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Studies on Topical Antiinflammatory Corticosteroids. III. Synthesis and Vasoconstrictive Activity of 11 β ,17 α ,21-Trihydroxy-2'-phenyl-2'H-2,4-pregnadieno[3,2-c]pyrazol-20-one Derivatives¹⁾

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17 α -Acyloxy-11 β ,21-dihydroxy-2'-phenyl-2'H-2,4-pregnadieno[3,2-c]pyrazol-20-one derivatives (**3a**, **3b**, **4**, **5a** and **5c**) were synthesized and tested for vasoconstrictive activities. Compound **3b** showed the most potent activity, which was greater than that of 9 α -fluoro-11 β ,21-dihydroxy-16 β -methyl-17 α -valeroyloxy-1,4-pregnadiene-3,20-dione (betamethasone 17-valerate, BV). The activities of all other compounds (**3a**, **4**, **5b** and **5c**) were rather weaker than that of the mother compound, 11 β ,17 α ,21-trihydroxy-2'-phenyl-2'H-2,4-pregnadieno[3,2-c]pyrazol-20-one (**1**). In contrast to the case of corticosteroids having a hydrocortisone-type skeleton, esterification of both the 17- and 21-hydroxy groups of the pyrazole-fused compound (**1**) or the substitution of the 21-hydroxy group of the 17-ester compound (**3**) with a chlorine atom are not always necessary for the exhibition of higher activity.

Keywords—corticosteroid; 11 β ,17 α ,21-trihydroxy-2'-phenyl-2'H-2,4-pregnadieno[3,2-c]pyrazol-20-one; 11 β ,17 α ,21-trihydroxy-2'-phenyl-2'H-2,4-pregnadieno[3,2-c]pyrazol-20-one 17,21-cyclic ortho ester; 17 α -acyloxy-11 β ,21-dihydroxy-2'-phenyl-2'H-2,4-pregnadieno[3,2-c]pyrazol-20-one; 17 α ,21-diacyloxy-11 β -hydroxy-2'-phenyl-2'H-2,4-pregnadieno[3,2-c]pyrazol-20-one; 17 α -acyloxy-21-chloro-11 β -hydroxy-2'-phenyl-2'H-2,4-pregnadieno[3,2-c]pyrazol-20-one; vasoconstrictive activity

Fried and co-workers²⁾ have synthesized a variety of pyrazole-fused corticosteroids, which showed significant enhancement of the antiinflammatory activity. However, since the 17-ester and 17,21-diester compounds of the corticosteroids have not been described, we were interested in the synthesis and activity of various 17-ester derivatives (**3**—**5**) of 11 β ,17 α ,21-trihydroxy-2'-phenyl-2'H-2,4-pregnadieno[3,2-c]pyrazol-20-one (**1**). This report deals with the synthesis of the 17-ester and 17,21-diester derivatives of the title corticosteroid and with the preliminary determination of their pharmacological activities.

Results and Discussion

Synthesis of 11 β ,17 α ,21-Trihydroxy-2'-phenyl-2'H-2,4-pregnadieno[3,2-c]pyrazol-20-one 17-Ester Derivatives (**3** and **4**)

The reaction of **1** obtained from 11 β ,17 α ,21-trihydroxy-4-pregnene-3,20-dione (hydrocortisone) according to the procedure of Hirschmann and co-workers³⁾ with ortho esters afforded 11 β ,17 α ,21-trihydroxy-2'-phenyl-2'H-2,4-pregnadieno[3,2-c]pyrazol-20-one 17,21-cyclic ortho esters (**2**) in good yields¹⁾ (Chart 1). The compounds (**2**) were purified by recrystallization from ether or ether: *n*-hexane (20—30: 1) and the results are summarized in

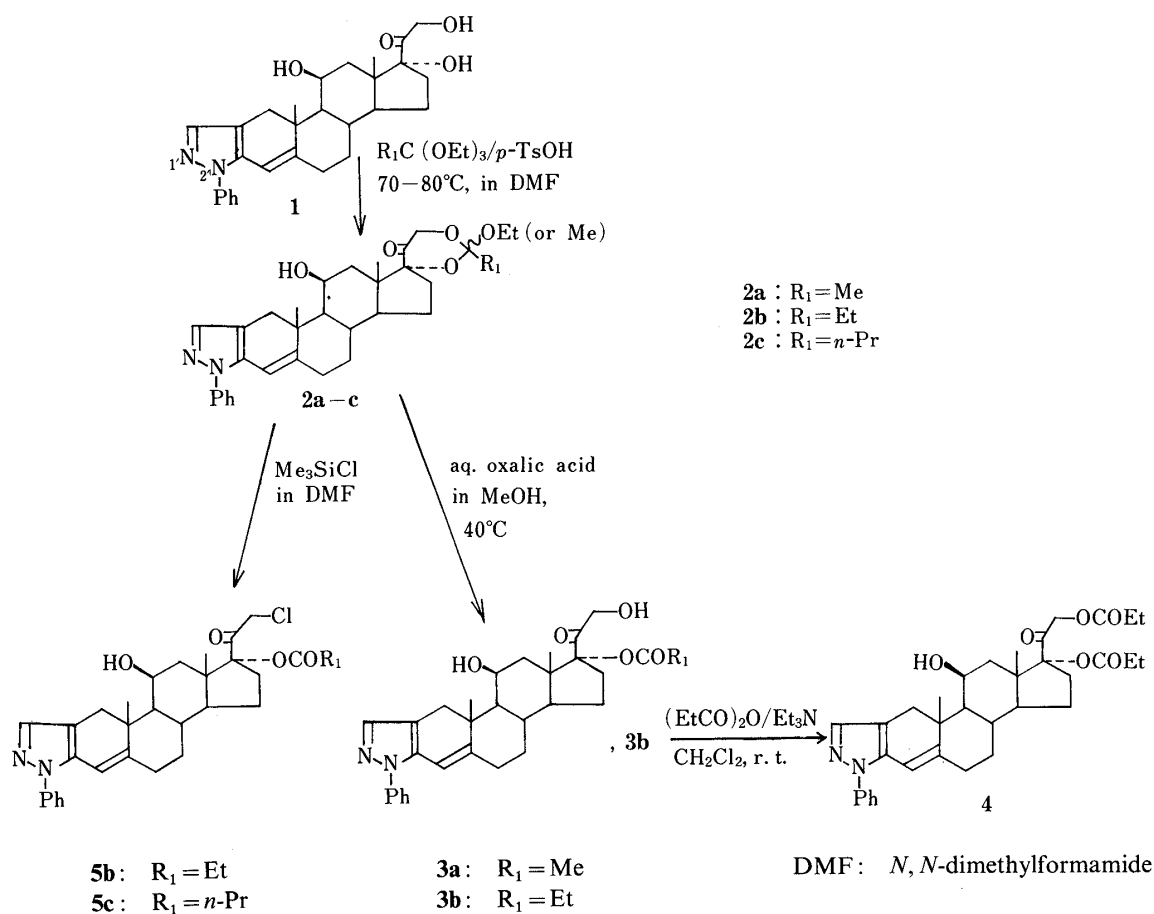


Chart 1

TABLE I. Yields, Melting Points and Elementary Analyses of 11β,17α,21-Trihydroxy-2'-phenyl-2'H-2,4-pregnadieno[3,2-c]pyrazol-20-one 17,21-Cyclic Ortho Esters (2)

Compd.	Yield ^{a)} (%)	mp (°C)	Formula	Analysis (%)		
				Found (Calcd)		
				C	H	N
2a	92.9	209.0–211.0	C ₃₂ H ₄₀ N ₂ O ₅	72.37 (72.15)	7.41 7.57	5.53 5.26
2b	75.0	216.0–217.0	C ₃₃ H ₄₂ N ₂ O ₅	72.65 (72.50)	7.69 7.74	5.23 5.12
2c	87.4	185.0–189.0	C ₃₃ H ₄₂ N ₂ O ₅	72.43 (72.50)	7.59 7.74	5.37 5.12

a) Isolated yield.

Table I.

Next, **2a** and **2b** were subjected to acid-catalyzed ring-opening¹⁾ by treatment with aqueous oxalic acid in MeOH, giving the corresponding 17α-acetoxy- and 17α-propanoyloxy-11β,21-dihydroxy-2'-phenyl-2'H-2,4-pregnadieno[3,2-c]pyrazol-20-ones (**3a** and **3b**) in good yields. Then, **3b** was reacted with propionic anhydride to give 17α,21-dipropanoyloxy-11β-hydroxy-2'-phenyl-2'H-2,4-pregnadieno[3,2-c]pyrazol-20-one (**4**) in good yield (Chart 1). The

TABLE II. Yields, Melting Points and Elementary Analyses of 17 α -Acyloxy-11 β ,21-dihydroxy-2'-phenyl-2'*H*-2,4-pregnadieno[3,2-*c*]pyrazol-20-one Derivatives (3, 4 and 5)

Compd.	Yield ^{a)} (%)	mp (°C)	Formula	Analysis (%)		
				Found (Calcd)		
				C	H	N
3a	65.4	234.0—236.0	C ₃₀ H ₃₆ N ₂ O ₅	71.71 (71.40)	7.24 (7.19)	5.54 (5.55)
3b	62.3	193.0—195.5	C ₃₁ H ₃₈ N ₂ O ₅	71.67 (71.79)	7.44 (7.38)	5.18 (5.14)
4	83.7	186.0—188.0	C ₃₄ H ₄₂ N ₂ O ₆	70.85 (71.06)	7.37 (7.37)	4.80 (4.87)
5b	57.0	240.0—241.0 (dec.)	C ₃₁ H ₃₇ ClN ₂ O ₄	69.47 (69.32)	6.89 (6.94)	5.31 (5.22)
5c	47.7	208.0—211.0	C ₃₂ H ₃₉ ClN ₂ O ₄	69.67 (69.74)	7.08 (7.13)	5.25 (5.08)

a) Isolated yield.

TABLE III. Vasoconstrictive Activities of 17 α -Acyloxy-11 β ,21-dihydroxy-2'-phenyl-2'*H*-2,4-pregnadieno[3,2-*c*]pyrazol-20-one Derivatives (3, 4 and 5)

Compd.	Vasoconstrictive activity ^{a)}		Compd.	Vasoconstrictive activity ^{a)}	
	After 2 h	After 6 h		After 2 h	After 6 h
Experiment 1			Experiment 2		
3a	1.00 ^{d, e)}	0.85 ^{d, e)}	5b	1.30 ^{d)}	1.05 ^{d)}
3b	2.20 ^{d, e)}	1.90 ^{e)}	5c	0.90 ^{d)}	0.50 ^{d)}
4	0.50 ^{d)}	0.65 ^{d)}	<i>Cf.</i>		
Control			2b	0.80 ^{d)}	0.50 ^{d)}
HC ^{b)}	0.65	0.45	2c	1.15	0.50 ^{d)}
BV ^{c)}	1.70	1.65	Control		
			1	1.85	1.50
			HC ^{b)}	0.95	0.45
			BV ^{c)}	2.55	2.20

a) Vaseline ointment (0.01%) was used and the activity is shown as averaged scores (maximal value, 3.00). The blanching scores are as follows: 3 for marked blanching; 2 for moderate effect; 1 for slight effect; 0 for no effect (normal skin). b) 21-Acetoxy-11 β ,17 α -dihydroxy-4-pregnene-3,20-dione (hydrocortisone 21-acetate, 0.1%). c) 9 α -Fluoro-11 β ,21-dihydroxy-16 β -methyl-17 α -valeroyloxy-1,4-pregnadiene-3,20-dione (betamethasone 17-valerate). d) $p < 0.05$ for BV. e) $p < 0.05$ for **1**, using Wilcoxon's signed-ranks test.⁸⁾

17-esters (**3a** and **3b**) and 17,21-diester (**4**) could be purified by simple recrystallization from ether or ether:*n*-hexane (20—30:1) after separation by preparative thin-layer chromatography (PTLC, silica gel, CH₂Cl₂:Et₂O = 3—4:1, twice).

Synthesis of 17 α -Acyloxy-21-chloro-11 β -hydroxy-2'-phenyl-2'*H*-2,4-pregnadieno[3,2-*c*]pyrazol-20-one Derivatives (**5**)

The ortho esters (**2b** and **2c**) were treated with trimethylsilyl chloride⁴⁾ to afford the corresponding 17 α -acyloxy-21-chloro-11 β -hydroxy-2'-phenyl-2'*H*-2,4-pregnadieno[3,2-*c*]pyrazol-20-one compounds (**5b** and **5c**) in moderate yields (Chart 1). The 21-chloro-17 α -acyloxy compounds (**5b** and **5c**) were purified in the same manner as above. The results are summarized in Table II.

Vasoconstrictive Activities

The 17-esters (**3a** and **3b**), 17,21-diester (**4**) and 21-chloro-17-esters (**5b** and **5c**) were tested for vasoconstrictive activities in ten healthy male volunteers⁵⁾ by the method reported previously,^{1b)} the results of which correlate well with the clinical efficacy for cutaneous disorders.^{6,7)} Statistical analysis was done by using Wilcoxon's signed-ranks test.⁸⁾ The results are summarized in Table III.

Among the 17-ester derivatives, the 17-propanoate (**3b**) exhibited the most potent activity, which was equal to or greater than that of 9 α -fluoro-11 β ,21-dihydroxy-16 β -methyl-17 α -valeroyloxy-1,4-pregnadiene-3,20-dione (betamethasone 17-valerate, BV) at 2 and 6 h, respectively. The activities of the 17-acetate (**3a**), 17,21-dipropanoate (**4**), 21-chloro-17-propanoate (**5b**) and 21-chloro-17-butanoate (**5c**) were not only weaker ($p < 0.05$) than that of BV at 2 and 6 h but also were rather weaker than that of the mother compound (**1**). In particular, it was unexpected that the activity of the diester (**4**), in which the 21-hydroxy group of the most potent compound (**3b**) carries a propanoyl group was remarkably reduced. Substitution of the 21-hydroxy group of the 17-monoesters (**3b** and **3c**) with a chlorine atom also considerably decreased the activity.

Generally, it is known that modification of corticosteroids by 17-esterification⁹⁾ or by 17,21-diesterification^{9a,10)} with lower aliphatic carboxylic acids or by chloro substitution¹¹⁾ of the 21-hydroxy group of 17-monoester compounds enhances the activity as compared with that of the mother compound. In fact, the activities of BV,^{9a,b)} 21-chloro-21-deoxy-betamethasone 17-propanoate¹¹⁾ and betamethasone 17,21-dipropanoate^{9a)} are considerably greater than that of the mother compound, betamethasone. However, our results in the present series of compounds are not in accordance with the well-known structure-activity correlation.

The original skeleton (**1**) of hydrocortisone fused with 2'-phenyl-2'-*H*-pyrazole becomes sterically bulky as compared with a simple hydrocortisone-type corticosteroid. Introduction of an ester group into **1** forms an even larger molecule, and as a result, the activity might be reduced due to the decrease of skin-permeability and/or absorption. Accordingly, it is concluded that modification by further esterification of corticosteroids with a sterically large skeleton may not always be a useful approach for obtaining higher activity.

Experimental

All melting points are uncorrected. Infrared (IR) and mass spectra (MS) were taken on a JASCO IRA-1 spectrophotometer and a Hitachi RM-50 spectrometer, respectively. Proton nuclear magnetic resonance (¹H-NMR) spectra were determined on a Hitachi R-24 (60 MHz) spectrometer using tetramethylsilane as an internal standard and chemical shifts are given in δ (ppm). The abbreviations used are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad.

General Procedure for the Preparation of 11 β ,17 α ,21-Trihydroxy-2'-phenyl-2'-*H*-2,4-pregnadieno[3,2-*c*]pyrazol-20-one 17,21-Cyclic Ortho Esters (2**)**—An ortho ester (2 mmol) and 11 β ,17 α ,21-trihydroxy-2'-phenyl-2'-*H*-2,4-pregnadieno[3,2-*c*]pyrazol-20-one (**1**, 1 mmol) were dissolved in *N,N*-dimethylformamide (DMF) (4 ml) and the solution was heated at 70–80 °C with stirring. Then, *p*-toluenesulfonic acid (0.05–0.1 mmol) was added to the solution and the reaction mixture was stirred for 30 min–1 h at the above temperature. After completion of the reaction, the mixture was cooled to room temperature and ethyl acetate (60 ml) and 0.5% Na₂CO₃ aq. solution (10 ml) were added. The organic layer was washed with water (30 ml $\times$ 3), dried over anhydrous Na₂SO₄, and concentrated *in vacuo*. The residue was purified by recrystallization from ether or ether:*n*-hexane, affording **2** in 75.0–92.9% yields. Spectral data for **2** are as follows.

11 β ,17 α ,21-Trihydroxy-2'-phenyl-2'-*H*-2,4-pregnadieno[3,2-*c*]pyrazol-20-one 17,21-Ethyl Orthoacetate (2a**)**—IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3440 (OH), 1725 (C=O). ¹H-NMR (CDCl₃): 0.92 (3H, s, C₁₈-H), 1.16 (3H, t, $J = 7.5$ Hz, CH₂CH₃), 1.34 (3H, s, C₁₉-H), 1.59 (3H, s, , 2.65, 3.00 (2H, dd, $J = 14$ Hz, C₁-H), 3.52 (2H, q, $J = 7.5$ Hz, CH₂CH₃), 3.86, 4.21 (2H, dd, $J = 14$ Hz, C₂₁-H), 4.43 (1H, br s, C₁₁-H), 6.15 (1H, s, C₄-H), 7.49 (6H, s, Ph, C₅-H). MS m/z : 532 (M⁺), 514, 504, 487, 486, 367, 247, 235, 222 (base peak), 221, 209, 207, 77, 43.

11 β ,17 α ,21-Trihydroxy-2'-phenyl-2'-H-2,4-pregnadieno[3,2-c]pyrazol-20-one 17,21-Ethyl Orthopropanoate (2b)—IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3450 (OH), 1725 (C=O). $^1\text{H-NMR}$ (CDCl_3): 0.91 (3H, s, $\text{C}_{18}\text{-H}$), 1.13 (6H, m, $\text{CH}_2\text{CH}_3 \times 2$), 1.32 (3H, s, $\text{C}_{19}\text{-H}$), 2.72, 3.04 (2H, dd, $J=14$ Hz, $\text{C}_1\text{-H}$), 3.50 (2H, q, $J=8$ Hz, OCH_2CH_3), 3.88, 4.24 (2H, dd, $J=16$ Hz, $\text{C}_{21}\text{-H}$), 4.46 (1H, br s, $\text{C}_{11}\text{-H}$), 6.17 (1H, s, $\text{C}_4\text{-H}$), 7.50 (6H, s, Ph, $\text{C}_5\text{-H}$). MS m/z : 546 (M^+), 528, 517, 501, 500, 444, 411, 367, 235, 222 (base peak), 221, 209, 207, 77, 57.

11 β ,17 α ,21-Trihydroxy-2'-phenyl-2'-H-2,4-pregnadieno[3,2-c]pyrazol-20-one 17,21-Methyl Orthobutanoate (2c)—IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3510 (OH), 1710 (C=O). $^1\text{H-NMR}$ (CDCl_3): 0.92 (3H, s, $\text{C}_{18}\text{-H}$), 0.95 (3H, t, $J=7.5$ Hz, $\text{CH}_2\text{CH}_2\text{CH}_3$), 1.34 (3H, s, $\text{C}_{19}\text{-H}$), 2.73, 3.05 (2H, dd, $J=15$ Hz, $\text{C}_1\text{-H}$), 3.27 (3H, s, OCH_3), 3.95, 4.23 (2H, dd, $J=16$ Hz, $\text{C}_{21}\text{-H}$), 4.55 (1H, br s, $\text{C}_{11}\text{-H}$), 6.16 (1H, s, $\text{C}_4\text{-H}$), 7.47 (6H, s, Ph, $\text{C}_5\text{-H}$). MS m/z : 546 (M^+), 530, 528, 514, 499, 481, 444, 411, 385, 367, 235, 222 (base peak), 221, 209, 207, 145, 91, 77.

17 α -Acetoxy-11 β ,21-dihydroxy-2'-phenyl-2'-H-2,4-pregnadieno[3,2-c]pyrazol-20-one (3a)—11 β ,17 α ,21-Trihydroxy-2'-phenyl-2'-H-2,4-pregnadieno[3,2-c]pyrazol-20-one 17,21-ethyl orthoacetate (2a; 160 mg, 0.3 mmol) was dissolved in MeOH (4 ml), followed by the addition of 2 N aqueous oxalic acid (0.5 ml) thereto. Then, the reaction mixture was stirred for 10 min at 40 °C and concentrated *in vacuo*. Ethyl acetate (50 ml) was added to the resulting residue and the solution was washed with water (30 ml $\times$ 3), dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was chromatographed on silica gel (PTLC, CH_2Cl_2 : $\text{Et}_2\text{O}=3\text{--}4:1$, twice) and the product was crystallized from ether, affording the title compound (3a, 99 mg) as colorless needles. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3440 (OH), 1725 (C=O), 1710 (C=O). $^1\text{H-NMR}$ (CDCl_3): 0.92 (3H, s, $\text{C}_{18}\text{-H}$), 1.29 (3H, s, $\text{C}_{19}\text{-H}$), 2.05 (3H, s, COCH_3), 2.65, 3.01 (2H, dd, $J=15$ Hz, $\text{C}_1\text{-H}$), 4.25 (2H, s, $\text{C}_{21}\text{-H}$), 4.47 (1H, br, $\text{C}_{11}\text{-H}$), 6.17 (1H, s, $\text{C}_4\text{-H}$), 7.59 (6H, s, Ph, $\text{C}_5\text{-H}$). MS m/z : 504 (M^+), 486, 445, 444, 411, 385, 367, 259, 235, 233, 222 (base peak), 221, 209, 207, 77, 43.

11 β ,21-Dihydroxy-17 α -propanoyloxy-2'-phenyl-2'-H-2,4-pregnadieno[3,2-c]pyrazol-20-one (3b)—According to the method described for 3a the title compound (3b) was obtained from 11 β ,17 α ,21-trihydroxy-2'-phenyl-2'-H-2,4-pregnadieno[3,2-c]pyrazol-20-one 17,21-ethyl orthopropanoate (2b; 224 mg, 0.41 mmol) in a yield of 132 mg as colorless needles. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3440 (OH), 1725 (C=O), 1720 (C=O). $^1\text{H-NMR}$ (CDCl_3): 0.94 (3H, s, $\text{C}_{18}\text{-H}$), 1.16 (3H, t, $J=8$ Hz, CH_2CH_3), 1.32 (3H, s, $\text{C}_{19}\text{-H}$), 2.64, 3.01 (2H, dd, $J=15$ Hz, $\text{C}_1\text{-H}$), 4.27 (2H, s, $\text{C}_{21}\text{-H}$), 4.50 (1H, br s, $\text{C}_{11}\text{-H}$), 6.13 (1H, s, $\text{C}_4\text{-H}$), 7.49 (6H, s, Ph, $\text{C}_5\text{-H}$). MS m/z : 518 (M^+), 504, 500, 445, 444, 432, 411, 259, 235, 222 (base peak), 221, 209, 207, 77, 57.

11 β -Hydroxy-17 α ,21-dipropanoyloxy-2'-phenyl-2'-H-2,4-pregnadieno[3,2-c]pyrazol-20-one (4)—11 β ,21-Dihydroxy-17 α -propanoyloxy-2'-phenyl-2'-H-2,4-pregnadieno[3,2-c]pyrazol-20-one (3b; 80 mg, 0.15 mmol) obtained above was dissolved in dry dichloromethane (6 ml), then propanoic anhydride (78 mg, 0.6 mmol) and triethylamine (0.5 ml) were added, and the reaction mixture was stirred for 5 h at ambient temperature. The solution was concentrated *in vacuo*, and the residue was directly chromatographed on silica gel (PTLC, CH_2Cl_2 : $\text{Et}_2\text{O}=5:1$, twice). The product was crystallized from ether, affording the title compound (4) in a yield of 72 mg as colorless needles. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3560 (OH), 1735 (C=O), 1730 (C=O), 1720 (C=O). $^1\text{H-NMR}$ (CDCl_3): 1.08 (3H, s, $\text{C}_{18}\text{-H}$), 1.22 (6H, m, $\text{CH}_2\text{CH}_3 \times 2$), 1.35 (3H, s, $\text{C}_{19}\text{-H}$), 2.63, 3.00 (2H, dd, $J=15$ Hz, $\text{C}_1\text{-H}$), 4.50 (1H, br s, $\text{C}_{11}\text{-H}$), 4.61, 4.95 (2H, dd, $J=16$ Hz, $\text{C}_{21}\text{-H}$), 6.18 (1H, s, $\text{C}_4\text{-H}$), 7.50 (6H, m, Ph, $\text{C}_5\text{-H}$). MS m/z : 574 (M^+), 556, 500, 467, 444, 411, 222, 221, 209, 207, 77, 74 (base peak), 73, 57.

11 β -Hydroxy-21-chloro-17 α -propanoyloxy-2'-phenyl-2'-H-pregnadieno[3,2-c]pyrazol-20-one (5b)—Compound 2b (110 mg, 0.2 mmol) obtained above was dissolved in dry DMF (3 ml) and then trimethylsilyl chloride (0.1 ml) was added to the solution with stirring. The reaction mixture was stirred for 1 h at ambient temperature, then concentrated *in vacuo*. The residue was directly chromatographed on silica gel (PTLC, CH_2Cl_2 : $\text{Et}_2\text{O}=5:1$, twice) and the product was crystallized from acetone:*n*-hexane, yielding the title compound (5b, 61 mg) as colorless needles. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3440 (OH), 1735 (C=O), 1720 (C=O). $^1\text{H-NMR}$ (CDCl_3): 0.95 (3H, s, $\text{C}_{18}\text{-H}$), 1.14 (3H, t, $J=7.5$ Hz, CH_2CH_3), 1.26 (3H, s, $\text{C}_{19}\text{-H}$), 2.46 (2H, q, $J=7.5$ Hz, CH_2CH_3), 2.71, 2.95 (2H, dd, $J=15$ Hz, $\text{C}_1\text{-H}$), 4.03, 4.27 (2H, dd, $J=16$ Hz, $\text{C}_{21}\text{-H}$), 4.55 (1H, br s, $\text{C}_{11}\text{-H}$), 6.16 (1H, s, $\text{C}_4\text{-H}$), 7.48 (6H, m, Ph, $\text{C}_5\text{-H}$). MS m/z : 538, 536 (M^+ , 1:3), 520, 518, 503, 482, 475, 457, 447, 445, 431, 429, 385, 367, 352, 273, 259, 235, 222 (base peak), 221, 209, 207, 77, 73.

11 β -Hydroxy-17 α -butanoyloxy-21-chloro-2'-phenyl-2'-H-2,4-pregnadieno[3,2-c]pyrazol-20-one (5c)—According to the method described above, the title compound (5c) was obtained from 2c (120 mg, 0.22 mmol) in a yield of 58 mg as colorless needles. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3550 (OH), 1735 (C=O), 1720 (C=O). $^1\text{H-NMR}$ (CDCl_3): 0.96 (3H, t, $J=7.5$ Hz, $\text{CH}_2\text{CH}_2\text{CH}_3$), 1.00 (3H, s, $\text{C}_{18}\text{-H}$), 1.33 (3H, s, $\text{C}_{19}\text{-H}$), 2.35 (2H, t, $J=7.5$ Hz, $\text{CH}_2\text{CH}_2\text{CH}_3$), 2.72, 3.05 (2H, dd, $J=15$ Hz, $\text{C}_1\text{-H}$), 4.12, 4.32 (2H, dd, $J=15$ Hz, $\text{C}_{21}\text{-H}$), 4.55 (1H, m, $\text{C}_{11}\text{-H}$), 6.16 (1H, s, $\text{C}_4\text{-H}$), 7.46 (6H, m, Ph, $\text{C}_5\text{-H}$). MS m/z : 552, 550 (M^+ , 1:3), 534, 532, 517, 515, 463, 447, 445, 431, 403, 385, 357, 342, 327, 263, 259, 235, 233, 222 (base peak), 221, 209, 207, 145, 91, 77.

References and Notes

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