causing the conversion of Cyt to Ura even after enzymatic repair. Furthermore, the configuration of these dimers was determined to be trans with the trans–syn isomer as the only or the predominant product. If a cis–syn isomer should form as reported,[4,5] in the study of Cyd and dCyd, its acid-catalyzed deamination product, cis–syn Ura<>Ura, should be extremely stable and easily identifiable. The information concerning the stereoconfiguration of these dimers is of particular importance when related to the photochemistry of nucleic acids.[29–33]

References and Notes

(1) R. B. Setlow and W. L. Carrier, *J. Mol. Biol.*, **17**, 237 (1966).
(2) R. Ben-Ishi, E. Ben-Hur, and Y. Hornfeld, *Isr. J. Chem.*, **6**, 769 (1968).
(3) A. J. Varghese and C. S. Rupert, *Photochem. Photobiol.*, **13**, 365 (1971).
(4) A. J. Varghese, *Biochemistry*, **10**, 2194 (1971).
(5) A. J. Varghese, *Photochem. Photobiol.*, **15**, 113 (1972).
(6) H. Taguchi, B. S. Hahn, and S. Y. Wang, 2nd Annual Meeting American Society of Photobiology, Vancouver, B.C., July 1974, p 21.
(7) B. S. Hahn, H. Taguchi, and S. Y. Wang, *Radiat. Res.*, **59**, 105 (1974).
(8) T. Ueda and J. J. Fox, *J. Med. Chem.*, **6**, 697 (1963).
(9) H. L. Wheeler and T. B. Johnson, *Am. Chem. J.*, **42**, 30 (1909).
(10) T. Ueda and J. J. Fox, *J. Org. Chem.*, **29**, 1770 (1964).
(11) G. W. Kenner, C. B. Reese, and A. R. Todd, *J. Chem. Soc.*, 855 (1955).
(12) I. Wempen, R. Dushinsky, L. Kaplan, and J. J. Fox, *J. Am. Chem. Soc.*, **83**, 4755 (1961).
(13) A. R. Katritzky and A. J. Waring, *J. Chem. Soc.*, 3046 (1963).
(14) J. J. Fox and D. Shugar, *Biochim. Biophys. Acta*, **9**, 369 (1952).
(15) P. Brooks and P. D. Lawley, *J. Chem. Soc.*, 1348 (1962).
(16) S. Y. Wang, *J. Am. Chem. Soc.*, **80**, 6196 (1958).
(17) H. Taguchi and S. Y. Wang, *J. Org. Chem.*, **42**, 3321 (1977); cf. ref 31.
(18) M. Green and S. S. Cohen, *J. Biol. Chem.*, **228**, 601 (1957).
(19) G. DeBoer and H. E. Johns, *Biochim. Biophys. Acta*, **204**, 18 (1970).
(20) I. L. Karle, in "Photochemistry and Photobiology of Nucleic Acids, Chemistry", Vol. 1, S. Y. Wang, Ed., Academic Press, New York, N.Y., 1976, Chapter 11, p 483.
(21) M. N. Khattak and S. Y. Wang, *Tetrahedron*, **28**, 945 (1972).
(22) E. J. Corey, J. D. Bass, R. LeMahieu, and R. B. Mitra, *J. Am. Chem. Soc.*, **86**, 5570 (1964).
(23) C. Fenselau, in "Photochemistry and Photobiology of Nucleic Acids, Chemistry", Vol. 1, S. Y. Wang, Ed., Academic Press, New York, N.Y., 1976, Chapter 9, p 420.
(24) D. M. Brown and M. J. E. Hewlins, *J. Chem. Soc. C*, 2050 (1968).
(25) M. Kasha, in "Light and Life", W. D. McElroy and B. Glass, Ed., Johns Hopkins University Press, Baltimore, Md., 1961, p 31.
(26) C. L. Angell, *J. Chem. Soc.*, 504 (1961).
(27) R. T. C. Brownlee, A. R. Katritzky, and R. D. Topom, *J. Chem. Soc.*, 726 (1966).
(28) A. R. Katritzky and J. M. Lagowski, *Adv. Heterocycl. Chem.*, **1**, 339 (1963).
(29) A. J. Varghese and S. Y. Wang, *Nature (London)*, **213**, 909 (1967).
(30) D. Weinblum, *Biochem. Biophys. Res. Commun.*, **27**, 387 (1967).
(31) H. Taguchi and S. Y. Wang, *Biochem. Biophys. Res. Commun.*, **73**, 356 (1976).
(32) M. H. Patrick and R. O. Rahn, in "Photochemistry and Photobiology of Nucleic Acids, Biology", Vol. 2, S. Y. Wang, Ed., Academic Press, New York, N.Y., 1976, Chapter 2, p 35.
(33) G. Fisher and H. E. Johns, in "Photochemistry and Photobiology of Nucleic Acids, Chemistry", Vol. 1, S. Y. Wang, Ed., Academic Press, New York, N.Y., 1976, Chapter 4, p 169.

Diterpenoid Total Synthesis, an A → B → C Approach. 12. Aromatic C Rings without Alkyl Substituents. Model Systems for Podocarpic Acid and Diterpenoid Alkaloids[1]

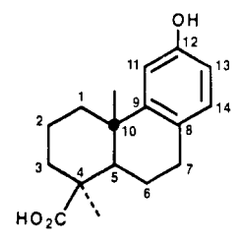
Walter L. Meyer,* Carl W. Sigel,[1d] R. John Hoff,[1e] Thomas E. Goodwin,[1f] Richard A. Manning, and Patricia G. Schroeder

Department of Chemistry, University of Arkansas, Fayetteville, Arkansas 72701

Received May 17, 1977

Examination of the general sequence **2** → **7** for addition of a 13-unsubstituted phenolic C ring[2] to decalones **2a–e** is described. Condensation of the decalones with HCO_2Et is uniformly efficient, but the rates and yields for conversion of the 8-hydroxymethylene derivatives to 8-formyl-Δ^8-7-octalones by reaction with DDQ vary remarkably. Addition of the sodium enolate of $MeCOCH_2CO_2$-*t*-Bu to α-formyl enones **4a–d** and acid-catalyzed cyclization of the adducts **5a–c** to tricyclic enediones **6a–c** proceed normally and in high yield. Aromatization of **6a–c** by $pyHBr_3$ affords not only 7-keto-12-phenols (**7**), the sole products from their 13-alkyl analogues, but also 13-bromo-7-keto-12-phenols and, at least in the case of **6a**, 13-bromo-Δ^{13}-7,12-enediones (**9**). Dehydrohalogenation of **9a** by collidine produces **7a**, a podocarpic acid model. Hydrogenolysis of the 12-(2′-benzoxazolyloxy) derivative of **7b** provides tetracyclic amide **19**, which has been formally converted to several diterpenoid alkaloids.[15]

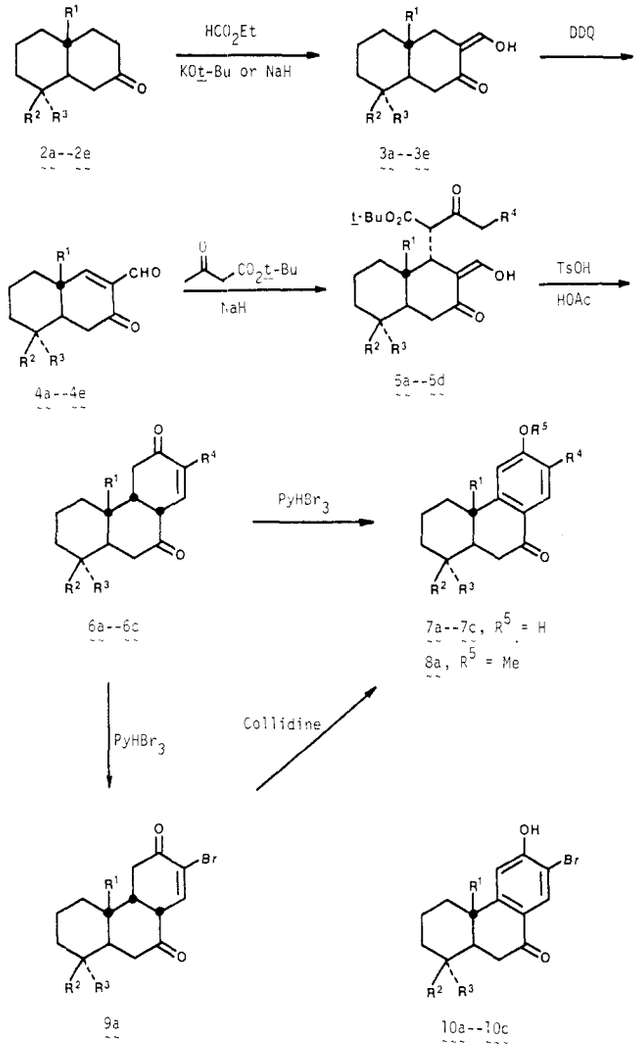
Total syntheses of several C-aromatic perhydrophenanthrene diterpenoids have demonstrated the efficiency of the general sequence **2** → **7** (Scheme I) for constructing a substituted aromatic ring at carbons 8 and 9 of a *trans*-7-decalone.[1a,2–4] A C-13 alkyl substituent (R^4) has been an important component of all the natural products we have previously prepared by this route, and we consider that one of the significant advantages of this synthetic procedure is its ability to include introduction of that group as an integral part of the annulation process. However, certain diterpenoids such as podocarpic acid (**1**) are devoid of such C-ring substitution, and this might also be true of other structures for which use of this ring elaboration plan would be desirable. Investigations reported here show that the synthesis is equally applicable to structures in which R^4 = H, but that modifications of the sequence may be necessary. They also reveal some unexpected effects of structure on the reaction of an α-hydroxymethylene ketone with DDQ (**3** → **4**). These conclusions result primarily from research into the synthesis of model compounds in the podocarpic acid and diterpenoid alkaloid series.



1

The decalones which were used in this work, **2a–e**, have been reported earlier,[5,6] and their condensation with ethyl formate is unexceptional. However, dehydrogenation of these hydroxymethylene ketones by DDQ under conditions which have given 75–95% yields of α-formyl enones **4** in other

Scheme I



a, R^1 = CN; R^2 = CO_2Et; R^3 = Me; R^4 = H

b, R^1,R^2 = CH_2NAcCH_2; R^3 = Me; R^4 = H

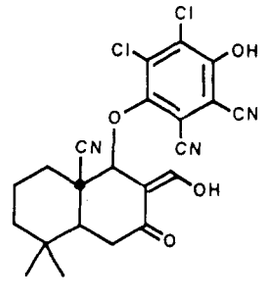
c, R^1,R^2 = CH_2NMsCH_2; R^3 = Me; R^4 = H

d, R^1 = CN; R^2 = R^3 = Me; R^4 = H

e, R^1 = CN; R^2 = Me; R^3 = CO_2Et; R^4 = H

series[1a,3,4] is not uniformly successful. The 4β-carbethoxy-10-cyano and *N*-acetylimino derivatives **3a** and **3b** react normally to afford the corresponding aldehydes **4a** and **4b** in 75–85% yield after 5 min at room temperature in dioxane containing acetic acid.[4] The 10-cyano-4,4-dimethyl compound **3d** also reacts rapidly under these conditions, but aldehyde **4d** is obtained in only 28% yield and is unaccompanied by residual **3d.** The remainder of the material from the latter reaction has not been isolated or identified, but it seems to be lost during bicarbonate treatment of the crude product to remove dichlorodicyanohydroquinone and this suggests the possible formation of a substance such as **11.** Analogous species have occasionally been encountered in other reactions of DDQ,[7] although conjugate addition of the hydroquinone to an α-formyl enone has not been a problem during oxidation of the other hydroxymethylene decalones we have examined. Reasons for this peculiar behavior of **3d** are not clear. However, we hesitate to ascribe it solely to an influence of the angular cyano group in view of the fact that **3a** and the $\Delta^{5,6}$ analogue of **3d**[5] react normally, and they both contain a similarly proximate nitrile.

Hydroxymethylene ketones **3c** and **3e** are dehydrogenated by DDQ in dioxane far more slowly than are their counterparts



11

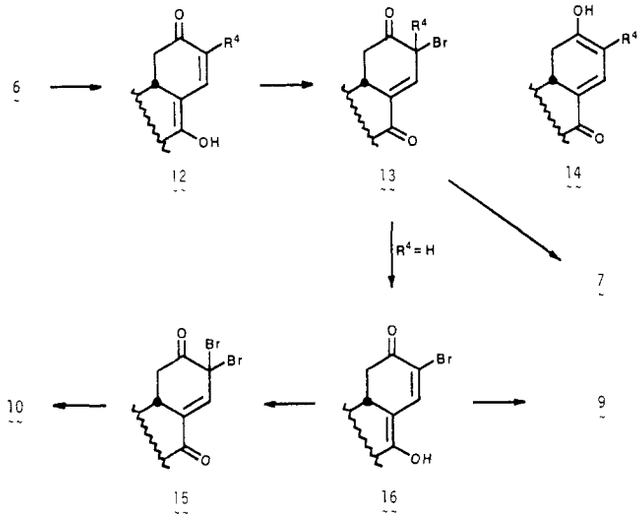
3a, 3b, etc. In fact, these reactions are so slow that 50% or more of the hydroxymethylene ketone remains after up to 18 h even in the presence of excess DDQ. The sulfonamido compound **3c** can be converted to its formyl enone **4c** in excellent yield (89%) by treatment with DDQ for 18 h in refluxing benzene,[8] but even these conditions do not substantially improve matters with **3e.** These differences in the rates of dehydrogenation of hydroxymethylene ketones by DDQ are particularly perplexing when they are brought about by structural changes as slight as the nature of a remote substituent on nitrogen (**3b** vs. **3c**) or the configuration at a remote center (**3a** vs. **3e**). The main comment we can presently make regarding the synthetic utility of this reaction is that it is surprisingly sensitive to subtle structural effects, and if the usual procedure is not effective with a particular compound a search for alternate reaction conditions may be fruitful.[9]

Addition of the sodium enolate of *tert*-butyl acetoacetate to α-formyl enones **4a–d** proceeds normally.[3–5,10] Acid-catalyzed conversion of the adducts to *trans-syn-cis*-$\Delta^{13,14}$-enediones **6a–c**[10] also occurs without incident,[11,12] but these enediones are more sensitive than are their 13-alkyl counterparts. In most cases the crude products appear to be substantially free of contaminants (^{1}H NMR), but attempted purification leads to considerable losses. Nonetheless, the crude materials suffice for further use, so the general sequence **2** → **6** is quite acceptable for synthesis of these compounds in overall yields of 50–60% from the decalones.

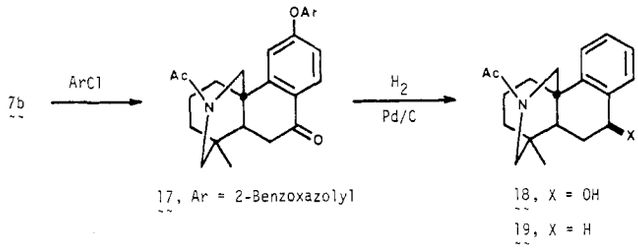
Reaction of enediones **6a–c** with pyridine hydrobromide perbromide[3] is significantly different from that of their 13-alkyl analogues. The latter substances are converted to 7-keto-12-phenols **7** (R^4 = alkyl) in high yield,[1a,3,4] the only complication arising from competitive 6α-bromination in the dehydroabietic acid series.[1a] Under comparable conditions ketophenol **7a** is produced in substantially lower yield from **6a,** and it is accompanied by a considerable amount of bromoenedione **9a** (IR and ^{1}H NMR identification) and a small amount of the corresponding 13-bromophenol **10a.** The bromoenedione becomes the major product and the amount of bromophenol is minimized when pyridine hydrobromide perbromide is added slowly, rather than rapidly, to **6a.** However, the bromoenedione is converted to ketophenol **7a** by collidine, so this two-step process represents a technique for aromatization of 13-unsubstituted enediones which is nearly as efficient (80% from **6a**) as is use of the brominating agent alone with the 13-alkyl compounds.[13]

These results are consistent with a course of events such as that shown in Scheme II for reaction of an enedione like **6** (R^4 = H or alkyl) with pyridine hydrobromide perbromide.[3,14] An alkyl group at C-13 blocks further enolization in the C-7–C-8–C-14–C-13–C-12 system of an initial 13-bromoenedione like **13,** and 1,4-dehydrohalogenation (or its equivalent) to ketophenol **7** (R^4 = H) is normally the favored process.[1a,3] However, in the absence of that alkyl group reenolization can compete with dehydrohalogenation, and an enol like **16**[14] can either ketonize (**9**) or brominate (**15** or an 8,13 dibromo isomer), with the latter event leading to bromophenol **10.**

Scheme II



Ketophenols **7b** and **7c** bear an obvious structural relationship to many diterpenoid alkaloids of the aconite–garrya family. Although it is not our plan to use these particular compounds as intermediates for elaboration of such structures, experimental relation of them to the natural products is desirable in order to confirm the structures of the ketophenols. For this purpose the phenolic and ketonic oxygens of the *N*-acetyl derivative **7b** were removed by the sequence **7b** → **17** → **19**.[1a] The reactions were conducted without ex-



tensive purification of intermediates or optimization of conditions, and are undoubtedly capable of improvement should that be desirable for other purposes. Nonetheless, the IR spectrum of amide **19** from this degradation is identical with that of an authentic sample.[15] This substantiates the structures which have been assigned to our compounds, particularly the trans A/B ring fusion in **2b** and **2c** and all of their progeny.[6] In addition, Tahara and Hirao have reported conversion of their enantiomer of **19** to intermediates which, in racemic form, have been transformed to (±)-atisine, (±)-veatchine, and (±)-garryine,[16] so this work also constitutes another total synthesis of these diterpenoid alkaloids, albeit only in the strictly formal sense.

Experimental Section

General procedures and techniques were the same as described earlier.[3] Unless otherwise specified, HCl, NaOH, KOH, NH_4OH, and $NaHCO_3$ solutions were aqueous and HOAc was glacial. Brine refers to saturated aqueous NaCl. General procedures for isolation of reaction products are abbreviated as follows: (A) the specified organic solution was washed with the indicated sequence of aqueous solutions followed by water or brine and dried ($MgSO_4$ or Na_2SO_4), and solvent was removed either in vacuo or by evaporation on the steam bath in a stream of dry N_2; (B) the indicated aqueous mixture was thoroughly extracted with the specified organic solvent followed by the steps in procedure A; (C) the reaction mixture was added to water or brine followed sequentially by the steps in procedures B and A. When no temperature is specified, operations were conducted at room temperature, ca. 23 °C. Mass spectral data is expressed in the form: *m/e* (percent base peak intensity). ^1H NMR spectra are reported for $CDCl_3$ solutions and IR spectra for $CHCl_3$ solutions unless otherwise indicated. Melting points (open capillary tubes) are corrected for stem exposure.

4β-Carbethoxy-10-cyano-8-hydroxymethylene-4α-methyl-5α-decal-7-one (3a). A solution of 500 mg (1.90 mmol) of **2a**, mp 68–75 °C,[6] in 30 mL of dry *t*-BuOH containing KO-*t*-Bu from prior dissolution of 500 mg (12.8 mg-atoms) of K was stirred for 15 min at 45 °C (N_2 atmosphere), treated dropwise during 30 min with 3 mL (37 mmol) of HCO_2Et in 15 mL of *t*-BuOH,[4] stirred at 45–50 °C for 9 h, treated with 1 mL of HCO_2Et, stirred at 50 °C for 5 h, and acidified to pH 6 with HOAc. The mixture was poured into brine and extracted with Et_2O and $CHCl_3$, which was extracted with 1% NaOH. Rapid acidification with 4 N HCl and isolation B ($CHCl_3$; 5% $NaHCO_3$ wash) afforded 455 mg (82%) of crude **3a** as tan crystals which recrystallized from hexane as colorless needles: mp 91–92 °C; UV max (95% EtOH) 270 nm (ε 9000); IR 2225, 1718, 1645, 1585 cm^{-1}; ^1H NMR τ 1.42 (s, 1 H), 5.80 (q, *J* = 7 Hz, 2 H), 8.70 (t, *J* = 7 Hz, 3 H), 8.75 (s, 3 H); mass spectrum 291 (42), 218)43), 217 (100), 190 (17), 148 (16), 41 (15).

Anal. Calcd for $C_{16}H_{21}NO_4$: C, 65.95; H, 7.27; N, 4.81. Found: C, 66.03; H, 7.21; N, 4.73.

4β,10-Acetyliminobismethyl-8-hydroxymethylene-4α-methyl-5α-decal-7-one (3b). Reaction of 800 mg (3.21 mmol) of once-distilled **2b**, bp 190–200 °C (0.25 mm),[6] with 2.2 mL of HCO_2Et and the KO-*t*-Bu from 800 mg (20.5 mg-atoms) of K in a total of 85 mL of *t*-BuOH was conducted as described for preparation of **3a**, but at ca. 23 °C throughout (HCO_2Et added in two portions: 1 mL in 10 mL of *t*-BuOH during 2 h, and after 6 h 1.2 mL in 10 mL of *t*-BuOH during 1 h). Isolation as described for **3a** afforded 795 mg (89%) of crude **3b** as a yellowish gum: UV max (95% EtOH) 281 (ε 7100); (base) 313 nm (ε 14 000); IR 1620 cm^{-1} (broad); ^1H NMR τ 1.26 (s) and 1.34 (s) (total 1 H), 5.88 and 7.32 (AB, *J* = 14 Hz) and 5.97 and 7.32 (AB, *J* = 14 Hz) (total 2 H), ~6.75 (br s, 2 H), 7.92 (s) and 7.94 (s) (total 3 H), 9.12 (s) and 9.14 (s) (total 3 H).[17] On some occasions the crude **3b** crystallized (mp 80–89 °C), but a suitable recrystallization technique was not found, and because many analogous compounds decompose extensively during attempted chromatography, sublimation, or distillation, crude **3b** was used directly.

8-Hydroxymethylene-4β,10-methanesulfonyliminobismethyl-4α-methyl-5α-decal-7-one (3c). Reaction of 500 mg (1.75 mmol) of crude **2c**, mp 182–185 °C,[6] with 2.85 g (38.5 mmol) of HCO_2Et and the KO-*t*-Bu from 546 mg (14.0 mg-atoms) of K in a total of 75 mL of *t*-BuOH was conducted as described for the preparation of **3b**, except that 30 min was allowed prior to addition of HCO_2Et (which was all added during 1 h) and reaction was continued for 12 h after addition of HCO_2Et. Acidification with HOAc[4,18] was followed by isolation C ($CHCl_3$; 5% $NaHCO_3$ wash) to provide 524 mg (96%) of crude **3c** as a yellowish solid: mp 177–184 °C. Sublimation [150–156 °C (1.0–0.25 mm); extensive material loss from decomposition] afforded an analytical sample: mp 185–187 °C dec; UV max (95% EtOH) 276 (ε 7500); (base) 316 nm (ε 12 500); IR 1640, 1580, 1340, 1150 cm^{-1}; ^1H NMR τ 1.41 (s, 1 H), 6.63 and 7.22 (AB, *J* = 12 Hz, 2 H), 6.69 and 7.24 (AB, *J* = 12 Hz, 2 H), 7.29 (s, 3 H), 9.13 (s, 3 H); mass spectrum 313 (34), 234 (100), 206 (63), 107 (33), 91 (34), 79 (34), 44 (62), 42 (57), 41 (59).

Anal. Calcd for $C_{15}H_{23}NO_4S$: C, 57.51; H, 7.35; N, 4.47; S, 10.22. Found: C, 57.60; H, 7.44; N, 4.48; S, 10.09.

10-Cyano-4,4-dimethyl-8-hydroxymethylene-5α-decal-7-one (3d). Reaction of 500 mg (2.44 mmol) of **2d**, mp 59–62 °C,[5] with 720 mg (9.73 mmol) of HCO_2Et and 174 mg (7.25 mmol) of NaH (as 300 mg of a 58% dispersion in mineral oil) in 20 mL of PhH was conducted as described for the 4,4,10-trimethyl analogue[3] to afford 480 mg (84%) of **3d** as pale yellow prisms, mp 104–114 °C, sublimation of which [110 °C (1 mm)] provided pure **3d** as colorless prisms: mp 113–116 °C; UV max (95% EtOH) 307 (ε 12 000); (base) 309 nm (ε 18 300); IR 2230, 1650, 1587 cm^{-1}; ^1H NMR τ −4.28 (br s, 1 H), 1.41 (s, 1 H), 8.90 (s, 3 H), 9.05 (s, 3 H); mass spectrum 233 (66), 218 (17), 136 (100), 98 (36), 70 (23), 41 (26).

Anal. Calcd for $C_{14}H_{19}NO_2$: C, 72.07; H, 8.21; N, 6.00. Found: C, 71.99; H, 8.30; N, 6.20.

4α-Carbethoxy-10-cyano-8-hydroxymethylene-4β-methyl-5α-decal-7-one (3e). Reaction of 318 mg (1.21 mmol) of **2e**, mp 84–85.5 °C,[6] with 1.7 g (23 mmol) of HCO_2Et and the KO-*t*-Bu from 356 mg (9.13 mg-atoms) of K in a total of 40 mL of *t*-BuOH was conducted at ~23 °C for 23 h as described for the preparation of **3c** to produce 307 mg (87%) of **3e** as a yellowish oil which crystallized. Recrystallization from $CHCl_3$–hexanes and trituration with hexanes afforded pure **3e** as colorless needles: mp 121.5–122 °C; UV max (95% EtOH) 275 (ε 11 400); (base) 310 nm (ε 20 800); IR 2220, 1718, 1650, 1590 cm^{-1}; ^1H NMR τ 1.42 (s, 1 H), 5.86 (q, *J* = 7 Hz, 2 H), 8.58 (s, 3

H), 8.75 (t, J = 7 Hz, 3 H); mass spectrum 291 (88), 218 (100), 217 (77), 190 (21), 98 (32), 83 (36), 55 (32), 41 (75).

Anal. Calcd for $C_{16}H_{21}NO_4$: C, 65.96; H, 7.27; N, 4.81. Found: C, 65.77; H, 7.22; N, 4.92.

4β-Carbethoxy-10-cyano-8-formyl-4α-methyl-5α-Δ⁸-octal-7-one (4a). A solution of 860 mg (2.96 mmol) of crude **3a** and 6 drops of HOAc in 17 mL of dioxane was treated with 762 mg (3.36 mmol) of 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ), mp 214–215 °C, stirred until homogeneous (5 min; N_2 atmosphere), and evaporated to dryness at 2 mm and ~23 °C (10 min required).[4] A $CHCl_3$ suspension of the residue was filtered and subjected to isolation A (5% $NaHCO_3$ wash; $CHCl_3$ back-wash[19]) to yield 683 mg (80%) of crude **4a** as a brown oil which could not be purified by crystallization or distillation; spectra showed no significant absorption from contaminants (~5% or less): IR 2220, 1720, 1700, 1690, 1615 cm^{-1}; ^1H NMR τ −0.13 (s, 1 H), 2.78 (s, 1 H), 5.76 (q, J = 7 Hz, 2 H), 8.68 (t, J = 7 Hz, 3 H), 8.71 (s, 3 H).

4β,10-Acetyliminobismethyl-8-formyl-4α-methyl-5α-Δ⁸-octal-7-one (4b). Reaction of 470 mg (1.70 mmol) of crude **3b** with 405 mg (1.78 mmol) of DDQ and 4 drops of HOAc in 12 mL of dioxane was conducted as described for the preparation of **4a**[19] to produce 400 mg (86%) of crude **4b** as a yellowish semisolid which recrystallized from EtOAc–cyclohexane as colorless prisms: mp 125–131 °C; IR 1700, 1685, 1635, 1608 cm^{-1}; ^1H NMR τ −0.07 (s) and −0.06 (s) (total 1 H), 2.67 (s, 1 H), 7.88 (s, 3 H), 9.07 (s) and 9.10 (s) (total 3 H);[17] mass spectrum 275 (13), 190 (11), 148 (100), 43 (19). Further recrystallization afforded an analytical sample of mp 152–153 °C.

Anal. Calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69. Found: C, 69.37; H, 7.54.

8-Formyl-4β,10-methanesulfonyliminobismethyl-4α-methyl-5α-Δ⁸-octal-7-one (4c). A solution of 100 mg (0.319 mmol) of crude **3c,** mp 176–182 °C dec, and 2 drops of HOAc in 2 mL of dry PhH was mixed with a solution of 79.0 mg (0.348 mmol) of DDQ, mp 211–213 °C, in 8 mL of hot PhH and the orange solution was boiled under reflux for 17 h (N_2 atmosphere), concentrated to 2 mL in a N_2 stream, diluted to 10 mL with $CHCl_3$, refluxed for 5 min, and filtered. The collected $DDQH_2$ was washed by suspension for 10 min in 10 mL of refluxing $CHCl_3$ and filtration. Combined filtrates were processed by isolation A (5% $NaHCO_3$ wash; $CHCl_3$ back-wash[19]) to provide 88 mg (89%) of crude **4c** as a yellowish solid, mp 213–224 °C dec, which recrystallized from CH_2Cl_2–pentane as colorless prisms: mp 218–220 °C dec; UV max (95% EtOH) 225 (ε 5900); (base) 318 nm (ε 15 200); IR 1705, 1682, 1612, 1344, 1155 cm^{-1}; ^1H NMR τ −0.02 (s, 1 H), 2.76 (s, 1 H), 7.25 (s, 3 H), 9.08 (s, 3 H); mass spectrum 311 (18), 232 (44), 148 (29), 122 (37), 91 (45), 79 (29), 77 (40), 55 (28), 44 (92), 42 (100).

Anal. Calcd for $C_{15}H_{21}NO_4S$: C, 57.86; H, 6.80; N, 4.50; S, 10.30. Found: C, 57.71; H, 6.65; N, 4.45; S, 10.08.

10-Cyano-4,4-dimethyl-8-formyl-5α-Δ⁸-octal-7-one (4d). Reaction of 500 mg (2.15 mmol) of **3d,** mp 102–111 °C, with 500 mg (2.20 mmol) of DDQ and 5 drops of HOAc in 5 mL of dioxane was conducted as described for the preparation of **4a.** The residue from the evaporation of dioxane was extracted five times with 6:1 Et_2O–$CHCl_3$, which was diluted with Et_2O and subjected to isolation A (brine and 5% $NaHCO_3$ wash) to afford 140 mg (28%) of **4d** as a yellow oil which appeared by ^1H NMR to be free of significant contamination: IR (CCl_4) 2216, 1700, 1690, 1610 cm^{-1}; ^1H NMR τ −0.11 (s, 1 H), 2.67 (s, 1 H), 8.84 (s, 3 H), 9.03 (s, 3 H). Attempted purification by crystallization or chromatography failed.

4α-Carbethoxy-10-cyano-8-formyl-4β-methyl-5α-Δ⁸-octal-7-one (4e). A stirred solution of 118 mg (0.405 mmol) of **3e,** mp 122.5–124 °C, and 0.1 mL of HOAc in 15 mL of dry dioxane was treated with 138 mg (0.608 mmol) of DDQ (N_2 atmosphere), heated under reflux for 5 h, diluted with $CHCl_3$, and evaporated to dryness in vacuo. A suspension of the residue in $CHCl_3$ was heated to boiling, filtered (hot $CHCl_3$ wash of residue), and processed by isolation A (1% $NaHCO_3$ wash; $CHCl_3$ back-wash) to provide 117 mg (100%) of a ca. 1:1 mixture (^1H NMR assay) of **3e** and **4e** as a pale yellow oil: ^1H NMR τ −0.08 (s, 1 H), 2.70 (s, 1 H), 5.85 (q, J = 7 Hz, 2 H), 8.52 (s, 3 H), 8.73 (t, J = 7 Hz, 3 H), plus resonances of **3e.** No successful method for purifying **4e** was found.

Ethyl 10-Cyano-7,12-dioxo-5α,8β,9β,17-norpodocarp-13-en-16-oate (6a). A mixture of 535 mg (3.39 mmol) of $CH_3COCH_2CO_2$-t-Bu, bp 95–100 °C (20–25 mm),[20] and 81 mg (3.4 mmol) of NaH (as 140 mg of a 58% dispersion in mineral oil) in 20 mL of dry PhH was stirred for 15 min (N_2 atmosphere), treated with 635 mg (2.20 mmol) of crude **4a** in 15 mL of PhH, stirred for 2 h, and acidified with HOAc (pH 6).[4] Isolation C ($CHCl_3$; 5% $NaHCO_3$ wash) left 920 mg of a mixture of **5a** (^1H NMR shows only one diastereomer[10]) and $CH_3COCH_2CO_2$-t-Bu as a tan oil (estimated ~75% **5a** by ^1H NMR): ^1H NMR τ 1.40 (s, 1 H), 5.82 (q, J = 7 Hz, 2 H), 7.77 (s, 3 H), 8.55 (s, 9 H), 8.62 (s, 3 H), 8.71 (t, J = 7 Hz, 3 H) plus resonances of CH_3CO-CH_2CO_2-t-Bu at τ 6.67 (s, 2 H), 7.77 (s, 3 H), 8.55 (s, 9 H). Purification was not attempted.

A solution of 920 mg of this crude **5a** and 100 mg of TsOH in 40 mL of HOAc was boiled under reflux for 2 h (N_2 atmosphere), 0.5 g of NaOAc was added, and most of the HOAc was removed in vacuo.[4] The residue was partitioned between $CHCl_3$ and water, which was subjected to isolation B ($CHCl_3$; 5% $NaHCO_3$ wash) to afford 520 mg (72% from **4a**) of crude **6a** as a brown semisolid, the spectra of which indicated only minimal contamination. Chromatography over Florisil (2 × 20 cm; Et_2O elution) provided 210 mg (29%) of **6a** as a colorless solid (mp 197–200 °C) which recrystallized from EtOAc as colorless needles: mp 200–202 °C; UV max (95% EtOH) 211 nm (ε 2100);[10] IR 2233, 1720, 1685 cm^{-1}; ^1H NMR τ 2.95 (d, J = 10 Hz, 1 H), 3.82 (dd, J = 6 and 10 Hz, 1 H), 5.79 (d, J = 7 Hz, 2 H), 6.07 (br t, J = ~6 Hz, 1 H), 8.68 (t, J = 7 Hz, 3 H), 8.77 (s, 3 H); mass spectrum 329 (37), 256 (27), 235 (97), 207 (33), 161 (75), 133 (100), 128 (52), 120 (53), 95 (50), 66 (36).

Anal. Calcd for $C_{19}H_{23}NO_4$: C, 69.28; H, 7.04; N, 4.25. Found: C, 69.19; H, 7.13; N, 4.39.

16,17-Acetylimino-5α,8β,9β-podocarp-13-ene-7,12-dione (6b). Reaction of 515 mg (1.87 mmol) of crude **4b** with the enolate from 450 mg (2.85 mmol) of $CH_3COCH_2CO_2$-t-Bu and 120 mg of a 58% NaH–mineral oil dispersion (2.90 mmol) in a total of 60 mL of PhH was conducted as described for the preparation of **5a,** affording 850 mg of a mixture of **5b** (^1H NMR shows two diastereomers, ca. 1:1 ratio[10,17]) and excess keto ester as a brown oil: ^1H NMR τ 1.58 (s) and 1.63 (s) (total 1 H), 7.78 (s, 3 H), 7.93 (s) and 7.97 (s) (total 3 H), 8.55 (s, 9 H), 9.12 (br s, 3 H) plus resonances of $CH_3COCH_2CO_2$-t-Bu.

Reaction of 850 mg of this crude **5b** with 120 mg of TsOH in 30 mL of HOAc for 2.5 h was conducted as described for the preparation of **6a** to afford 600 mg of brown gum, which was washed with hexane to leave 470 mg (80% from **4b**) of crude **6b** as a tan solid: mp 138–155 °C; IR 1715, 1680, 1630 cm^{-1}; ^1H NMR τ 3.05 (d, J = 10 Hz, 1 H), 3.87 (dd, J = 6 and 10 Hz, 1 H), 7.87 (s) and 7.92 (s) (total 3 H),[17] 8.74 (s, impurity), 9.12 (br s, 3 H).[17] Enedione **6b** decomposed during attempted chromatography or recrystallization, and thus was not purified further.

16,17-Methanesulfonylimino-5α,8β,9β-podocarp-13-ene-7,12-dione (6c). A mixture of 120 mg (5.00 mmol) of NaH (obtained by repeatedly washing a 58% NaH–mineral oil dispersion with hexanes) and 270 mg (1.71 mmol) of $CH_3COCH_2CO_2$-t-Bu in 9 mL of freshly distilled Me_2SO was stirred for 30 min, treated with 177 mg (0.569 mmol) of **4c,** mp 210–217 °C dec, stirred for 6 min (N_2 atmosphere), and acidified with HOAc.[10] Isolation C (CH_2Cl_2) left 235 mg (88%) of crude **5c** as a yellowish glass (^1H NMR shows predominantly or only one isomer[10,21]). Trituration with hexanes and washing with Et_2O afforded **5c** as a colorless amorphous powder: mp 173–176 °C dec; IR 1720, 1700, 1622, 1570, 1330, 1145 cm^{-1}; ^1H NMR τ −4.55 (br s, 1 H), 1.57 (s, 1 H), 6.25 (d, J = 5 Hz, 1 H), 6.58 (d, J = 12.5 Hz, 2 H), 6.73 (d, J = 5 Hz, 1 H), 7.26 (d, J = 12.5 Hz, 2 H), 7.29 (s, 3 H), 7.77 (s, 3 H), 8.61 (s, 9 H), 9.12 (s, 3 H).[21]

Anal. Calcd for $C_{23}H_{35}NO_7S$: C, 58.83; H, 7.51; N, 2.89; S, 6.83. Found: C, 58.91; H, 7.68; N, 3.08; S, 6.77.

Reaction of 125 mg (0.267 mmol) of crude **5c,** mp 160–169 °C dec, with 51 mg (0.29 mmol) of $TsOH·H_2O$ in 15 mL of HOAc for 0.75 h was conducted as described for the preparation of **6a** to provide 116 mg of crude **6c** as a tan oil. Trituration and repeated washing with Et_2O afforded 94 mg (100%) of yellowish solid mixture containing ~70% of **6c** and 30% of an unknown contaminant (^1H NMR assay): mp 150–159 °C; IR 1710, 1680, 1602, 1332, 1150 cm^{-1}; ^1H NMR τ 3.05 (d, J = 10 Hz, 1 H), 3.86 (dd, J = 6 and 10 Hz, 1 H), 7.17 (s, 3 H), 9.13 (s, 3 H), and resonance from the 30% contaminant at τ 2.65 (dd, J = 10 and 2 Hz, 1 H), 3.97 (dd, J = 10 and 2 Hz, 1 H), 7.25 (s, 3 H), 9.10 (s, 3 H).[22] Attempted purification by recrystallization, sublimation, or chromatography led to decomposition, so this material was aromatized directly.

9α-(1′-Carbo-*tert*-butoxy-2′-oxopropyl)-10-cyano-4,4-dimethyl-8-hydroxymethylene-5α-decal-7-one (5d). Reaction of the enolate from 115 mg (0.728 mmol) of $CH_3COCH_2CO_2$-t-Bu and 16 mg (0.67 mmol) of NaH (as a 58% dispersion from which mineral oil was not removed) in 8 mL of Me_2SO (15 min for enolate formation) with 120 mg (0.519 mmol) of crude **4d** was conducted as described for the preparation of **5c** to afford 160 mg (79%) of crude **5d.** Washing with pentane left **5d** as a yellow powder (^1H NMR shows only one diastereomer[10]): mp 130–140 °C; ^1H NMR τ −4.33 (br s, 1 H), 1.43 (s, 1 H), 6.22 (d, J = 4 Hz, 1 H), 6.55 (d, J = 4 Hz, 1 H), 7.82 (s, 3 H), 8.68 (s, 9 H), 8.90 (s, 3 H), 9.04 (s, 3 H); mass spectrum 389 (11), 333 (35), 306 (50), 290 (56), 272 (97), 232 (52), 136 (93), 57 (100), 55 (40),

43 (79), 41 (62).

Ethyl 10-Cyano-12-methoxy-7-oxo-5α,17-norpodocarpa-8,11,13-trien-16-oate (8a). A solution of 48 mg (0.15 mmol) of **6a**, mp 197–200 °C, in 5 mL of HOAc was treated dropwise during 2 h with 47 mg (0.15 mmol) of pyridine hydrobromide perbromide ($pyHBr_3$; mp 132–135 °C)[23] in 5 mL of HOAc (N_2 atmosphere) and stirred for 6 h. Isolation C ($CHCl_3$; 5% $NaHCO_3$ wash) left 50 mg of a yellowish gum which appeared to consist predominantly of **9a** (^1H NMR). This could be crystallized from EtOAc: IR 2230, 1718, 1692 cm^{-1}; ^1H NMR τ 2.53 (d, J = 6 Hz, 1 H), 5.75 (q, J = 7 Hz, 2 H), 8.67 (t, J = 7 Hz, 3 H), 8.74 (s, 3 H). Normally the crude product was dissolved in 5 mL of *sym*-collidine, heated at ~90 °C for 3 h (N_2 atmosphere),[24] and processed by isolation C ($CHCl_3$; 2 N HCl and $NaHCO_3$ wash) to provide 50 mg (105%) of crude **7a** as a colorless solid: mp 190–230 °C; IR (KBr) 3320 (br), 1710, 1650, 1570 cm^{-1}; ^1H NMR (Me_2CO-d_6) τ 2.05 (d, J = 8.5 Hz, 1 H), 2.88 (d, J = 2 Hz, 1 H), 3.03 (dd, J = 2 and 8.5 Hz, 1 H), 5.81 (q, J = 7 Hz, 2 H), 8.68 (s, 3 H), 8.71 (t, J = 7 Hz, 3 H). TLC and ^1H NMR indicated the presence of a contaminant believed to be **10a** [~20%; τ 1.78 (s, 1 H), 2.58 (s, 1 H), 8.74 (s, 3 H)] which was very difficult to remove by recrystallization, sublimation, or chromatography, so the phenol was etherified for final characterization. A mixture of 50 mg of crude **7a**, mp 190–220 °C, 0.125 mL of Me_2SO_4, 2 g of anhydrous K_2CO_3, and 10 mL of dry Me_2CO was stirred at reflux for 9 h (N_2 atmosphere) and filtered,[4] Me_2CO was distilled in vacuo, and the residue was dissolved in $CHCl_3$. Isolation A (NH_4OH wash) left 54 mg of crude **8a**, mp 187–193 °C, which was fractionally sublimed to afford 40 mg (80% based on **6a**) of pure **8a** as colorless prisms, mp 197–200 °C. The analytical sample was resublimed: mp 197–200 °C; UV max (95% EtOH) 270 nm (ϵ 10 000); IR (KBr) 2215, 1720, 1670, 1590 cm^{-1}; ^1H NMR τ ~1.93, 2.99, and 3.07 (ABC, $J_{13,14}$ = 8.5, $J_{11,13}$ = 2.5, $J_{11,14}$ = 0 Hz, 3 H), 5.78 (q, J = 7 Hz, 2 H), 6.13 (s, 3 H), 8.68 (t, J = 7 Hz, 3 H), 8.68 (s, 3 H).

Anal. Calcd for $C_{20}H_{23}NO_4$: C, 70.36; H, 6.79; N, 4.00. Found: C, 69.99; H, 6.86; N, 3.89.

16,17-Acetylimino-5α-podocarpa-8,11,13-triene (19). A solution of 470 mg (1.49 mmol) of crude **6b**, mp 138–155 °C, in 30 mL of HOAc was treated with 330 mg (1.08 mmol) of $pyHBr_3$, mp 132–135 °C, in one portion (rapid precipitate formation[25]) and stirred for 45 min (N_2 atmosphere).[3] Isolation C ($CHCl_3$; 5% $NaHCO_3$ wash) provided 500 mg of a multicomponent mixture (TLC), which was taken up in $CHCl_3$ and extracted with 2% NaOH[26] which was immediately acidified with 2 N HCl and processed by isolation B ($CHCl_3$; 5% $NaHCO_3$ wash) to afford 130 mg (38%) of crude **7b** as a brown solid. Recrystallization from Me_2CO–MeOH afforded **7b** contaminated with a second compound (TLC), presumably **10b**, as tan prisms: mp 210–214 °C; IR 1675, 1625, 1580 cm^{-1}; ^1H NMR (80 °C)[17] τ 2.07 (d, J = 8.5 Hz, 1 H), 2.83–3.28 (m, 2 H), 7.88 (s, 3 H), 9.07 (s, 3 H), plus 1.83 (s) and 2.69 (s) presumably from **10b**. Phenol **7b** was not easily separated from the contaminant by recrystallization, chromatography (Al_2O_3), or fractional sublimation, so this mixture was used directly.

A mixture of 77 mg (0.25 mmol) of the crystalline **7b**, mp 210–214 °C, 60 mg (0.39 mmol) of 2-chlorobenzoxazole, and 200 mg of anhydrous K_2CO_3 in 20 mL of dry Me_2CO was stirred and boiled under reflux for 24 h,[1a] taken to dryness in vacuo, and partitioned between $CHCl_3$ and water which was processed by isolation B ($CHCl_3$). The residual 110 mg of crude oily **17** was chromatographed over 6 g of Florisil (5 × 10 cm; hexane, hexane–PhH, PhH, PhH–Et_2O, Et_2O, $CHCl_3$, and $CHCl_3$–MeOH elution). Excess chlorobenzoxazole was eluted with 50:50 hexane–PhH, and the 98:2 $CHCl_3$–MeOH fraction afforded 60 mg (57%) of **17** as a colorless amorphous solid: IR 1670, 1625, 1560 cm^{-1}; ^1H NMR τ 1.80 (d, J = 8.5 Hz, 1 H), 2.17–2.83 (m, 6 H), 5.38 (d, J = 14 Hz) and 5.63 (d, J = 14 Hz) (total 1 H), 6.48 (d, J = 14 Hz) and 6.56 (d, J = 14 Hz) (total 1 H), 7.27 (d, J = 14 Hz, 2 H), 7.90 (s, 3 H), 9.05 (s, 3 H).

A solution of 60 mg (0.14 mmol) of the chromatographed **17** in 10 mL of 95% EtOH was hydrogenated at 1 atm over 30 mg of 30% Pd/C for 18 h.[1a] The residue after filtration of Pd/C and evaporation was taken up in Et_2O, which was processed by isolation A (5 N KOH wash) to leave 25 mg of an oil which appeared to contain a small amount of **18** (IR) in addition to **19**: IR 3420 (w, **18**?), 1720 (w), 1625 cm^{-1}; ^1H NMR (CCl_4; 60 °C[17]) τ 2.67–3.17 (m, 4 H), 8.02 (s, 3 H), 9.07 (s, 3 H). Chromatography over 0.5 g of neutral Al_2O_3 (activity I; PhH, PhH–Et_2O, Et_2O, Et_2O–EtOAc, EtOAc elution) afforded in the PhH–Et_2O fraction 7 mg (18%) of **19** as an oil which slowly crystallized: mp 95–108 °C; IR (CCl_4) 1635 cm^{-1}, identical from 4000 to 800 cm^{-1} with a spectrum of authentic **19** provided by Professor A. Tahara.[15]

16,17-Methanesulfonylimino-12-hydroxy-7-oxo-5α-podocarpa-8,11,13-triene (7c). A solution of 94 mg (0.27 mmol) of crude **6c**, mp 150–159 °C, and 85 mg (0.28 mmol) of $pyHBr_3$ in 7 mL of HOAc was stirred for 0.5 h (N_2 atmosphere)[3] and added to 100 mL of 2% NaOH which was basified to pH ~10 with solid NaOH, diluted with 100 mL of 2% NaOH, washed with $CHCl_3$, and acidified with concentrated HCl. Isolation B ($CHCl_3$) left 51 mg (54%) of crude **7c** as a colorless powder, mp 255–268 °C dec. This was washed with $CHCl_3$ and recrystallized from MeOH (dry ice–Me_2CO bath) to afford **7c** as a colorless amorphous solid: mp 269–271 °C dec; UV max (95% EtOH) 220 (ϵ 10 000), 277 (13 000); (base) 242 (ϵ 5600), 332 nm (23 600); IR (KBr) 3280, 1650, 1575, 1330, 1288, 1154 cm^{-1}; ^1H NMR (Me_2CO-d_6) τ 2.02 (s, 1 H), 2.12 (d, J = 8.5 Hz, 1 H), 2.97 (d, J = 2.5 Hz, 1 H), 3.18 (dd, J = 8.5 and 2.5 Hz, 1 H), 7.20 (s, 3 H), 9.04 (s, 3 H).

Anal. Calcd for $C_{18}H_{23}NO_4S$: C, 61.86; H, 6.65; N, 4.00; S, 9.17. Found: C, 61.75; H. 6.65; N, 4.02; S, 9.17.

Registry No.—**2a**, 16981-46-7; **2b**, 62461-28-3; **2c**, 62461-29-4; **2d**, 56666-22-9; **2e**, 16981-47-8; **3a**, 63784-50-9; **3b**, 63784-51-0; **3c**, 63784-52-1; **3d**, 63784-53-2; **3e**, 63784-54-3; **4a**, 63784-55-4; **4b**, 63784-56-5; **4c**, 63784-57-6; **4d**, 63784-58-7; **4e**, 63784-70-3; **5a**, 63784-59-8; **5b** isomer 1, 63784-60-1; **5b** isomer 2, 63814-61-9; **5c**, 63784-61-2; **5d**, 63784-62-3; **6a**, 62461-84-1; **6b**, 62461-85-2; **6c**, 62461-86-3; **7a**, 63784-63-4; **7b**, 63797-56-8; **7c**, 63784-64-5; **8a**, 63784-65-6; **9a**, 63784-66-7; **10a**, 63784-67-8; **10b**, 63784-68-9; **17**, 63784-69-0; **19**, 38750-33-3; $CH_3COCH_2CO_2$-*t*-Bu, 1694-31-1; 2-chlorobenzoxazole, 615-18-9.

References and Notes

(1) (a) Part 11: W. L. Meyer and C. W. Sigel, *J. Org. Chem.*, **42**, 2769 (1977). (b) Abstracted in part from Ph.D. Dissertations of C.W.S., R.J.H., T.E.G., and R.A.M. and the M.S. Thesis of P.G.S., Indiana University, 1967, and University of Arkansas, 1972, 1974, 1971, and 1968, respectively. (c) Supported in part by Research Grant AM-10123 from the National Institute of Arthritis and Metabolic Diseases and by the University of Arkansas Research Reserve Fund; the UV and mass spectrometers were obtained with partial support of National Science Foundation Grants GP-8286 and GP-6978, respectively. (d) National Institutes of Health Predoctoral Fellow; 1965–1967. (e) Eastman Kodak Research Fellow, 1969–1970. (f) National Science Foundation Trainee, 1969–1970 and 1971–1972; National Aeronautics and Space Administration Trainee, 1970–1971; Phillips Petroleum Company Fellow, 1972–1973.

(2) For convenience all bicyclic and tricyclic compounds in this paper will be numbered by the steroid—terpenoid convention as in **1**, with the gem-disubstituted ring of decalins being ring A. The configurational notations α and β denote a trans or cis relation to the C-10 angular group, respectively. All synthetic substances were prepared only in racemic form, although the prefix (±) is omitted and only one enantiomer is depicted.

(3) W. L. Meyer, G. B. Clemans, and R. A. Manning, *J. Org. Chem.*, **40**, 3686 (1975).

(4) W. L. Meyer, R. A. Manning, E. Schindler, R. S. Schroeder, and D. C. Shew, *J. Org. Chem.*, **41**, 1005 (1976).

(5) W. L. Meyer, R. W. Huffman, and P. G. Schroeder, *Tetrahedron*, **24**, 5959 (1968).

(6) W. L. Meyer, T. E. Goodwin, R. J. Hoff, and C. W. Sigel, *J. Org. Chem.*, **42**, 2761 (1977).

(7) S. K. Pradham and H. J. Ringold, *J. Org. Chem.*, **29**, 601 (1964); A. B. Turner and H. J. Ringold, *J. Chem. Soc. C*, 1720 (1967).

(8) Oxidation of **3c** in hot *t*-BuOH also proceeds well, but is hampered by competitive HOAc-catalyzed conversion of **3c** to its *tert*-butyl enol ether, cf. footnote 13 of ref 4.

(9) We do not believe that these reactivity differences are due to differences in purity of the DDQ which was used in various reactions (although that is certainly a variable which can also produce capricious results) or to differences in technique among experimentalists. Although no single individual in our laboratory has conducted all of the dehydrogenations discussed here, each of these reactions has been examined by one or more persons, each of whom has also reproduced one or more of the successful reported dehydrogenations[1a,3,4] using the same DDQ.

(10) W. L. Meyer, R. A. Manning, P. G. Schroeder, and D. C. Shew, *J. Org. Chem.*, **42**, 2754 (1977).

(11) Further reactions were not examined in the 4,4-dimethyl-10-cyano and 4α-carbethoxy-10-cyano series owing to the inaccessibility of **4d** and **4e** in adequate quantity or purity.

(12) Cf. footnote 12 of ref 9.

(13) Detailed optimization of aromatization conditions and a search for **9b** and **9c** in the hydroxide-insoluble fraction were not pursued with **6b** and **6c**, but all data which were obtained in those series are in accord with qualitative similarity between their reactivity and that of **6a**.

(14) Scheme II portrays reactions through enols **12** and **16** rather than **14** (R^4 = H or alkyl and R^4 = Br) only for brevity. The latter are reasonable alternatives, although molecular models suggest that the trans-syn tricyclic system is less strained with a double bond at 7,8 than it is at 8,14, cf. ref 10. Initial bromination at C-8 is not discussed because it should lead to **7** whether R^4 is alkyl or H.[3] Pathways involving Br_2 addition to double bonds of various enediones can also be envisioned, but seem less likely because compound **12** of ref 1a undergoes 6-bromination and not $\Delta^{8,14}$ bromine addition.

(15) A. Tahara, K. Hirao, and Y. Hamazuki, *Chem. Ind. (London)*, 850 (1965); A. Tahara and K. Hirao, *Tetrahedron Lett.*, 1453 (1966). We are grateful to Dr. Tahara for the IR spectrum of his enantiomer of **19**.

(16) W. Nagata, T. Sugasawa, M. Narisada, T. Wakabayashi, and Y. Hayase, J. Am. Chem. Soc., 85, 2342 (1963); W. Nagata, M. Narisada, T. Wakabayashi, and T. Sugasawa, ibid., 86, 929 (1964).
(17) ^{1}H NMR spectra of the *N*-acetyl derivatives in this series indicate that they exist as nearly 50:50 mixtures of two conformers about the N–CO bond, with interconversion being slow on the NMR time scale at ambient probe temperature, cf. ref 6.
(18) Acidification with HCl induces variable amounts of *tert*-butyl enol etherification, cf. ref 4.
(19) It is particularly important to carefully reextract the $NaHCO_3$ wash solution so as to avoid loss of the formyl enone into the aqueous phases.
(20) We thank the Eastman Chemical Co. for a generous sample of this substance.
(21) In some preparations additional resonance from CH_3CO (τ 7.91) and $(CH_3)_3C$ (τ 8.55) indicate the presence of up to ~20% of a second diastereomer.[10]
(22) The ^{1}H NMR properties of this by-product, insofar as they are discernable in the spectrum of the mixture, would be consistent with its formulation as a trans-anti-trans diastereomer of **6c**. In view of the fact that we have not encountered such a stereoisomer in any other analogous system, however, we hesitate to make such an assignment until the substance can be examined in pure form.
(23) L. F. Fieser, "Experiments in Organic Chemistry", 3rd ed, D. C. Heath, Boston, Mass., 1957, p 65.
(24) C. W. Shoppee, S. K. Roy, and B. S. Goodrich, J. Chem. Soc., 1583 (1961).
(25) Precipitation at this point has not been observed in analogous reactions, and is probably due to salt formation at the amide function.
(26) Use of more concentrated alkali brings about partial hydrolysis of the amide.

Synthesis of 6*H*,12*H*-indazolo[2,1,*a*]-6,12-diiminoindazoles and 3-Imino-2-phenylindazolines from Azo Compounds and Isocyanides in the Presence of Octacarbonyldicobalt[1]

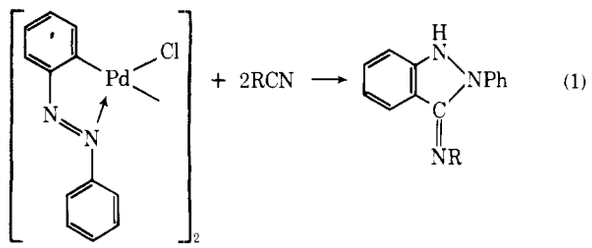
Yasuhiro Yamamoto* and Hiroshi Yamazaki

The Institute of Physical and Chemical Research, Wako-shi, Saitama 351, Japan

Received July 19, 1977

The reactions of azobenzenes and isocyanides in the presence of $Co_2(CO)_8$ gave 6*H*,12*H*-indazolo[2,1,*a*]-6,12-diiminoindazoles (**1**) and 3-imino-2-phenylindazolines (**2**). Orthometalation by a cobalt atom, which is considered as a first step in these reactions, occurs nucleophilically. The reaction mechanism is discussed.

Reactions of aromatic azo compounds with carbon monoxide are catalyzed by $Co_2(CO)_8$ to produce 3-oxo-2-phenylindazolines and 2,4-dioxo-1,2,3,4-tetrahydroquinazolines.[2] Similar reactions in the presence of $Ni(CO)_4$ give 6*H*,12*H*-indazolo[2,1,*a*]-6,12-dioxoindazoles.[3] We recently showed that reaction of cyclopalladation complexes of azobenzene with isocyanides gave 3-imino-2-phenylindazolines stoichiometrically (eq 1).[6] In attempts to examine the catalytic scope of

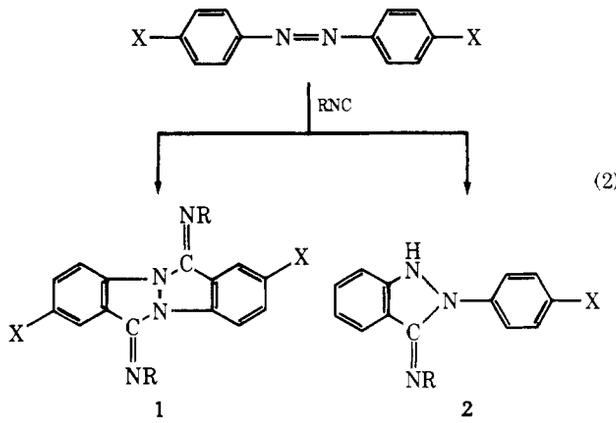


(1)

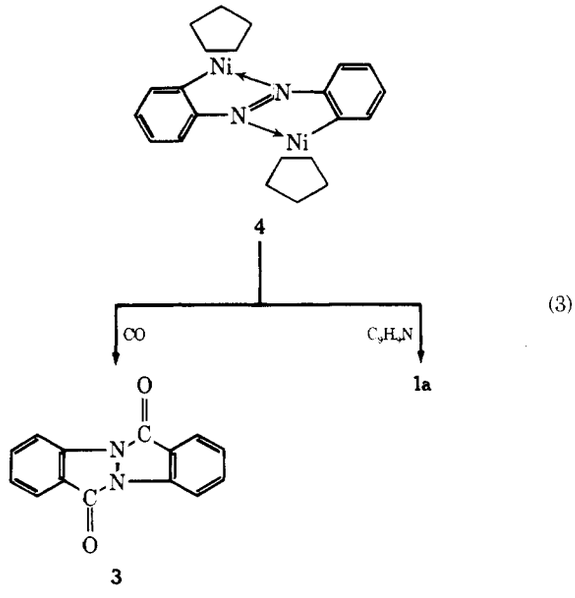
these reactions, the reactions of azobenzene derivatives with isocyanides were carried out in the presence of $Co_2(CO)_8$. We found that the aforementioned reactions produced 6*H*,12*H*-indazolo[2,1,*a*]-6,12-diiminoindazoles and 3-imino-2-phenylindazolines, depending on the substituent of RNC.

A mixture of azobenzene, 2,6-xylyl isocyanide, and $Co_2(CO)_8$ was heated in toluene at 120–125 °C. Chromatography of the mixture on alumina gave a yellow crystalline compound **1a** with the empirical formula $C_{30}H_{26}N_4$, M^+ 442 (442.54). The NMR spectrum showed one singlet due to the methyl groups at δ 2.16 ppm, suggesting a symmetrical molecular structure. The UV absorption pattern is similar to that of 6*H*,12*H*-indazolo[2,1,*a*]-6,12-dioxoindazole (**3**). The reaction of 2,6-xylyl isocyanide with a nickel azobenzene complex (**4**)[7] gave **1a** (eq 3).

A similar reaction with carbon monoxide produced **3** (eq 3). These results showed that **1a** is 6*H*,12*H*-indazolo[2,1,*a*]-6,12-[dixylyl]iminoindazole. Similar compounds were obtained when *p*-chloro- and *p*-methylazobenzene or 4-



(2)



(3)