, University of Maryland, Stewart, J. M., Ed.
(24) Conventional C, H, N analyses using an automatic analyzer gave consistently low N values for these osmium complexes. It is necessary to use the Kirsten-Dumas method in order to obtain satisfactory N analyses.

Total Synthesis of the C19–C29 Aliphatic Segment of (+)-Rifamycin S[1]

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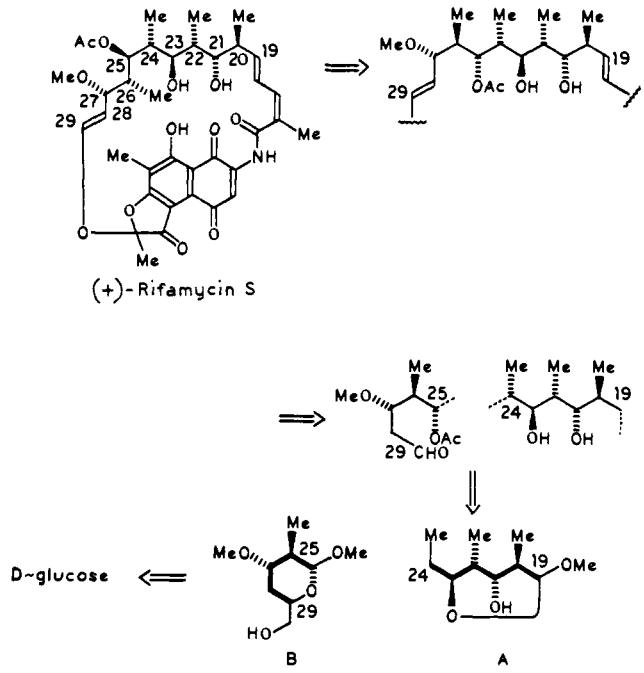
Received May 11, 1982

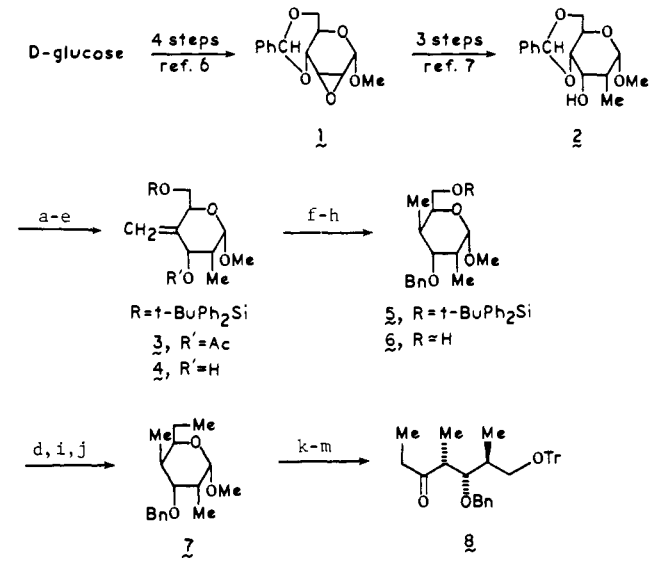
Among the landmark achievements in natural product synthesis in 1980 was Kishi's conquest of the rifamycin S structure.[2] In considering synthetic approaches[3] to this formidable target,[4] one is faced with several challenging problems, not the least of which is the construction of the sequence of alternating methyl and hydroxyl groups situated in the C19–C29 aliphatic segment and encompassing eight contiguous asymmetric centers. We report on the assembly of the aliphatic segment of rifamycin S based on a strategy that recognizes *hidden carbohydrate-type* symmetry[5] as illustrated in Scheme I. Bond disconnection at C24–C25 generates two segments representing C19–C24 and C25–C29, which can be related to two *"chiral templates"*[5] derived from D-glucose and designated as precursors A and B.

Precursor A. The synthesis of precursor A as shown in Scheme II starts with the readily available and crystalline epoxide **1**,[6] which

Scheme I



Scheme II[a]



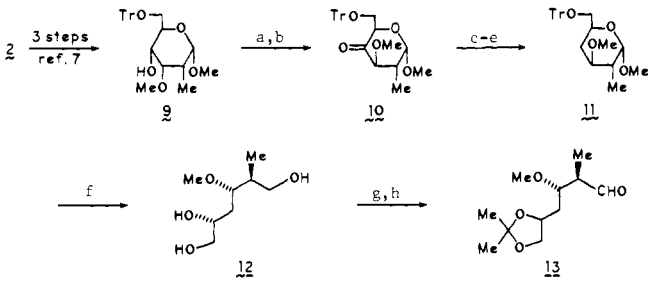
[a] Key: (a) Ac_2O, CH_2Cl_2, DMAP, 91%; (b) 50% aqueous AcOH; (c) diphenyl-*tert*-butylsilyl chloride pyridine, 0 °C, 18 h, 88% (two steps); (d) $COCl_2$, Me_2SO, CH_2Cl_2, Et_3N, −60 to 25 °C, quantitative; (e) $Ph_3P{=}CH_2$, toluene, then KCN, MeOH, 88%; (f) 20% $Pd(OH)_2/C,H_2$, dioxane, then BnBr, THF, KH, 92%; (g) flash chromatography, EtOAc-hexanes 15:85; (h) *n*-Bu_4NF, THF, 76%; (d) 86%; (i) $Ph_3P{=}CH_2$, toluene, 87.5%; (j) 5% Rh/Al_2O_3, H_2, toluene, quantitative; (k) 25% aqueous AcOH, 50 °C, 1 h, then $NaBH_4$, EtOH, 86%; (l) TrCl, pyridine, 65 °C, 20 h, 92%; (m) pyridinium chlorochromate, CH_2Cl_2, 4-Å sieves; see: Herscovici, J.; Antonaki , K. *J. Chem. Soc. Chem. Commun.* 1980 561.

was converted into **2** by methodology developed in our assembly of the erythronolide A secoacid skeleton.[7,8] Elaboration of the

(1) Portions of this work were presented at the Euchem Conference on "Uses of Carbohydrates as Starting Materials for Organic Synthesis", Belle-Ile-en-Mer, France, June 3–6, 1979; Euchem Stereochemistry Conference, Bürgenstock, Switzerland, April 27–May 3, 1980; 28th IUPAC Congress, Vancouver, Canada, August 16–21, 1981, OR 088.
(2) Nagaoka, H.; Rutsch, W.; Schmid, G.; Johnson, M. R.; Kishi, Y. *J. Am. Chem. Soc.* **1980**, *102*, 7962–7965. Iio, H., Nagaoka, H.; Kishi, Y. *Ibid.* **1980**, *102*, 7965–7967. See also ref 22.
(3) See for example: (a) Corey, E. J.; Hase, T. *Tetrahedron Lett.* **1980**, 335–338. (b) Nakata, M.; Takao, H.; Ikeyama, Y.; Sakai, T.; Tatsuta, K.; Kinoshita, M. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1749–1756 and previous papers.
(4) For a recent review, see: Wehrli, W. *Top. Curr. Chem.* **1977**, *72*, 21–49 and references cited therein. See also: Prelog, V.; Oppolzer, W. *Helv. Chim. Acta* **1973**, *56*, 2279–2315.
(5) Hanessian, S. *Acc. Chem. Res.* **1979**, *12*, 159–165.
(6) Wiggins, L. F. *Methods Carbohydr. Chem.* **1963**, *2*, 188–191.
(7) Hanessian, S.; Rancourt, G.; Guindon, Y. *Can. J. Chem.* **1978**, *56*, 1843–1846. Hanessian, S.; Rancourt, G. *Ibid.* **1977**, *55*, 1111–1113. Hanessian, S.; Rancourt, G. *Pure Appl. Chem.* **1977**, *49*, 1201–1214.
(8) Satisfactory elemental analyses and spectroscopic data were obtained for new compounds reported herein. Optical rotations were measured in chloroform at concentrations of 1%. NMR spectra were recorded on Brucker 90 MHz and 400 MHz spectrometers. Mass spectra were recorded on an MM-1212 low-resolution (chemical ionization) and an MS-902 high-resolution (electron impact) instruments.

0002-7863/82/1504-6164$01.25/0

Scheme III[a]



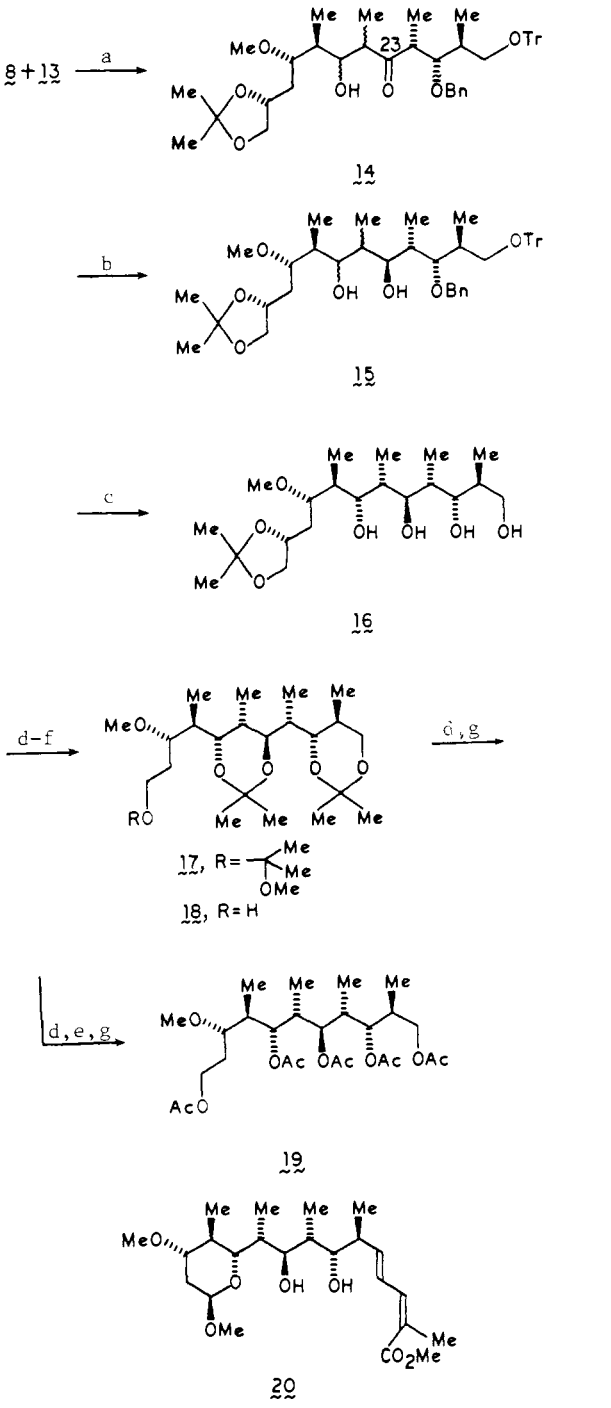
[a] Key: (a) Ethyldimethylaminopropyl carbodiimide, HCl, Me_2SO, quantitative; (b) NaOMe, MeOH, 85%; (c) $NaBH_4$, MeOH, 97%; (d) SO_2Cl_2, pyridine −75 to 25 °C, 18 h, 75%; (e) *n*-Bu_3SnH, AiBN, toluene, reflux, quantitative; (f) 50% aqueous AcOH, 80 °C, 2.5 h, then $NaBH_4$, EtOH, 80%; (g) 2,2-dimethoxypropane, TsOH·H_2O, THF, 78%; (h) pyridinium chlorochromate, 4-Å sieves, CH_2Cl_2, 5 min, 72%.

C-methyl substituent corresponding to C22 was achieved via a stereoselective hydroxyl-assisted catalytic hydrogenation of the allylic alcohol derivative **3**, $[\alpha]_D$ +104.3°, which was readily available from **2**. The resulting epimeric mixture (4:1 axial/equatorial) was benzylated and separated by chromatography to give the desired intermediate **5**, $[\alpha]_D$ +25.6° (^1H NMR δ 0.94 (C-2 Me), 0.79 (C-4 Me), and the latter was homologated to **7**, $[\alpha]_D$ +37° (^1H NMR δ 4.44 (d, J = 4.4 Hz, (H-1), 0.94 (C-2 Me), 0.86 (C-4 Me)) in good overall yield. Having thus taken advantage of the inherent conformational and topological properties of cyclic carbohydrate-derived intermediates in securing the three asymmetric carbon atoms corresponding to C20–C22, we were ready to consider various transforms into acyclic structures representing the six-carbon framework spanning C19–C24 of the target.[9] In one such option, **7** was transformed into the acyclic ketone **8**, mp 91–92 °C, $[\alpha]_D$ −8.9°, whose synthetic utility as a carbanionic equivalent of the C19–C24 segment of rifamycin S can be clearly appreciated.

Precursor B. Intermediate **2** used in the previous sequence was the starting point for the elaboration of precursor B, in which we intended to incorporate the asymmetric centers corresponding to C26 and C27 (Scheme III). Thus, manipulation of **2** by a three-step high-yielding sequence involving crystalline intermediates[7] afforded the known crystalline derivative **9**. Convergence with the desired template (precursor B) required inversion at C3 and deoxygenation at C4. The first operation was achieved by an oxidation–epimerization process[7] which led to the crystalline ketone **10**, mp 137.5–138.5 °C, $[\alpha]_D$ +130.1°, and the second was achieved by reduction of **10** to the alcohol, chlorination,[10] and tributyltin hydride mediated reductive dechlorination[11] to give **11**, $[\alpha]_D$ +76.1°. Once again, the cyclic templates having served their purpose, it was time to exploit their utility as acyclic derivatives. A two-step sequence provided the triol **12**, which presented unique opportunities for functionalization at the C1 position (C25 in rifamycin S).[12] Of the several options available, it was decided to utilize the extended C25–C29 segment as an electrophilic partner represented by aldehyde **13** (^1H NMR δ 9.81 (CHO), 3.47 OMe), 1.11 (C-2 Me), etc.; Scheme III).

Depoloyed with a number of useful intermediates, we were now in a position to address the question of assembling the acyclic carbon backbone of our target by one of several carbon–carbon bond-forming reactions as per our original sythetic blueprint. One attractive option called for engaging intermediates **8** and **13** in a cross-aldol reaction via a metal enolate.[13,14] We reasoned that by virtue of the presence of a β-alkoxy substituent in the ketone component, it could be possible to generate metal-coordinated

Scheme IV[a]



[a] Key: (a) 8 in THF, −78 °C, LDA, 30 min, add 13, −70 °C, 10 min, 76%; (b) Dibal, toluene, −78 °C, 2 h, then 25 °C; (c) 10% Pd/C, H_2, MeOH, separate major isomer, 73%; (d) 70% aqueous AcOH, 45 °C, 90 min, ~quantitative; (e) aqueous $NaIO_4$, MeOH, 10 min, then $NaBH_4$; (f) 2,2-dimethoxypropane, CSA, 36 h, 60%; (g) Ac_2O, EtOAc, DMAP, 50 °C, 3 h, 80%.

(9) Other derivatives incorporating epoxide (C23–C24), aldehyde (C23), and phenyl sulfoxide (C24) functions were prepared and their electrophilic and nucleophilic reactivities studied.

(10) See for example: Jennings, H. J.; Jones, J. K. N. *Can. J. Chem.* **1965**, *43*, 2372-2386. Hanessian, S.; Vatèle, J.-M., *Tetrahedron Lett.* **1981**, *22*, 3579–3582.

(11) Arita, H.; Ueda, N.; Matsushima, Y. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 567–569.

(12) Other derivatives incorporating dithian (C25), phenyl sulfoxide (C25); β-keto phosphonate (C24, C25), and carbomethoxy (C25) functions were prepared, and their nucleophilic and electrophilic reactivities were studied.

(13) Heathcock, C. H. *Science* (*Washington, D.C.*) **1981**, *214*, 395–400. Heathcock, C. H. In "Comprehensive Carbanion Chemistry"; Durst, T., Buncel, E., Eds.; Elsevier, Amsterdam, Vol. II in press.

(14) For some recent examples see: Evans, D. A.; McGee, L. R. *J. Am. Chem. Soc.* **1981**, *103*, 2876–2878 and references cited therein. See also ref 2 as cited by Yamamoto et al. (Yamamoto, Y.; Yatagai, H.; Naruta, Y.; Maruyama, K. *Ibid.* **1980**, *102*, 7107–7109).

species from the prerequisite *Z* enolate such that we could bias the stereoselection in favor of the syn (erythro) diastereoisomers and, perhaps more specifically, the 24*S*,25*R* component.[15,16] A cross-aldol reaction between the lithium enolate derived from **8** and the aldehyde **13** was effected under time and temperature controlled conditions to afford a mixture of two diastereomeric products **14**, $[\alpha]_D$ −17.16°, in 76% yield (Scheme IV), in which the desired 24*S*,25*R* syn isomer was a major component (>7:3).

At this juncture, it was therefore of paramount importance to secure an appropriate degradation product of rifamycin S that contained the intact C19–C29 segment and to be able to establish the constitutional and configurational identity of the aldol product **14**. Degradation of rifamycin S is known to provide a dienic ester fragment **20**.[17] This was further manipulated[18] to give the acetal **17**, mp 73–74 °C, $[\alpha]_D$ +20°, and the pentaacetate derivative **19**, $[\alpha]_D$ ~0°,[19] which were suitable compounds for our correlation. Reduction of the C23 carbonyl function with diisobutylaluminum hydride proceeded with high stereoselectivily (>10:1) to give the desired **15**. Catalytic hydrogenolysis produced major compound **16**,[20] $[\alpha]_D$ −3.2°, which was further transformed into the crystalline hemiacetal and syrupy pentaacetate derivatives **17** and **19**, respectively, and found to be identical in all respects with samples obtained from **20** (TLC, $[\alpha]_D$, 400 MHz and two-dimensional ^{1}H NMR, mass spectroscopy).

Since intermediates such as **16** and **18** can be easily converted to one of Kishi's advanced intermediates, our approach as reported herein represents a formal synthesis of the optically active antibiotic.[21,22]

Acknowledgment. We acknowledge financial assistance provided by the National Engineering and Science Council of Canada, the CNRS for a fellowship to J.-R.P. (1978–1979), le Ministère de l'éducation du Québec and the University of Montreal. We also thank Dr. M. T. Phan Viet for recording the 400-MHz spectra and Dr. K. Tatsuta for a sample of a degradation product of rifamycin S; see ref 17.

Registry No. 2, 75879-81-1; **2**, acetyl derivative, 82707-13-9; **3**, 82707-02-6; **3**, α-OH derivative, 82731-51-9; **3**, keto derivative, 82731-52-0; **4**, 82707-03-7; **5**, 82707-04-8; **6**, 82707-05-9; **6**, debenzyl derivative, 82731-53-1; **6**, aldehyde derivative, 82707-14-0; **7**, 82769-13-9; 7, didehydro derivative, 82768-70-5; **8**, 82707-06-0; **8**, α-OH, detrityl derivative, 82707-15-1; **8**, α-OH derivative, 82707-16-2; **9**, 64526-83-6; **10**, 64526-85-8; **11**, 82707-07-1; **11**, β-chloro derivative, 82707-17-3; **12**, 82731-48-4; **13**, 82707-08-2; **13**, hydroxy derivative, 82707-18-4; **14**, 82707-09-3; **15**, 82707-10-6; **16**, 82707-11-7; **17**, 82731-49-5; **18**, 82707-12-8; **19**, 82731-50-8; (+)-rifamycin S, 13553-79-2.

Supplementary Material Available: NMR spectral data and physical constants for selected intermediates (13 pages). Ordering information is given on any current masthead page.

(15) Heathcock, C. H.; Pirrung, M. C.; Lampe, J.; Buse, C. T.; Young, S. D. *J. Org. Chem.* **1981**, *46*, 2290–2300 and references cited therein. Heathcock, C. H.; Young, S. D.; Hagen, J. P.; Pirrung, M. C.; White, C. T.; Van Der Veer, D. *Ibid.* **1980**, *45*, 3846–3856.

(16) The selectivity in the aldol condensation can be rationalized based in part on a coordinated transition state[15] involving the benzyloxy group.

(17) Kinoshita, M.; Tatsuta, K.; Nakata, M. *J. Antibiot.* **1978**, *31*, 630–632.

(18) The following steps were involved: (a) O_3; (b) $NaBH_4$; (c) Ac_2O, DMAP, AcOEt; (d) *n*-Bu_3SnH, AIBN, toluene; (e) TsOH, aqueous MeOH; (f) $NaBH_4$; (g) 2,2-dimethoxypropane, CSA.

(19) The structure and identity of **19** and complete chemical shift assignments were further confirmed by a completed ^{1}H NMR decoupling experiments and two-dimensional NMR in the C–Me region at 400 MHz (supplementary material available).

(20) Chromatographic separation on silica gel with CH_2Cl_2–EtOH (96:14) as the eluant.

(21) During the course of this work, another carbohydrate-based approach to the aliphatic segment of rifamycin S was reported by using a different strategy; see ref 3b.

(22) For a highly stereocontrolled syntheses of the optically active form of the aliphatic segment of rigamycin S, see: Nagaoka, H.; Kishi, Y. *Tetrahedron* **1981**, *37*, 3873–3888.

Additions and Corrections

General Methods of Synthesis of Indole Alkaloids. 14.[1,2] Short Routes of Construction of Yohimboid and Ajmalicinoid Alkaloid Systems and Their ^{13}C Nuclear Magnetic Resonance Spectral Analysis [*J. Am. Chem. Soc.* **1976**, *98*, 3645]. ERNEST WENKERT,* CHING-JER CHANG, H. P. S. CHAWLA, DAVID W. COCHRAN, EDWARD W. HAGAMAN, JAMES C. KING, and KAZUHIKO ORITO.

Page 3650, Table II: The δ value of C(3) of compound **24** should read "59.6".

Total Synthesis of the Yohimbines [*J. Am. Chem. Soc.* **1979**, *101*, 5370]. ERNEST WENKERT,* TIMOTHY D. J. HALLS, GERHARD KUNESCH, KAZUHIKO ORITO, RICHARD L. STEPHENS, WAYNE A. TEMPLE, and JHILLU YADAV.

Page 5376, reference 2 (missing fourth line): R. N. Guthikonda, *J. Am. Chem. Soc.*, **94**, 5109 (1972); (d) L. Töke, K. Honty, ...

Reactions of Metal–Metal Multiple Bonds. 8. Forming Mo–Mo Quadruple Bonds by Reductive Elimination (Alkyl Group Disproportionation) in the Reactions of 1,2-$Mo_2R_2(NMe_2)_4$ Compounds (M≡M) with Carbon Dioxide and 1,3-Diaryltriazines [*J. Am. Chem. Soc.* **1982**, *104*, 2138]. M. J. CHETCUTI, M. H. CHISHOLM,* K. FOLTING, D. A. HAITKO, and J. C. HUFFMAN.

Page 2144, last sentence in **Preparation of $Mo_2(O_2CNMe_2)_4$**: The sentence should read as follows—Anal. Calcd: C, 26.48; H, 4.41; N, 10.29. Found: C, 26.48; H, 4.25; N, 10.09.

Coordination Chemistry of Metal Surfaces. 3.[1] Benzene and Toluene Interactions with Nickel Surfaces [*J. Am. Chem. Soc.* **1981**, *103*, 773]. C. M. FRIEND and E. L. MUETTERTIES.*

Page 777, Figure 8: The scale for the abscissa was incorrect. Figure 8 should be: