26.17 (t), 25.61 (t), 23.67 (t), 23.15 (t), 14.19 (q), 13.91 (q); HRMS, $[M + 1]^+$, calcd for $C_{18}H_{32}NO$ 278.24839, found (m/z) 278.25068.

5c: colorless oil; ^1H NMR ($CDCl_3$) δ 7.3 (m, 5 H), 3.03 (dd, J = 10, 4 Hz), 2.87 (dd, J_{AB} = 14.4 Hz, J = 10 Hz), 2.75 (dd, J_{AB} = 14.4 Hz, J = 8 Hz), 2.32 (s, 6 H), 1.65 (m), 1.4–1.5 (m, 4 H), 1.2–1.4 (m, 7 H), 0.93 (t, J = 7 Hz, 3 H), 0.91 (t, J = 7 Hz, 3 H), O*H* too broad to be observed under ambient conditions at 400 MHz; ^{13}C NMR ($CDCl_3$) δ 141.04 (s), 129.05 (d, 2 C), 128.27 (d, 2 C), 125.93 (d), 74.50 (s), 70.11 (t), 44.11 (q, 2 C), 36.62 (t), 35.96 (t), 25.68 (t), 25.55 (t), 23.71 (t), 23.42 (t), 14.14 (q, 2 C); HRMS, $[M + 1]^+$, calcd for $C_{19}H_{34}NO$ 292.26404, found (m/z) 292.26310.

5d: ^1H NMR ($CDCl_3$) δ 3.8 (br, O*H*), 2.52 (q, J = 7.2 Hz), 2.27 (s, 6 H), 1.55 (m), 1.2–1.4 (m, 11 H), 0.91 (d, J = 7.5 Hz, 3 H), 0.87 (t, J = 7.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 75.98 (s), 69.02 (d), 36.94 (t), 34.93 (t), 25.43 (t), 25.16 (t), 23.04 (t), 22.87 (t), 14.04 (q), 13.97 (q), 9.11 (q), $N(CH_3)_2$'s were severely broadened (δ 43 and 45) under ambient conditions at 100 MHz; HRMS, $[M + 1]^+$, calcd for $C_{13}H_{30}NO$ 216.23274, found (m/z) 216.23404.

Acknowledgment. We thank the National Institutes of Health (Grant GM-38014), the Research Corporation, the donors of The Petroleum Research Fund administered by the American Chemical Society, The Camille and Henry Dreyfus Foundation, and Boston University Seed Grant Committee for support. We also thank John Lloyd and Dr. Gerd Dielmann of Finnigan-MAT and Michael Creech of Boston University for the high-resolution mass spectra.

Notes

A Novel Ring System: 6a-Aminofuro[2,3-*b*]furans

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Although a fair amount of work has been published on heterocycles containing two fused five-membered rings, less is known about compounds in which furan rings are involved.[1,2] The parent furo[2,3-*b*]furan system and substituted derivatives are apparently unknown.

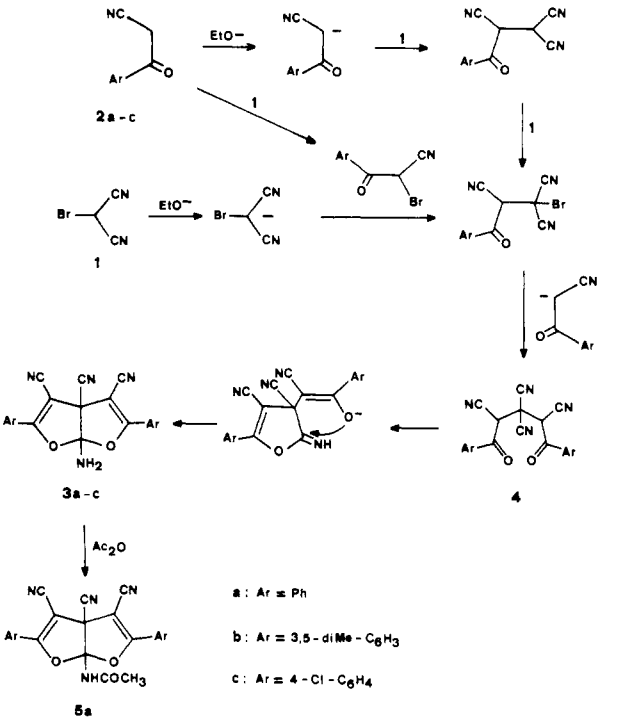
We report in this paper the reaction of bromomalonitrile (1) with ω-cyanoacetophenone (**2a**) in the presence of alkoxide from which a furo[2,3-*b*]furan results in a single step (Scheme I).

The reaction is easily performed in ethanol at room temperature by stirring a mixture of **2a** and bromomalononitrile (1). A crystalline solid is obtained in moderate yield (30%). The microanalytical and mass spectral data correspond to two units of ω-cyanoacetophenone per unit of malononitrile.

An unambiguous structural assignment could not be achieved from the analytical and the deceptively simple spectral data alone, and X-ray crystallographic analysis was therefore performed. Compound **3a** was found to be a novel furo[2,3-*b*]furan heterocyclic system, containing a most unusual functional grouping at carbon 6a (–O–C(NH_2)–O–), a primary amide acetal.

A perspective drawing of **3a** is shown in Figure 1, with the atomic labeling. The molecule presents a pseudo mirror plane. Each half is nearly situated in a plane, the dihedral angle being about 119.5°. Both five-membered rings are planar. Rings I and II and the C_{16}–N_{17} nitrile group are nearly planar. On the contrary, rings III and IV and the C_{20}–N_{17} nitrile group are farther from planarity

Scheme I



(see paragraph at the end of the paper about supplementary material). This nonsymmetrical molecular geometry in the solid state is probably a requirement of the molecular arrangement in the crystal; the NMR spectra suggest a perfect symmetry in solution, however.

The reaction can also be applied to substituted ω-cyanoacetophenones. The corresponding compounds **3** can be very easily isolated by simple filtration in moderate yields. The presence of electron-donating groups (e.g., methoxy) in the para position of the ω-cyanoacetophenones seems to prevent this reaction.

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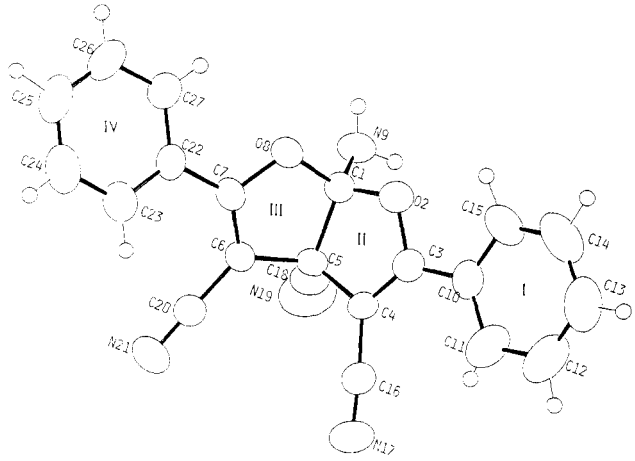

Figure 1. Perspective drawing of **3a**.

The mechanistic interpretation of this process is not easy because of the complex chemistry[3] of bromomalononitrile. However, formation of intermediate **4**, involving two units of ω-cyanoacetophenone and one of malononitrile, seems necessary. Cyclization of **4** leads to an iminofuran ring, which, in turn, undergoes a further cyclization to bicyclic system **3**. As for the formation of intermediate **4**, we could suggest a number of possibilities, taking into account that 1 mol of bromomalononitrile per mol of ω-cyanoacetophenone is required for the reaction to be successful.[4] Half a mole of bromomalononitrile acts as a reagent and the other half as a brominating agent. Generation of **4** could thus be explained, as shown in Scheme I, by bromination and nucleophilic substitution.[5] A one-electron-transfer mechanism could be involved. On the other hand, similar pK_a values for ω-cyanoacetophenone (7.5)[6] and bromomalononitrile (7.58)[7] prevent ruling out either of the two proposed possibilities.

Experimental Section

Melting points were determined on a Büchi apparatus in capillary tubes and are uncorrected. Infrared spectra were obtained on Perkin-Elmer 257 and 781 spectrometers as KBr disks. The nuclear magnetic resonance spectrometers used were a Varian T-60A for the ^1H NMR spectra and a Bruker WM 400 (100.6 MHz) for the ^{13}C NMR spectra. Chemical shifts are given in ppm, downfield from internal tetramethylsilane. Reactions were monitored by TLC, using silica gel as the adsorbent and toluene–ethyl acetate as the eluent.

X-ray Crystallographic Measurements. Crystal Data: $C_{21}H_{12}O_2N_4$, monoclinic, $P2_1/n$, a = 14.467 (1) Å, b = 14.537 (1) Å, c = 8.537 (1) Å, β = 94.087 (3)°, V = 1790.8 (2) Å^3, Z = 4, D_c = 1.3068 g cm^{-3}, M = 352.351, $F(000)$ = 728, μ = 6.757 cm^{-1}.

Unit cell parameters were obtained from a least-squares fit of 75 angles in the range $2 < \theta < 45°$. A total of 3043 reflections were collected on a Philips PW1100 four-circle diffractometer with graphite-monochromated Cu Kα radiation in the range $2 < \theta < 65°$, using the $\omega/2\theta$ scan mode. Two reference reflections monitored every 90 min showed no crystal decomposition or instrumental instability (R_{int} = 0.01). Systematic absences were consistent with the $P2_1/n$ space group. A total of 1798 reflections were considered observed, with the $I > 3\sigma(I)$ criterion.

The structure was solved with MULTAN 80.[8] All H atoms appeared in a difference map, and they were included in the refinement with isotropic temperature factors. An empirical weighting scheme[9] was applied as to give no trends in $\langle w\Delta^2F\rangle$ vs $\langle F_o\rangle$ and vs $\langle \sin\theta/\lambda\rangle$. Final mixed refinement gave R = 0.062 (R_w = 0.068) for 292 variables with $(\Delta/\sigma)_{max}$ = 0.04 and $(\Delta/\sigma)_{av}$ = 0.01. Maximal residual electronic density was 0.22 e Å^{-3}. Scattering factors were taken from ref 10. Most calculations were performed with the XRAY system[11] and PARST[12] on a Vax 11/750 computer.

6a-Amino-2,5-diaryl-3,3a,4-tricyanofuro[2,3-*b*]furans (3). General Procedure. The appropriate ω-cyanoacetophenone **2** (14 mmol) was dissolved in ca. 25 mL of ethanol containing 14 mmol of sodium ethoxide. Bromomalononitrile (**1**) (14 mmol) was then added, and the reaction mixture was stirred at room temperature for 3 h. The solid that precipitated was then collected by filtration and washed with ethanol. The compound thus obtained showed no impurities by TLC. Analytical samples were further purified by recrystallization from the appropriate solvent.[13]

6a-Amino-3,3a,4-tricyano-2,5-diphenylfuro[2,3-*b*]furan (3a). This compound was obtained according to the general procedure in 30% yield. It was also prepared by substituting dibromomalononitrile (7 mmol), as the potassium bromide complex, for bromomalononitrile, following a similar procedure: yield 24%; mp 193–194 °C dec (from methylene chloride); IR (KBr) 3390, 3300 (NH_2), 2210 (CN), 1630 (C=C) cm^{-1}; ^1H NMR (C_3SOCD_3) δ 7.7–8.2 (m, 10 H, arom), 4.9 (bs, 2 H, NH_2); ^{13}C NMR (CD_3SOCD_3) δ 59.8 (>C*–CN), 82.3 (=C*–CN), 113.0, 113.7 (CN), 125.3, 127.5, 129.4 (CH arom), 133.7 (C arom, ipso), 126.4 (C–NH_2), 167.5 (C–Ph);[14] mass spectrum, m/e 352 (M^+, <1), 286 (<1), 209 (8), 207 (13), 145 (3), 122 (7), 106 (8), 105 (100). Anal. Calcd for $C_{21}H_{12}N_4O_2$: C, 71.58; H, 3.43; N, 15.90. Found: C, 71.53; H, 3.36; N, 15.99.

6a-Amino-3,3a,4-tricyano-2,5-bis(3,5-dimethylphenyl)-furo[2,3-*b*]furan (3b). This compound was obtained in 31% yield by following the general procedure: mp 219–221 °C dec (from methylene chloride); IR (KBr) 3370, 3320 (NH_2), 2210 (CN), 1620 (C=C) cm^{-1}; ^1H NMR (CD_3SOCD_3) δ 7.2–7.7 (m, 6 H arom), 5.05 (bs, 2 H, NH_2), 2.35 (s, 12 H, CH_3); ^{13}C NMR (CD_3SOCD_3) δ (SFORD multiplicities) 20.7 (q, CH_3), 59.4 (s, >C*–CN), 81.9 (s, =C*–CN), 112.8, 113.5 (s, CN), 124.9 (d, C_2' arom), 125.1 (s, C_1' arom), 126.1 (s, C–NH_2), 135.1 (d, C_4' arom), 138.7 (s, C_3' arom), 167.6 (s, C–Ph); mass spectrum, m/e 408 (M^+, <1), 366 (<1), 342 (<1), 282 (<1), 235 (10), 194 (2), 173 (10), 150 (6), 134 (10), 133 (100), 105 (49). Anal. Calcd for $C_{25}H_{20}N_4O_2$: C, 73.53; H, 4.90; N, 13.70. Found: C, 73.57; H, 4.70; N, 13.74.

6a-Amino-2,5-bis(4-chlorophenyl)-3,3a,4-tricyanofuro-[2,3-*b*]furan (3c). This compound was obtained in 36% yield by following the general procedure: mp 214–216 °C dec (from benzene); IR (KBr) 3395, 3300 (NH_2), 2210 (CN), 1635 (C=C) cm^{-1}; ^1H NMR (CD_3SOCD_3) δ 7.2–7.8 (q, 8 H arom), 5.0 (bs, 2 H, NH_2); mass spectrum, m/e 420 (M^+, <1), 342 (<1), 243 (11), 241 (5), 179 (5), 156 (13), 141 (33), 139 (107). Anal. Calcd for $C_{21}H_{10}N_4O_2Cl_2$: C, 59.88; H, 2.39; N, 13.30; Cl, 16.83. Found: C, 59.80; H, 2.42; N, 13.48; Cl, 16.60.

6a-(Acetylamino)-3,3a,4-tricyano-2,5-diphenylfuro[2,3-*b*]furan (5a). Compound **3a** (1 mmol) was refluxed in acetic

(3) For a review on the chemistry of bromo- and halogenomalononitriles, see: Freeman, F. *Synthesis* **1981**, 925.

(4) The reaction can also be carried out by using 0.5 mol of dibromomalononitrile (as its KBr complex) with similar results.

(5) Despite the positive character of the bromine atom in bromomalononitrile, nucleophilic substitutions are known. The brominating ability of bromomalononitrile is also known (see ref 3).

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(12) Nardelli, M. *Comput. Chem.* **1983**, *7*, 95.

(13) Attempts to crystallize compounds **3** from oxygenated solvents (alcohols, ethers) led to extensive decomposition.

(14) In the ^1H-coupled spectrum, this peak appears as a triplet resulting from the long-range coupling ($^3J_{CH}$ = 4 Hz) with the C_2' aromatic protons. Its chemical shift is in good agreement with values reported for the C_2 carbon in 2-phenyl-substituted 4*H*-pyrans. See: Pascual, C.; Martín, N.; Seoane, C. *Magn. Reson. Chem.* **1985**, *23*, 793.

anhydride (ca. 10 mL) for 30 min. The cold mixture was poured on 250 mL of ice water. A dark red oil was formed, which became solid after 24 h. The solid was collected and purified by preparative TLC (silica gel, 15:1 Cl_3CH/MeOH): yield 80%; mp 147–148 °C (from methanol–water); IR (KBr) 3660, 3520, 3360, 3260 (NH, H_2O), 2210 (CN), 1720 (C=O), 1630 (C=C) cm^{-1}; ^1H NMR (CD_3SOCD_3) δ 10.8 (bs, 1 H, NH), 7.3–8.2 (m, 10 H arom), 2.1 (CH_3CO); mass spectrum, m/e 394 (M^+, 9), 352 (2), 308 (2), 281 (2), 209 (2), 106 (8), 105 (100), 77 (28). Anal. Calcd for $C_{23}H_{14}N_4O_3 \cdot 0.5H_2O$: C, 68.48; H, 3.75; N, 13.88. Found: C, 68.38; H, 3.70; N, 13.80.

Acknowledgment. Support of this work by a grant from the Comisiõn Asesora de Investigaciõn Científica y Técnica de la Presidencia del Bogierno of Spain (Grant PB86-0570) is gratefully acknowledged.

Registry No. 1, 1885-22-9; **2a**, 614-16-4; **2b**, 85692-25-7; **2c**, 4640-66-8; **3a**, 115437-98-4; **3b**, 115437-99-5; **3c**, 115438-00-1; **5a**, 115438-01-2; dibromomalononitrile, 1885-23-0.

Supplementary Material Available: Full X-ray data for **3a** (6 pages). Ordering information is given on any current masthead page.

Organomercury Chemistry of Iridoid Glucosides. 1. Chemoselective Hydroxymercuration–Demercuration of Aucubin: A Cheaper and Efficient Approach to Epimeric Isoeucommiols and 6,7-Bis(hydroxymethyl)-*cis*-2-oxabicyclo[3.3.0]oct-7-enes[1]

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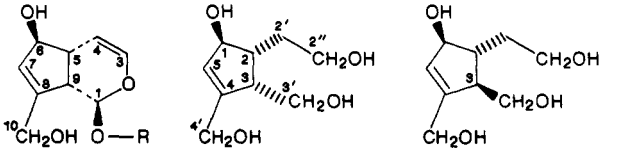
The utilization of iridoid glucosides, mainly of aucubin **1**, the most abundant and widespread member of this group, as chiral natural precursors for the synthesis of prostaglandins and other biologically active cyclopentanoid compounds has in recent years received considerable attention in our laboratory[3] and elsewhere.[4]

We recently reported[3f] the synthesis of a new intermediate for methyl jasmonate and the PG's from isoeucommiol **2**, a chiral cyclopentene tetrol, which was obtained[5] through expensive enzymatic hydrolysis (β-glucosidase) of **1** and $NaBH_4$ reduction of its aglycon **3** (aucubigenin).

Previously—by acid-catalyzed cyclization of **2**—we had obtained the 6α,7-bis(hydroxymethyl)-*cis*-2-oxabicyclo-[3.3.0]oct-7-ene **4**, precursor of modified PG's.[3a,b]

Taking advantage of the chemoselectivity of the hydroxymercuration–demercuration (OM–DM) reaction[6] toward the enol ether double bond of **1**, we have realized a more efficient and inexpensive synthesis of **2**, which led also to its unknown C-3 epimer **5**.

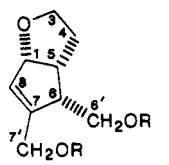
Compound **4** and its C-6 epimer **7** have also been obtained by this procedure. The stereochemistry of **7** renders it particularly useful for prostaglandin syntheses.



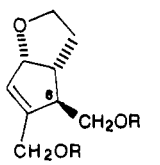
1, R = β-Gluc; **3**, R = H

2

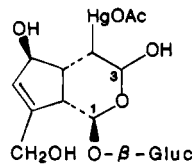
5



4, R = H



7, R = H



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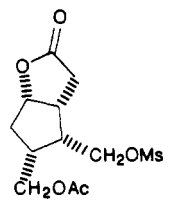

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Results and Discussion

In the course of our studies on the transformation of **2**[3f] we verified the unexpected unreactivity of its trisubstituted double bond toward the classical OM–DM procedure,[7a,b] even under different experimental conditions and in spite of literature reports on similar unsaturated systems.[7,8]

Failure of this attempt, however, paved the way for a chemoselective application of the OM–DM reaction to the direct transformation **1** → **2**, on the assumption that the Δ^7 double bond of **1** would be as unreactive as the identically substituted double bond of **2**.

Reaction of the enol ether double bond of **1** with $Hg(OAc)_2$ in THF–H_2O afforded the organomercurial **6** containing a new hemiacetal function at C-3. Successive reductive replacement of mercury by hydrogen ($NaBH_4$, DM stage) allowed reduction of hemiacetal functions at C-3 and at C-1 to CH_2OH groups with loss of the D-glucose moiety. The product[9] of this clean and high-yield (85%) reaction showed, in different eluents, an R_f value identical with that of isoeucommiol **2** prepared from aucubigenin **3**.[5]

As this new route to isoeucommiol **2** might allow a "one-pot" reaction for the patented conversion[3a,b] **1** → **2** → **4**, the OM–DM of **1** was repeated by acidifying the THF–H_2O solution obtained after filtration of Hg°. Unpredictably, two products were obtained with very close

(1) Abstracted in part from the "Dottorato di Ricerca" Thesis of Davini, E., University of Rome, 1984–86.

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(4) See ref 3d and references therein.

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(9) The ^1H NMR spectrum (300 MHz) of isolated product showed, besides the signals of **2**, the presence of additional low-intensity signals attributable to traces (10–20%) of a not separable contaminant, whose structure and formation will be explained later in this paper.

0022-3263/88/1953-5343$01.50/0