threo), 4.85 (1 H, HC(OH), AB system, J = 5.4 Hz, erythro), 7.0–7.35 (10 H, Ph H, m); mass spectrum (70 eV), m/e 210 ($M^+ - H_2O$), 178, 121, 107.

2,3-Di-2-pyridyl-2,3-butanediol (14u) and 2,3-Di-4-pyridyl-2,3-butanediol (14v). For detailed separation of *dl* and meso isomers and spectroscopic assignments see ref 18.

Registry No. (±)-**12g**, 93453-79-3; (±)-**12h**, 93453-80-6; (±)-**12n**, 57377-60-3; **12g**, 91-01-0; *dl*-**13a**, 93453-74-8; *meso*-**13a**, 62154-11-4; *dl*-**13b**, 22985-88-2; *meso*-**13b**, 22985-87-1; *dl*-**13c**, 22985-90-6; *meso*-**13c**, 4217-65-6; *dl*-**13d**, 93453-75-9; *meso*-**13d**, 93453-77-1; *dl*-**13e**, 93528-45-1; *meso*-**13e**, 93528-46-2; *dl*-**13f**, 93453-76-0; *meso*-**13f**, 93453-78-2; *dl*-**13m**, 16020-87-4; *meso*-**13m**, 16020-86-3; *dl*-**13n**, 63882-18-8; *meso*-**13n**, 63846-48-0; *dl*-**13p**, 93453-81-7; *meso*-**13p**, 93453-82-8; **13g**, 464-72-2; *dl*-**14r**, 655-48-1; *meso*-**14r**, 579-43-1; *threo*-**14t**, 50778-88-6; *erythro*-**14t**, 50778-87-5; *dl*-**14u**, 20445-39-0; *meso*-**14u**, 20445-38-9; *dl*-**14v**, 83179-65-1; *meso*-**14v**, 83179-64-0; $TiCl_3$, 7705-07-9; *p*-$MeOC_6H_4C(O)CH_3$, 100-06-1; *p*-$MeC_6H_4C(O)CH_3$, 122-00-9; $PhC(O)CH_3$, 98-86-2; *p*-$ClC_6H_4C(O)CH_3$, 99-91-2; *p*-$CF_3C_6H_4C(O)CH_3$, 709-63-7; *p*-$CNC_6H_4C(O)CH_3$, 1443-80-7; PhC(O)C(O)Ph, 134-81-6; (±)-PhC(O)CH(OH)Ph, 579-44-2; (±)-PhC(O)CH(OMe)Ph, 5987-95-1; 2-$PyC(O)CH_3$, 1122-62-9; 4-$PyC(O)CH_3$, 1122-54-9; *p*-$HOC_6H_4C(O)CH_3$, 99-93-4; *p*-$NH_2C_6H_4C(O)CH_3$, 99-92-3; *p*-$NH_3^+C_6H_4C(O)CH_3$, 93453-73-7; $PhC(O)CH_2CH_3$, 93-55-0; $PhC(O)CH_2Ph$, 451-40-1; PhC(O)-*t*-Bu, 938-16-9; PhC(O)Ph, 119-61-9.

New Preparation and Controlled Alkaline Hydrolysis of 21-Bromo-20-ketopregnenes. A Facile Synthesis of Deoxycorticoids[1]

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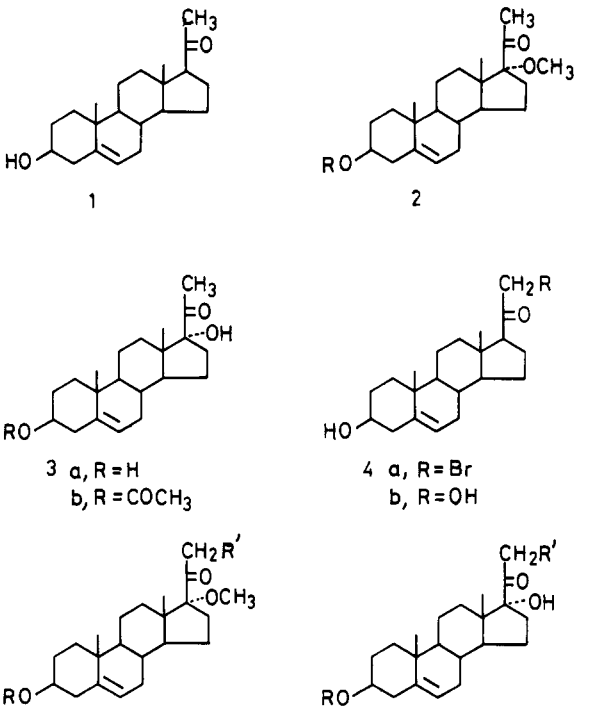
Syntheses of deoxycorticoids **7b**, **8b**, and **9b** are described. Treatment of 20-oxo steroid 1 with 3 mol equiv of $CuBr_2$ in MeOH in the presence or absence of pyridine gave the 21-bromide **4a** or the 17α-methoxide **2** in high yields, respectively. When 6 mol equiv of the brominating reagent was used in the absence of pyridine, the 21-bromo 17α-methoxide **5a** was formed. 17α-Hydroxy 20-ones **3** could be similarly converted to the 21-bromides **6a** and **6b**. Oxidation of **4a**, **5a**, and **6a** with CrO_3 and subsequent isomerization of a double bond at C-5 with acid gave the corresponding 4-en-3-ones **7a**, **8a**, and **9a**, of which **7a** and **9a** were efficiently hydrolyzed to **7b** and **9b** under controlled conditions with a K_2CO_3–H_2O–acetone system. On the other hand, **8a** was converted to **8b** by reaction with $NaOCH_3$ in MeOH.

Introduction of the 21-hydroxyl function into the 17-acetyl side chain of a 20-ketopregnene is of central importance in the partial synthesis of corticoids. One of the attractive chemical methods involves direct C-21 halogenation of a 20-ketopregnane and subsequent displacement of the resulting 21-halo compound by acetate or hydroxide.

Direct halogenation of a 20-oxo steroid lacking a substituent (e.g., OH or CH_3) at C-17 with the common reagent such as Br_2 generally does not give a satisfactory yield of the 21-bromo derivative,[2] although Ringold and Stork[3] reported a versatile method for direct C-21 iodination of 20-ketopregnenes with a 4-en-3-one or 5-en-3β-ol system. While displacement of a 21-bromo 20-one by hydroxyl can be accomplished by careful control of reaction conditions,[4] it is preferable to use acetate instead, because a Favorskii rearrangement[5] is involved in the reaction and the product, 21-hydroxy 20-one, is sensitive to basic reagents.

Glazier[6] reported that the reaction of 3β-hydroxy-5-pregnen-20-one (**1**) with $CuBr_2$ in MeOH resulted in the formation of 17α-methoxy derivative (**2**) in a modest yield without affecting the integrity of the olefinic bond at C-5. We recently discovered a high yield and controlled stereoselective alkaline hydrolysis of steroidal 16α-bromo 17-ones[7,8] and 2α-bromo 3-ones.[9]

Chart I



We now report the previously unreported direct bromination at C-21 of 20-ketopregnenes **1**, **2**, and **3** with

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(2) For a review see: Oliveto, E. P. "Organic Reactions in Steroid Chemistry"; Fried, J., Edwards, J. A., Eds.; Van Norstrand Reinhold: New York, 1972; Vol. II, p 127.
(3) Ringold, H. J.; Stork, G. *J. Am. Chem. Soc.* **1958**, *80*, 250.
(4) Kritchevsky, T. H.; Gallagher, T. F. *J. Am. Chem. Soc.* **1951**, *73*, 184.
(5) Kirk, D. N.; Hartshorn, M. P. "Steroid Reaction Mechanism"; Elsevier Publishing Co.: Amsterdam, 1968; p 388.
(6) Glazier, E. R. *J. Org. Chem.* **1962**, *27*, 4397.
(7) Numazawa, M.; Osawa, Y. *J. Am. Chem. Soc.* **1980**, *102*, 5402.

0022-3263/85/1950-0081$01.50/0

Table I. Bromination of 20-Oxo Steroids 1, 2, and 3 with $CuBr_2$[a]

	condition					
no.	$CuBr_2$, mol equiv	solvent	C_5H_5N	time, h	product	isolated yield, %
1	3	MeOH	no	24	**2**	65
1	3	MeOH	yes	24	**4a**	71
1	6	MeOH	no	24	**5a**	54
2	3	MeOH	no	24	**5a**	78
2	3	MeOH	yes	24	**5a**	<1[b]
2	3	THF	no	4	**5a**	<1[c]
3a	3	THF	no	2	**6a**	10
3a	3	THF	yes	2	**6a**	<1[b]
3a	3	MeOH	no	6	**6a**	<1[c]
3b	3	MeOH	no	12	**6b**	10
3b	3	THF	no	2	**6b**	45
3b	3	THF	yes	3	**6b**	<1[b]

[a] A solution of 20-oxo steroid (0.96 mmol) in a solvent (30 mL) was heated under reflux for an appropriate time in the presence or absence of pyridine (3 mol equiv.) After the usual workup, the crude products obtained were purified by silica gel column chromatography with a *n*-hexane-AcOEt (3:1) system as the mobile phase. [b] More than 95% of the substrate was recovered. [c] Formation of a complex mixture of products was observed on thin-layer chromatogram and the product could not be isolated as a pure form.

$CuBr_2$ in the presence or absence of pyridine in which a C-5 double bond does not interfere. Utilization of the controlled hydrolytic method in the syntheses of 21-hydroxy-20-oxo steroids **4b**, **5c**, **6c**, and **8b**, deoxycorticosterone (**7b**), and cortexolone (**9b**) are also described.

Results and Discussion

Bromination of Steroidal 20-Ones. The bromination of 20-ketopregnenes **1**, **2**, and **3** with $CuBr_2$ was initially explored under a variety of conditions to directly obtain the corresponding 21-bromo compounds **4a**, **5a**, **6a**, and **6b** (Table I), which are promising intermediates for the construction of the 17-side chain of deoxycorticoids. We have recommended the use of three rather than two mol equiv of $CuBr_2$ for the synthesis of 16α-bromo 17-ones in much improved yields.[10] Thus, reaction of **1** with 3 mol equiv of $CuBr_2$ in MeOH afforded 17α-methoxide **2** in 65% yield compared with 33% reported.[11] Methoxylation presumably occurs by way of acid-catalyzed nucleophilic substitution by MeO^- at C-17 of the initially produced 17α-bromide.[6] The reagent (6 mol equiv) gave 21-bromo 17α-methoxide **5a** in high yield. Bromination of **2** with the same reagent also gave **5a**, indicating that complete reaction of **1** with $CuBr_2$ proceeds by way of **2**.

Reaction of 17α-hydroxy 20-ones **3** with $CuBr_2$ in THF gave the corresponding 21-bromides **6a** and **6b** in modest yields. The choice of solvent was important (Table I). These reactions represent the first direct brominations at C-21 of 17α-substituted 20-ketopregnene without affecting the isolated double bond at C-5.

Bromination of 20-oxo steroid **1** with 3 mol equiv of $CuBr_2$ in the presence of 3 mol equiv of pyridine, with the thought of producing an improved yield of 17α-methoxide **2** analogous to the results of Sollmon and Dodson,[12] gave unexpectedly 21-bromo 20-one **4a** as the major product (Table I). **2** was not formed at all. This surprising results, the regioselective and direct C-21 bromintion of **1** with $CuBr_2$, can be rationalized on the basis that the function of pyridine is probably to promote enolization in the Hofman sense toward C-21[13] in analogy with that of CaO[3] used in the direct iodination. However, pyridine lowered yields of other 21-bromo-20-oxo derivatives, **5a**, **6a**, and **6b**, to a great extent. The results show that in the bromination with $CuBr_2$ structural features and substituents in the vicinity of the 20-carbonyl as well as the reaction conditions are important.

3β-Hydroxy 5-enes **4a**, **5a**, and **6a** could be efficiently converted to the 4-en-3-one derivatives **7a**, **8a**, and **9a** by oxidation with 8 N CrO_3 followed by isomerization of a C-5 double bond by acid, respectively.

Chart II

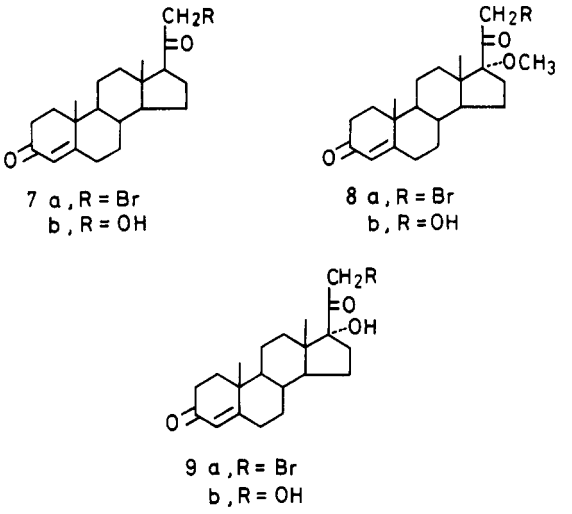

Table II. Hydrolysis of 21-Bromo 20-One with Base[a]

	condition		21-hydroxy 20-one isolated
base (mol equiv)	solvent (mL)	time, min	yield, %
	(A) Substrate **4a**–Product **4b**		
NaOH (1.2 or 12)	60% EtOH (40)	20 or 10	82 or 70
NaOH (1.2)	67% pyridine (15)	15	0[b]
NaOH (1.2)	67% DMF (15)	30	95
K_2CO_3 (1.0)	60% acetone (25)	120	78
	(B) Substrate **7a**–Product **7b**		
NaOH (1.2 or 12)	60% EtOH (40)	15 or 10	60 or 58
NaOH (1.2)	67% pyridine (8)	60	41
NaOH (1.2)	67% DMF (15)	15	85
K_2CO_3 (1.0)	60% acetone (25)	30	93

[a] To a solution of **4a** or **7a** (100 mg, 0.25 mmol) in aqueous solvent was added 1 N NaOH solution or K_2CO_3 and the reaction mixture was stirred at room temperature (NaOH) or heated under reflux (K_2CO_3). [b] Insoluble material was produced before addition of NaOH.

Hydrolysis of 21-Bromo-20-oxo Steroids. Treatment of 21-bromo-20-oxo derivatives **4a** and **7a** with 1.2 equiv of NaOH in 60% DMF or with 1.0 mol equiv of K_2CO_3 in 60% acetone[7-10] afforded the corresponding 21-hydroxides **4b** and **7b** in very high yields, respectively (Table II). Pyridine was not a good solvent for the hydrolysis, because the substrates reacted immediately with the solvent to

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(10) Numazawa, M.; Nagaoka, M.; Osawa, Y. *J. Org. Chem.* **1982**, *47*, 4024.

(11) The probable formation (ca. 7%) of 17β-methoxy isomer was detected by ^1H NMR analysis of the reaction products, although the isomer could not be isolated as a pure form. The isomer: ^1H NMR ($CDCl_3$) δ 0.73 (3 H, s, 18-CH_3), 1.00 (3 H, s, 19-CH_3), 2.17 (3 H, s, 21-CH_3), 3.15 (3 H, s, 17β-OCH_3).

(12) Sollmon, P. B.; Dodson, R. M. *J. Org. Chem.* **1961**, *26*, 4180.

(13) Kirk, D. N.; Hartshorn, M. P. "Steroid Reaction Mechanism"; Elsevier Publishing Co.: Amsterdam, 1968; p 168.

Table III. Hydrolysis of 21-Bromo-17α-hydroxy 20-One with Base[a]

condition			21-hydroxy 20-one isolated yield, %
base (mol equiv)	solvent (mL)	time, min	
	(A) Substrate **6b**–Product **6c**		
NaOH (1.2)	76% EtOH (50)	10	60
NaOH (1.2)	67% pyridine (10)	10	0[b]
NaOH (1.2)	80% DMF (16)	10	25
K_2CO_3 (1.0)	60% acetone (50)	10	99
	(B) Substrate **9a**–Product **9b**		
NaOH (1.2 or 10)	76% EtOH (25)	20 or 10	52 or 40
NaOH (1.2)	67% pyridine (6)	30	20
NaOH (1.2)	80% DMF (10)	10	36
K_2CO_3 (1.0)	60% K_2CO_3 (50)	10	68

[a] To a solution of 100 mg of **6b** or **6c** (0.25 mmol) in aqueous solvent was added 1 N NaOH solution or K_2CO_3. The reaction was carried out as shown in Table II. [b] Insoluble material was produced before addition of NaOH.

probably produce 21-pyridino derivatives.[14] Kritchevsky and Gallagher[4] reported that replacement of the bromine of a 21-bromo-17α-hydroxy 20-one by hydroxyl could be achieved with an excess amount of alkali in aqueous EtOH. Treatment of **4a** and **7a** with a limited amount of NaOH (1.2 or 12 equiv) in 60% EtOH gave also **4b** and **7b** but the yields were much improved, compared with that reported.[4] It is noteworthy that the formation of the 17α-isomer of **7b** was not observed in the hydrolysis of **7a**.[15]

Hydrolysis of 21-bromo-17α-hydroxy 20-ones **6b** and **9a** with the bases under similar conditions as above gave primarily the same results as above (Table III). Marked differences between 5-ene and 4-en-3-one derivatives observed in the hydrolysis with pyridine as the solvent (Table II and III) might be due to a conformational transmission of distortion through rings B, C, and D and the carbon at C-20, although the exact reason is not clear.

Compounds **7b** and **9b** were identical with the natural products in all respects and their over all yields, without purification and isolation of intermediates, were approximately 55% and 35%, respectively.

Attempted hydrolysis of 21-bromides **5a** and **8a** having a 17α-methoxy substituent under the controlled conditions was unsuccessful, leading to the formation of a complex mixture of polar products from which no material with a 21-hydroxy 20-one system could be isolated. We finally could get 21-hydroxides **5c** and **8b** by treatment of **5a** and **8a** with an excess amount of $NaOCH_3$ in MeOH at room temperature. **5c** and **8b** should probably be produced by hydrolysis during acid treatment of the corresponding 21-methyl ethers initially formed. The results suggest that the 17α-methoxy group may cause a change of the reactivity at C-21 of a 21-bromo 20-one toward alkali by conformational and/or stereoelectronic effect through C-20 position.

Conclusion

Efficient syntheses of deoxycorticoids **7b** and **9b** were achieved by both discovery of direct bromination at C-27 of 20-ketopregnenes 1 and **3a** with $CuBr_2$ and new utilization of the controlled alkaline hydrolysis[7-10] of the bromo ketones **7a** and **9a**. The advantages of the procedure are to be found in the accessiblity of starting material, the relative few steps in the reaction sequence, the simplicity, and the availability of the reagents.

Experimental Section

3β-Hydroxy-17α-methoxy-5-pregnen-20-one (2) was obtained (65%) from 3β-hydroxy-5-pregnen-20-one (1): mp 206–209 °C (acetone) (lit.[6] mp 206–210 °C); ^{1}H NMR (60 MHz, $CDCl_3$) δ 0.60 (3 H, s, 18-CH_3), 1.00 (3 H, s, 19-CH_3), 2.13 (3 H, s, 21-CH_3), 3.13 (3 H, s, 17α-OCH_3), 3.50 (1 H, br m, 3α-H), 5.40 (1 H m, 6-H).

21-Bromo-3β-hydroxy-5-pregnen-20-one (4a) was obtained (71%) from 1: mp 156–158 °C (acetone) (lit.[16] mp 159–159.5 °C); ^{1}H NMR ($CDCl_3$) δ 0.67 (3 H, s, 18-CH_3), 1.62 (3 H, s, 19-CH_3), 3.50 (1 H, br m, 3α-H), 3.92 (2 H, s, 21-CH_2), 5.38 (1 H, m, 6-H); IR (KBr) 3550, 1719 and 1060 cm^{-1}; MS, m/z 394 and 396 (M^+), 376 and 378 ($M^+ - H_2O$).

21-Bromo-3β-hydroxy-17α-methoxy-5-pregnen-20-one (5a) was obtained (54%) from 1: mp 215–217 °C (acetone); ^{1}H NMR ($CDCl_3$) δ 0.63 (3 H, s, 18-CH_3), 1.00 (3 H, s, 19-CH_3), 3.18 (3 H, s, 17α-OCH_3), 3.50 (1 H, br m, 3α-H), 4.05 (1 H, d, J = 15.0 Hz, 21-H_a), 4.32 (1 H, d, J = 15.0 Hz, 21-H_b), 5.35 (1 H, m, 6-H); IR (KBr) 3500, 1715 and 1050 cm^{-1}; MS, m/z 426 and 424 (M^+), 303 ($M^+ - COCH_2Br$). Anal. Calcd for $C_{22}H_{33}BrO_3$: C, 62.12; H, 7.82; Br, 18.78. Found: C, 62.00; H, 7.88; Br, 18.58.

21-Bromo-3β-acetoxy-17α-methoxy-5-pregnen-20-one (5b). Compound **5a** (50 mg, 0.18 mmol) was acetylated in the usual fashion with pyridine and Ac_2O. From acetone, there was obtained colorless prisms (41 mg, 75%): mp 179–180 °C; ^{1}H NMR ($CDCl_3$) δ 0.95 (3 H, s, 18-CH_3), 1.02 (3 H, s, 19-CH_3), 2.00 (3 H, s, 3-$OCOCH_3$), 3.17 (3 H, s, 17α-OCH_3), 4.03 (1 H, d, J = 14.0 Hz, 21-H_a), 4.28 (1 H, d, J = 14.0 Hz, 21-H_b), 4.55 (1 H, br m, 3α-H), 5.42 (1 H, m, 6-H); IR (KBr) 1715, 1702 and 1242 cm^{-1}. Anal. Calcd for $C_{24}H_{35}BrO_4$: C, 61.67; H, 7.55; Br, 7.09. Found: C, 61.79; H, 7.75; Br, 16.99.

21-Bromo-3β,17α-dihydroxy-5-pregnen-20-one (6a) was obtained (10%) from 3β,17α-dihydroxy-5-pregnen-20-one (**3a**): mp 228–229 °C (acetone); ^{1}H NMR ($CDCl_3$) δ 0.67 (3 H, s, 18-CH_3), 0.98 (3 H, s, 19-CH_3), 3.50 (1 H, br m, 3α-H), 4.17 (1 H, d, J = 15.0 Hz, 21-H_a), 4.50 (1 H, d, J = 15.0 Hz, 21-H_b), 5.33 (1 H, m, 6-H); IR (KBr) 3520 and 1720 cm^{-1}. Anal. Calcd for $C_{21}H_{31}BrO_3$: C, 61.32; H, 7.60; Br, 19.42. Found: C, 61.62; H, 7.52; Br, 19.50.

21-Bromo-3β-acetoxy-17α-hydroxy-5-pregnen-20-one (6b) was obtained (45%) from 3β-acetoxy-17α-hydroxy-5-pregnen-20-one (**3b**): mp 213–215 °C (AcOEt); ^{1}H NMR ($CDCl_3$) δ 0.70 (3 H, s, 18-CH_3), 1.03 (3 H, s, 19-CH_3), 2.03 (3 H, s, 3-$OCOCH_3$), 4.12 (1 H, d, J = 14.0 Hz, 21-H_a), 4.50 (1 H, d, J = 14.0 Hz, 21-H_b), 4.67 (1 H, br m, 3α-H), 5.42 (1 H, m, 6-H); IR (KBr) 3550, 1720 and 1710 cm^{-1}; MS, m/z 391 and 393 ($M^+ - CH_3COOH$). Anal. Calcd for $C_{23}H_{33}BrO_4$: C, 60.93; H, 7.33; Br, 17.62. Found: C, 61.20; H, 7.32; Br, 17.55.

Conversion of 5-En-3β-ols 4a, 5a, and 6a to 4-En-3-ones 7a, 8a, and 9a. Compound **4a**, **5a**, or **6a** (1.4 mmol) was dissolved in 100 mL of acetone. To this solution was added dropwise 0.5 mL of 8 N CrO_3 solution with stirring below 5 °C and then the solution was allowed to stand for 5 min. After this time, the mixture was poured into ice–water (500 mL). The precipitates (496–510 mg) were collected by filtration, dried under vacuum, and then dissolved in 15 mL of acetone. p-Toluenesulfonic acid monohydrate (46 mg, 0.24 mmol) was added to the solution and the mixture was allowed to stand for 3 h and then poured into water followed by extraction with AcOEt (2 × 200 mL). The organic layer was washed with $NaHCO_3$ solution and water, dried (Na_2SO_4), and evaporated to give a solid (410–430 mg).

21-Bromo-4-pregnene-3,20-dione (7a) was obtained (63%) from **4a**: mp 184–185 °C dec (acetone) (lit.[16] mp 190–191 °C); ^{1}H NMR ($CDCl_3$) δ 0.70 (3 H, s, 18-CH_3), 1.18 (3 H, s, 19-CH_3), 3.90 (2 H, s, 21-CH_2), 5.73 (1 H, s, 4-H).

21-Bromo-17α-methoxy-4-pregnene-3,20-dione (8a) was obtained (62%) from **5a**: mp 150–152 °C; ^{1}H NMR ($CDCl_3$) δ

(14) The product could not be isolated as pure form because of its extremely low solubility in solvent. However, elemental analysis (Calcd for $C_{28}H_{36}BrNO_2$: C, 65.82; H, 7.65; N, 2.95; Br, 16.84. Found: C, 65.85; H, 7.88; N, 3.04; Br, 14.55) and an IR spectrum (KBr) (1730, 1638 cm^{-1}) of the crude product obtained from **4a** suggest it to probably be the 21-pyridino derivative of **4a**.

(15) When the fraction corresponding to **7b** was subjected to high-pressure liquid chromatography [column, Radial-Pak C_{18} (10 × 0.8 id cm); solvent, MeOH/H_2O 8/2, v/v, flow rate 2 mL/min], a single peak (retention time, 7.8 min) was observed. The ^{1}H NMR stectrum also did not show signals corresponding to the 17α-isomer of **7b**.

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0.65 (3 H, s, 18-CH_3), 1.17 (3 H, s, 19-H_3), 3.17 (3 H, s, 17α-OCH_3), 4.17 (2 H, s, 21-CH_2), 5.90 (1 H, s, 4-H); IR (KBr) 1720, 1670 and 1615 cm^{-1}. Anal. Calcd for $C_{22}H_{31}BrO_3$: C, 62.41; H, 7.38; Br, 18.87. Found: C, 62.25; H, 7.27; Br, 18.75.

21-Bromo-17α-hydroxy-4-pregnene-3,20-dione (9a) was obtained (65%) from **6a**: mp 217–219 °C (lit. mp 223–224 °C dec,[17] mp 187–189 °C[18]); ^1H NMR ($CDCl_3$) δ 0.70 (3 H, s, 18-CH_3), 1.20 (3 H, s, 19-CH_3), 4.15 (1 H, d, J = 15.0 Hz, 21-H_a), 4.43 (1 H, d, J = 15.0 Hz, 21-H_b), 5.73 (1 H, s, 4-H).

3β,21-Dihydroxy-5-pregnen-20-one (4b) was obtained (95%) from **4a**: mp 172–175 °C (acetone) (lit.[19] mp 171–173 °C); ^1H NMR ($CDCl_3$) δ 0.67 (3 H, s, 18-CH_3), 1.00 (3 H, s, 19-CH_3), 3.50 (1 H, br m, 3α-H), 4.18 (2 H, s, 21-CH_2), 5.37 (1 H, m, 6-H); IR (KBr) 3350 and 1703 cm^{-1}.

3β,21-Dihydroxy-17α-methoxy-5-pregnen-20-one (5c). To a solution of **5a** (1 g, 2.36 mmol) in 100 mL of dry MeOH was added dropwise 182 mL of 28% $NaOCH_3$ (400 equiv) methanolic solution with stirring under ice cooling. The reaction mixture was further stirred at room temperature for 30 min. After this time, the mixture was diluted with AcOEt (500 mL) and the organic layer was washed with 5% HCl, 5% $NaHCO_3$ and NaCl solutions, subsequently, and dried (Na_2SO_4). After evaporation of the solvent the residue was subjected to silica gel column. Elution with *n*-hexane–AcOEt (5:1, v/v) gave crude product, which was crystallized from acetone to give **5c** (330 mg, 39%) as colorless prisms: mp 191–193 °C; ^1H NMR ($CDCl_3$) δ 0.60 (3 H, s, 18-CH_3), 1.02 (3 H, s, 19-CH_3), 3.17 (3 H, s, 17α-OCH_3), 3.53 (1 H, br m, 3α-H), 4.17 (1 H, d, J = 20.0 Hz, 21-H_a), 4.53 (1 H, d, J = 20.0 Hz, 21-H_b), 5.37 (1 H, m, 6-H); IR (KBr) 3490, 3400, 1720, 1080 and 1050 cm^{-1}; MS, m/z 362 (M^+), 330 ($M^+ - CH_3OH$). Anal. Calcd for $C_{22}H_{34}O_4$: C, 72.90; H, 9.45. Found: C, 72.85; H, 9.75.

3β-Acetoxy-17α,21-dihydroxy-5-pregnen-20-one (6c) was obtained (99%) from **6b**: mp 214–218 °C (acetone) (lit.[20] mp 225–230 °C); ^1H NMR ($CDCl_3$) δ 0.67 (3 H, s, 18-CH_3), 1.03 (3 H, s, 19-CH_3), 2.03 (3 H, s, 3-$OCOCH_3$), 4.23 (1 H, d, J = 18.0 Hz, 21-H_a), 4.33 (1 H, br m, 3α-H), 4.73 (1 H, d, J = 18.0 Hz, 21-H_b), 5.43 (1 H, m, 6-H).

21-Hydroxy-4-pregnene-3,20-dione (7b) was obtained (93%) from **7a**: mp 137–138.5 °C (acetone) (lit.[21] mp 141–142 °C); ^1H NMR ($CDCl_3$) δ 0.73 (3 H, s, 18-CH_3), 1.18 (3 H, s, 19-CH_3), 4.18 (2 H, s, 21-CH_2), 5.73 (1 H, s, 4-H); IR (KBr) 3480, 1692, 1663 and 1608 cm^{-1}.

17α-Methoxy-21-hydroxy-4-pregnene-3,20-dione (8b) was obtained (45%) from **8a**: mp 168–171 °C (acetone); ^1H NMR ($CDCl_3$) δ 0.65 (3 H, s, 18-CH_3), 1.20 (3 H, s, 19-CH_3), 3.17 (3 H, s, 17α-OCH_3), 4.20 (1 H, d, J = 20.0 Hz, 21-H_a), 4.58 (1 H, d, J = 20.0 Hz, 21-H_b), 5.75 (1 H, s, 4-H); IR (KBr) 3425, 1708, 1665 and 1610 cm^{-1}. Anal. Calcd for $C_{22}H_{32}O_4$: C, 73.30; H, 8.95. Found: C, 73.02; H, 6.21.

17α,21-Dihydroxy-4-pregnene-3,20-dione (9b) was obtained (68%) from **9a**: mp 196–199 °C (acetone) (lit.[22] mp 200–205 °C); ^1H NMR ($CDCl_3$) δ 0.72 (3 H, s, 18-CH_3), 1.18 (3 H, s, 19-CH_3), 4.25 (1 H, d, J = 20.0 Hz, 21-H_a), 4.75 (1 H, d, J = 20.0 Hz, 21-H_b), 5.70 (1 H, s, 4-H); IR (KBr) 3500, 3480, 1710 and 1664 cm^{-1}.

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