aqueous solution (pH >10) was washed with ethyl acetrate (50 mL), adjusted to pH 1.0 (concentrated HCl), and extracted with ethyl acetate (3 × 50 mL). The combined ethyl acetate extracts were dried ($MgSO_4$) and evaporated to yield a tan precipitate. Crystallization from methanol–water yielded 380 mg (71%) of **2** as off-white flakes: mp 148.5–149.5 °C; IR (KBr) 3400, 3050, 2940, 1720, 1585, 1400, 1375, 1275, 1245, 1115, 1105, 795, 770 cm^{-1}; NMR (acetone-d_6) δ 8.25 (m, 1, Ar H-8), 7.80 (m, 1, Ar H-5), 7.40 (m, 4, Ar H-3, -4, -6, -7), 6.90 (m, J = 3, 6 Hz, 1, Ar H-2), 6.15 (s, 2, OH and COOH), 4.65 (t, J = 4 Hz, 1, CH), 4.45 (d, J = 4 Hz, 2, CH_2); UV (MeOH) λ_{max} 291 nm (log ϵ 3.64), 236 (log ϵ 3.91); mass spectrum (CI, methane), m/z 233 (QM) (93), 232 (M^+, 27), 215 (21), 187 (base peak), 169 (21), 145 (53), 144 (22). Anal. Calcd for $C_{13}H_{12}O_4$: C, 67.23; H, 5.20. Found: C, 67.28; H, 5.42.

(2*S*)-(+)-2-Hydroxy-3-(1-naphthoxy)propionic Acid ((2*S*)-2). 2-Hydroxy-3-(1-naphthoxy)propionic acid (**2**: 3.0 g, 13 mmol) was added to 1.58 g (13 mmol) of (−)-α-methylbenzylamine in 40 mL of ethanol. Repeated fractional crystallization (ethanol) of the resulting diastereomeric salts yielded 490 mg (11%) of the (−) salt: mp 172–176 °C; $[\alpha]_D^{20}$ −31.0° (c 1.0, MeOH). The salt was then decomposed in acidic water (50 mL) and extracted with EtOAc (2 × 50 mL). The EtOAc extract was dried ($MgSO_4$) and evaporated to yield a tan solid. Crystallization from chloroform–hexane yielded 200 mg of (2*S*)-**2** as tan needles: mp 132–133 °C; $[\alpha]_D^{20}$ +6.0° (c 1.0, MeOH); circular dichroism (c 0.10, Cupra A), $[\theta]_{790}$ +50, $[\theta]_{675}$ +155, $[\theta]_{625}$ 0, $[\theta]_{565}$ −120, $[\theta]_{415}$ −10, $[\theta]_{320}$ −430, $[\theta]_{315}$ 0, $[\theta]_{295}$ +115; circular dichroism of methyl ester (c 0.10 MeOH), $[\theta]_{300}$ 0, $[\theta]_{285}$ +210, $[\theta]_{270}$ 0.

(2*R*)-(−)-2-Hydroxy-3-(1-naphthoxy)propionic Acid ((2*R*)-2). From 3.0 g (13 mmol) of **2** and 1.58 g (13 mmol) of (+)-α-methylbenzylamine fractional crystallization (EtOH) afforded 570 mg (12%) of the (+) salt: mp 170–172 °C; $[\alpha]_D^{20}$ +31.0° (c 1.0, MeOH). Conversion of the salt to the free acid afforded 250 mg of (2*R*)-**2** as tan needles: mp 132–133 °C; $[\alpha]^{20}_D$ −6.1° (c 1.0, MeOH); circular dichroism (c 0.10, Cupra A), $[\theta]_{790}$ −30, $[\theta]_{680}$ −160, $[\theta]_{630}$ 0, $[\theta]_{565}$ +115, $[\theta]_{415}$ 0, $[\theta]_{325}$ +460, $[\theta]_{315}$ 0, $[\theta]_{295}$ −140; circular dichroism of methyl ester (c 0.10 MeOH), $[\theta]_{300}$ 0, $[\theta]_{285}$ −230, $[\theta]_{270}$ 0.

(2*S*)-(+)-3-(1-Naphthoxy)-1,2-propanediol ((2*S*)-6). Borane (18 mg, 0.66 mmol, 0.66 mL of a 1.0 M solution in THF) was added dropwise at −15 °C to a solution of 100 mg (0.44 mmol) of (2*R*)-2-hydroxy-3-(1-naphthoxy)propionic acid ((2*R*)-**2**) in 1.0 mL of THF in a Reactivial. The container was sealed. The solution was allowed to warm to room temperature and stirred for 24 h. Excess diborane was destroyed by the addition of 2 mL of a 1:1 THF–H_2O mixture. The aqueous layer was saturated with K_2CO_3, the THF layer removed, and the aqueous layer extracted with ether (3 × 5 mL). The THF and ether extracts were combined, dried ($MgSO_4$), and evaporated to yield a white solid. Crystallization from benzene yielded 50 mg (50%) of (2*S*)-**6** as white flakes: mp 108–109 °C (lit.[11] mp 108–110 °C); $[\alpha]_D^{20}$ +6.9° (c 1.0 MeOH); IR (KBr) 3225, 2970, 1575, 1500, 1450, 1400, 1265, 1240, 1110, 1080, 985, 785, 770 cm^{-1}; NMR (acetone-d_6) δ 8.25 (m, 1, Ar H-8), 7.80 (m, 1, Ar H-5), 7.45 (m, 4, Ar H-3, -4, -6, -7), 6.90 (m, 1, Ar H-2), 4.20 (m, 1, CHOH), 4.00 (br s, 2, OH), 3.80 (m, 2, CH_2OH); $[\alpha]_D^{20}$ +6.9° (c 1.0, EtOH); circular dichroism (c 0.10, Cupra A–MeOH, 4:1), $[\theta]_{780}$ 0, $[\theta]_{550}$ −20, $[\theta]_{400}$ 0, $[\theta]_{330}$ +95, $[\theta]_{325}$ 0.

(2*R*)-(−)-3-(1-Naphthoxy)-1,2-propanediol ((2*R*)-6). This compound was prepared from (2*R*)-3-(tosyloxy)propane-1,2-diol acetonide as previously reported:[11] mp 108–110 °C (lit.[11] mp 109–111 °C); IR (KBr) 3250, 1590, 1465, 1410, 1295, 1255, 1115, 1080, 1005, 780 cm^{-1}; $[\alpha]_D^{20}$ −8.1°; circular dichroism (c 0.11, Cupra A–MeOH, 4:1), $[\theta]_{780}$ 0, $[\theta]_{555}$ +30, $[\theta]_{360}$ 0, $[\theta]_{325}$ −90, $[\theta]_{320}$ 0.

Acknowledgment. We acknowledge support of this work by the U.S. Public Health Service by Research Grant GM-25373 and by National Research Service Award GM-07750.

Registry No. (2*R*)-**2**, 80789-57-7; (2*R*)-**2** (+)-α-methylbenzylamine salt, 80789-58-8; (2*S*)-**2**, 80789-59-9; (2*S*)-**2** (−)-α-methylbenzylamine salt, 80789-60-2; (±)-**2**, 80844-62-8; **3**, 80789-61-3; **4**, 60148-34-7; **4** oxime, 80789-62-4; (±)-**5**, 80789-63-5; (2*R*)-**6**, 61248-78-0; (2*S*)-**6**, 56715-19-6; 1-naphthol, 90-15-3; α-bromoacetaldehyde diethyl acetal, 2032-35-1.

2-Methyl-5-*tert*-butylcyclohexane-1,3-dione and Related 2-Alkylcyclohexane-1,3-diones from 1,3-Dimethoxybenzenes

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Received September 18, 1981

In connection with vitamin D analogue syntheses and studies on the mechanism of asymmetric aldol condensation reactions, we required a facile preparation of 2-methyl-5-*tert*-butylcyclohexane-1,3-dione (**1a**,[2] Chart I). We report its preparation as well as that of 2-alkylcyclohexane-1,3-diones **2a–c** needed in related ongoing studies. Rather than directly preparing 2-unsubstituted cyclohexane-1,3-diones and then alkylating, a sequence known to proceed with modest efficiency at best,[3] we extended the method of Piers and Grierson[4] for incorporating the alkyl group between the two carbonyl moieties.

The 5-*tert*-butyl derivatives **1a** and **1b** were synthesized from the cyclohexadiene **3a**. Alkylation[4] of **3a** (*tert*-butyllithium in THF, −78 °C, 10 min; CH_3I, −78 °C to room temperature; 93% distilled yield) afforded **4a**, which upon hydrolysis (1 M HCl) gave **1a** in essentially quantitative yield. Direct hydrolysis of **3a** afforded the dione **1b**.[2] A recent report[5] described the sequence **5** → **6** → **7** → **8** in which the R group is introduced in the first step by using a tertiary carbinol. Rather than utilizing **8a** for the reduction, we have found that exhaustive Birch reduction (Li, *t*-BuOH, NH_3–THF) of the previously unreported **7** (R = *t*-Bu)[5] afforded **3a** directly in 82% yield.

Similar Birch reduction of **8b**[6] and **8c**[4] afforded **3b** and **3c**, respectively. Alkylation of **3b** (methyl iodide), **3c** (ethyl iodide), and **3c** (isopropyl bromide) as above for **3a** afforded **4b–d**, which upon hydrolysis gave the known diketones **2c**[3d] (80% based on **3b**), **2a**[2b] (78% based on **3c**), and **2b**[3e,7] (64% based on **3c**).

(1) (a) Universidad de Santiago. (b) University of California, Riverside.

(2) The title diketone **1a** appears to be unknown, but the demethyl compound **1b** has been reported: Dunkelblum, E.; Levene, R.; Klein, J. *Tetrahedron* **1972**, *28*, 1009–1024. The isomeric 2-*tert*-butylcyclohexane-1,3-dione has also been synthesized: Newkome, G. R.; Montelaro, R. C.; Sauer, J. D.; Wander, J. D. *J. Chem. Soc., Chem. Commun.* **1972**, 905.

(3) (a) Methylation of cyclohexane-1,3-dione proceeds in 54–56% yield. Mekler, A. B.; Ramachandra, S.; Swaminathan, S.; Newman, M. S. "Organic Syntheses"; Wiley: New York, 1973; Collect. Vol. 5 V, pp 743–746. A typical yield in our hands was about 51%. (b) ethylation of cyclohexane-1,3-dione proceeds in ~30% yield, a result reproducible in our hands. Smith, H. *J. Chem. Soc.* **1953**, 803–810. Newkome, G. R.; Roach, L. C.; Montelaro, R. C.; Hill, R. K. *J. Org. Chem.* **1972**, *37*, 2098–2101. Coke, J. L.; Williams, H. J.; Natarajan, S. *Ibid.* **1977**, *42*, 2380–2382. (c) Methylation of dimedone is reported to proceed in 70% yield, although our yields have averaged 53%. Clark, R. D.; Ellis, J. E.; Heathcock, C. H. *Synth. Commun.* **1973**, *3*, 347–354. (d) Methylation of 5-methylcyclohexane-1,3-dione affords 48% of product. Leed, A. R.; Boettger, S. D.; Ganem, B. *J. Org. Chem.* **1980**, *45*, 1098–1106. The first crop yield with this procedure was 21–35% (three trials) in this laboratory. (e) The isopropyl derivative **2b** has been prepared by the classical Claisen route: Newkome's improved route[3b] and ref 7.

(4) Piers, E.; Grierson, J. R. *J. Org. Chem.* **1977**, *42*, 3755–3757. In our hands, we were unable to improve our yields significantly using hexamethylphosphoramide as co-solvent in the alkylation step.

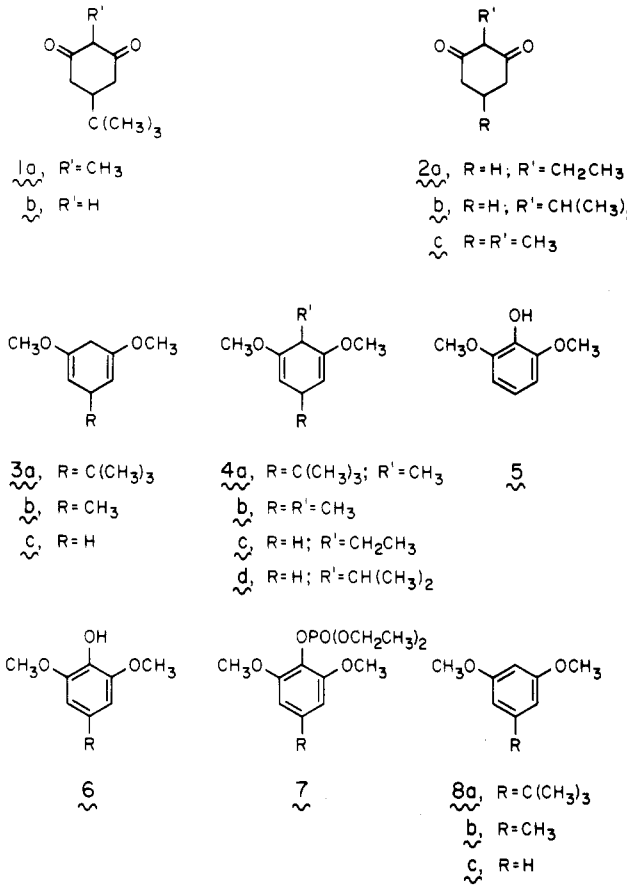
(5) Dominianni, S. J.; Ryan, C. W.; DeArmitt, C. W. *J. Org. Chem.* **1977**, *42*, 344–346. For a related study, see also: Focella, A.; Teitel, S.; Brossi, A. *Ibid.* **1977**, *42*, 3456–3457.

(6) Birch, A. J.; Rickards, R. W. *Aust. J. Chem.* **1956**, *9*, 241–243.

(7) Bhattacharyya, P. C. *J. Indian Chem. Soc.* **1965**, *42*, 467–469. Newkome's paper[3b] gives a melting point of 150–151 °C for **2b**.

0022-3263/82/1947-1576$01.25/0

Chart I



In summary, these prototype Birch reduction–alkylation–hydrolysis sequences further extend the method of Piers and Grierson to afford the desired *tert*-butyl derivative 1 and related 2-alkylcyclohexane-1,3-diones. In particular, the sequence described for the preparation of **1a** from **5** should be generally useful for obtaining a variety of 2,5-dialkyl derivatives.

Experimental Section

General Methods. ^1H nuclear magnetic resonance spectra (NMR) were recorded at 90 MHz on a Varian EM-390 spectrometer (in $CDCl_3$ with $(CH_3)_4Si$ as internal standard; chemical shifts are given as δ values and coupling constants, J, in hertz). Mass spectra (70 eV) were recorded on an ARI MS-9 mass spectrometer. Kugelrohr distillation boiling points (bp) refer to the external oven air-bath temperatures. Microanalyses were performed by Elek Microanalytical Labs (Torrance, CA). Dry tetrahydrofuran (THF) refers to solvent freshly distilled from $LiAlH_4$ under N_2. All operations involving organometallic reagents were conducted under a dry, inert atmosphere. Ammonia was passed directly from an anhydrous ammonia cylinder through a drying tower (KOH pellets) and then condensed into the reaction vessel (−78 °C).

4-*tert*-Butyl-2,6-dimethoxyphenyl Diethyl Phosphate (7, R = *tert*-Butyl). A mixture of *tert*-butyl alcohol (14.8 g, 0.20 mol), 2,6-dimethoxyphenol (**5**; 31 g, 0.20 mol), and methanesulfonic acid (40 mL) was reacted and worked up exactly as previously described.[5] The crude product **6** (R = *tert*-butyl; 42.5 g, ~100%; dried under high vacuum), used directly in the next step, exhibited the following appropriate NMR signals: δ 6.54 (2 H, s), 5.42 (1 H, s), 3.80 (6 H, s), 1.27 (9 H, s). To the stirred ice-cooled solution of crude phenol **6** (R = *tert*-butyl; 42.5 g, 0.20 mol) in CCl_4 (30 mL) was added diethyl phosphonate (30 mL, 0.23 mol). Triethylamine (32 mL, 0.23 mol) was added dropwise (syringe) to the mixture, and the mixture was stirred at 0 °C (1 h) and then at room temperature overnight. Dichloromethane (50 mL) was added to the mixture, and then the stirred mixture was quenched with 15% aqueous NaOH solution (15 mL). The organic phase was extracted with an additional portion of the 15% aqueous NaOH solution (40 mL), the combined aqueous phase was back-extracted with CH_2Cl_2 (2 × 30 mL), and then the combined CH_2Cl_2 extracts were washed with water and saturated aqueous $NaHCO_3$. After the organic phase was dried ($MgSO_4$), the solvent was removed under vacuum. Crystallization from hexanes by repetitive filtration of ice-cooled solutions followed by concentration afforded 51 g (74% based on **5**) of colorless phosphate **7** (R = *tert*-butyl; mp 54–58 °C), sufficiently pure for Birch reduction. Recrystallization (Skellysolve B) afforded light tan plates: mp 76–78 °C; NMR δ 6.56 (2 H, s, arom), 4.25 (4 H, dq, $J \approx 7.2$, 7.2 Hz, CH_2O), 3.80 (6 H, s, OCH_3), 1.36 (6 H, dt, $J \approx 1.5$, 7.2 Hz, CH_3 of ethyl), 1.29 (9 H, s, *tert*-butyl); mass spectrum, *m/e* (relative intensity; >10%) 347 (11, M + 1), 346 (62, M), 331 (49), 271 (16), 195 (31), 192 (31), 178 (17), 177 (base), 155 (17), 149 (11), 127 (13), 109 (13), 91 (19), 81 (11).

3-*tert*-Butyl-1,5-dimethoxy-1,4-cyclohexadiene (3a). A solution of phosphate **7** (R = *tert*-butyl; 17.4 g, 0.05 mol) in THF (30 mL) and *tert*-butyl alcohol (75 mL) was added (via syringe, N_2) to anhydrous liquid ammonia (160 mL) without stirring three-necked flask equipped with a mechanical stirrer, dry ice condenser, and N_2 and septum inlets). Lithium metal (~0.8 g of wire cut up in small pieces) was added (slow mechanical stirring; no blue color was observed) over 1 h. Additional lithium metal (2 g) was added at a rate sufficient to maintain a blue color (4.5 h). The reaction mixture was quenched (methanol, 20 mL), and then the ammonia was allowed to evaporate overnight under N_2. A conventional workup with water and ether including drying of the ether phase (Na_2SO_4) and concentration afforded quite pure (NMR) diene **3a**. Kugelrohr distillation [bp 52–54 °C (0.02 mm)] afforded 8.2 g (82%) of product: NMR δ 4.6 (2 H, m, vinyl), 3.45 (6 H, s, OCH_3), 2.6 (3 H, m, allylic), 0.78 (9 H, s, *tert*-butyl); calcd for $C_{12}H_{20}O_2$ *m/e* 196.1464, found *m/e* 196.1477.

3-*tert*-Butyl-1,5-dimethoxy-6-methyl-1,4-cyclohexadiene (4a) and 5-*tert*-Butyl-2-methylcyclohexane-1,3-dione (1a). To a cooled (−78 °C) magnetically stirred solution of diene **3a** (4.03 g, 0.0207 mol) in THF (50 mL) was added *tert*-butyllithium (0.0225 mol, 15.0 mL, 1.5 M in pentane) dropwise by means of a syringe. After 15 min at −78 °C, freshly distilled methyl iodide (2.0 mL, ~4.6 g, 0.032 mol) was added via syringe to the stirred orange-yellow solution. After 10 min, the reaction mixture (white suspension) was brought to room temperature (~30 min), quenched with water, and then worked up in the usual fashion (ether and water; dried with Na_2SO_4; concentrated) to afford a pale yellow liquid in essentially quantitative yield (pure by NMR). Kugelrohr distillation [bp 70–72 °C (1.5 mm)] afforded **4a** (4.01 g, 93%) as a colorless liquid: NMR δ 4.62 (2 H, m, vinyl), 3.50 (6 H, s, OCH_3), 2.7 (2 H, m, allylic), 1.19 (3 H, d, $J \approx 6$ Hz, allylic CH_3), 0.88 (9 H, s, *tert*-butyl); calcd for $C_{13}H_{22}O_2 - H_2$ *m/e* 208.1464, found *m/e* 208.1472.

The neat liquid **4a** (2.0 g, 9.6 mmol) was treated with 0.25 mL of aqueous HCl (1 M), and the two-phase mixture was heated on a water bath (80–90 °C) for 5 min. Alternatively, acetone may be used as a cosolvent.[4] The resulting solid foam **1a** was removed by filtration and crystallized (ethyl acetate): ~quantitative based on **4a**; mp 213.0–216.5 °C dec; NMR δ 2.6–1.5 (8.1 H, complex m and CH_3 s at δ 1.64), 0.89 (9.0 H, s, *tert*-butyl). Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95; *m/e* 182.1307. Found: C, 72.94; H, 9.65; *m/e* 182.1311.

5-*tert*-Butylcyclohexane-1,3-dione (1b). A sample of **3a** was hydrolyzed in precisely the same manner as described for its 2-methyl derivative **1a** (preceding experiment). Filtration of the product afforded **1b** in essentially quantitative yield. Crystallization (water) afforded the pure material: mp 139.5–141 °C (lit.[2] mp 147–148 °C from acetone); NMR δ 10.3 (0.5 H, br s, enol OH), 5.45 (0.5 H, br s, enol CH), 2.8–1.6 (6 H, m), 0.92 and 0.90 (9 H, 2 s, *tert*-butyl of ~1:1 mixture of enol and keto forms).

1,5-Dimethoxy-3-methyl-1,4-cyclohexadiene (3b). The Birch reduction was carried out by the procedure described above: **8b** (20.0 g, 0.128 mol), THF (98 mL), *tert*-butyl alcohol (115 g), NH_3 (400 mL), lithium (8.20 g, 1.17 mol), methanol (100 mL for quench); lithium addition time was ~2.5 h. Workup (ether and water; Na_2SO_4 drying), concentration (**Caution**: the bath temperature should be kept below 40 °C to avoid loss of product during rotary evaporation), and Kugelrohr distillation [bp 50 °C (0.25 mm)] afforded pure **3b**: NMR δ 4.5 (2 H, m, vinyl) 3.51 (6

H, s, OCH_3), 3.2–2.7 (3 H, complex m, allylic), 1.08 (3 H, d, $J \approx 6$ Hz, allylic CH_3). Hydrolysis of the diene **3b** by the procedure used for the conversion of **4a** to **1a** afforded the known 5-methylcyclohexane-1,3-dione: 76% yield based on **8b** (12.6 g, from ethyl acetate); mp 124–125 °C (lit.[6] mp 127–128 °C).

1,5-Dimethoxy-3,6-dimethyl-1,4-cyclohexadiene (4b) and 2,5-Dimethylcyclohexane-1,3-dione (2c). The diene **3b** (924 mg, 5.8 mmol) was methylated (CH_3I, 0.91 g, 6.4 mmol) and then worked up by the procedure described above for the conversion of **3a** to **4a**. The crude product appeared pure by NMR: δ 4.5 (2 H, m, vinyl), 3.50 (6 H, s, OCH_3), 3.1–2.5 (2 H, m, allylic), 1.19 and 1.18 (3 H, 2 overlapping d, $J \approx 6$ Hz, ~2:1 ratio of one of the allylic methyls of two stereoisomers), 1.03 (3 H, d, $J \approx 6$ Hz, second allylic methyl of both stereoisomers). Hydrolysis (1 M HCl) of **4b** as described above for preparing **1a** from **4a** afforded an 80% yield (650 mg from **3b**; crystallization from water) of dione **2c**, mp 168.5–171 °C (lit.[3d] mp 170–172 °C). A sample of **2c** prepared by the literature[3d] procedure had a melting point of 169–171 °C (from ethyl acetate). Both samples of **2c** exhibited identical NMR spectra.

3-Ethyl-2,4-dimethoxy-1,4-cyclohexadiene (4c) and 2-Ethylcyclohexane-1,3-dione (2a). For alkylation of **3c**[4] (1.262 g, 9.01 mmol), the procedure used for the preparation of **4a** was followed except that ethyl iodide (1.90 g, 12.2 mmol) was used. Workup and Kugelrohr distillation [bp 70–72 °C (3.0 mm)] afforded 1.263 g (83% yield) of **4c**: NMR δ 4.7 (2 H, m, olefinic), 3.50 (6 H, s, OCH_3), 2.8 (3 H, m, allylic), 1.9–1.5 (2 H, m, ethyl CH_2), 0.68 (3 H, t, $J \approx 6.2$ Hz); calcd for $C_{10}H_{16}O_2$ m/e 168.1151, found m/e 168.1138. Hydrolysis (by the procedure described above for preparing **1a**) of **4c** afforded after crystallization (ethyl acetate) the pure diketone **2a**: 92% yield (78% based on **3c**); mp 173–176 °C (lit.[3b] mp 172–175 °C). The NMR spectrum of **2a** proved to be identical with that of an authentic specimen prepared in this laboratory by the literature procedure.[3b]

3-Isopropyl-2,4-dimethoxy-1,4-cyclohexadiene (4d) and 2-Isopropylcyclohexane-1,3-dione (2b). For alkylation of **3c** (700 mg), the procedure used for the preparation of **4a** was followed except that isopropyl bromide (0.8 mL) was used as the alkylating agent. Workup and Kugelrohr distillation [bp 76–79 °C (3.2 mm)] afforded a 71% yield of **4d**: NMR δ 4.7 (2 H, m, olefinic), 3.50 (6 H, s, OCH_3), 2.7 (3 H, m, allylic), 2.1 (1 H, m, isopropyl methine), 0.89 (6 H, d, $J \approx 6$ Hz, $C(CH_3)_2$); calcd for $C_{11}H_{18}O_2$ m/e 182.1307, found m/e 182.1304. Hydrolysis with aqueous HCl by the above procedure afforded after crystallization a 90% yield (64% based on **3c**) of pure diketone **2b**: mp 143–145 °C (from ethyl acetate), mp 139–142 °C (from water) (lit.[7] mp 140–143 °C).

Acknowledgment. This study was supported by National Institutes of Health Grant No. AM-16595 and was performed at the University of California at Riverside.

Registry No. 1a, 80753-98-6; **1b**, 49673-64-5; **2a**, 18456-78-5; **2b**, 3401-01-2; **2c**, 61621-47-4; **3a**, 80753-99-7; **3b**, 28495-21-8; **3c**, 37567-78-5; **4a**, 80754-00-3; **4b**, 54118-01-3; **4c**, 54117-99-6; **4d**, 80754-01-4; **5**, 91-10-1; **6** (R = *t*-Bu), 6766-84-3; **7** (R = *t*-Bu), 80754-02-5; **8b**, 4179-19-5; 5-methylcyclohexane-1,3-dione, 4341-24-6.

Regioselective Diamine–Dialdehyde Condensation. Annelated Azepinopurine

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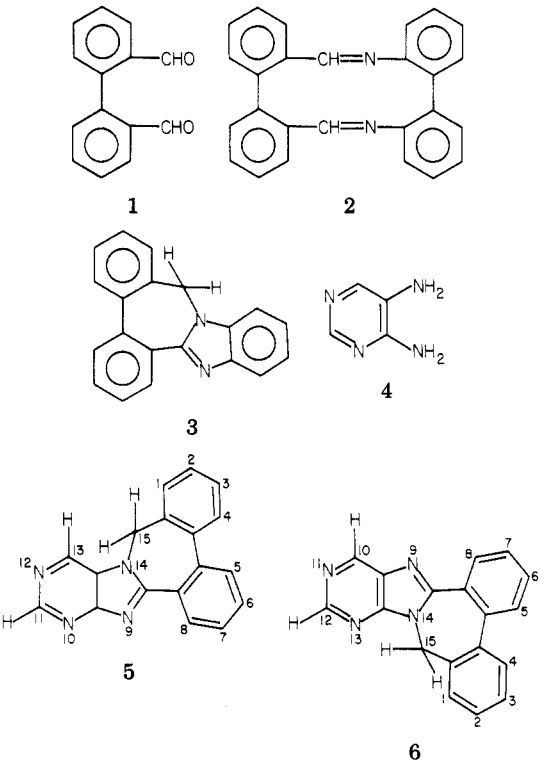
Received July 2, 1981

Diamine–dialdehyde condensations provide a valuable entry into heteroannulenes and condensed heterocyclic series.[1] The method has been studied in terms of bis Schiff bases vs. bicyclic "hydride shift" products. It may be illustrated by the double condensations of biphenyl-2,2′-dicarboxaldehyde (**1**, Chart I): it reacted with 2,2′-diaminobiphenyl to give 9,20-diazatetrabenzo[*a*,*c*,*g*,*i*]dodecene (**2**)[2,3] and with *o*-phenylenediamine to give 15*H*-dibenzo[*c*,*e*]benzimidazo[2,1-*a*]azepine (**3**).[4] We describe here the condensation of **1** and 4,5-diaminopyrimidine (**4**), an unsymmetrical heterocyclic diamine. α-Dicarbonyl compounds (including glyoxal) have previously been condensed with **4** and its derivatives to give pteridines.[5,6a]

Chart I



1 2 3 4 5 6

The reaction of **1** and **4** was conducted in boiling acetic acid. The bicyclic "hydride shift" structure of the product was concluded from the ^1H NMR spectrum (in CF_3CO_2H) which showed an AB quartet at 5.92 and 5.26 ppm (J = 14 Hz) due to two aliphatic geminal protons. Two isomeric "hydride shift" products may account for the spectroscopic data: 15*H*-dibenzo[3,4:5,6]azepino[2,1-*f*]purine (**5**) and 15*H*-dibenzo[3,4:5,6]azepino[1,2-*e*]purine (**6**). In **5**, the origin of the azepino nitrogen is the 5-amino group of **4**, while in **6**, it is the 4-amino group of **6**. Compound **5** is a 7*H*-purine derivative while **6** is a 9*H*-purine derivative. The decision between **5** and **6** was based on the results of the X-ray crystallographic investigation. The evidence established the structure of the product as **5**.

Consider the structures of **5** and **6**. They differ (inter alia) in the positions of the atoms of the pyrimidine rings: N(10) and N(12) in **5** became C(10) and C(12) in **6**, while C(11) and C(13) in **5** became N(11) and N(13) in **6**. The X-ray scattering power of carbon and nitrogen atoms does not differ significantly. Therefore, the distinction between

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0022-3263/82/1947-1578$01.25/0