# N-Arylurethane Neighboring Group Participation During Solvolysis of 3-Methoxy-17-N-phenylcarbamoyloxy-16-p-tolylsulfonyloxymethylestra-1,3,5(10)triene Stereoisomers<sup>1</sup>

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ABSTRACT: During alkaline methanolysis of the four stereoisomers 1-4 of 3methoxy-17-N-phenylcarbamoyloxy-16-p-tolylsulfonyloxymethylestra-1,3,5(10)-triene, a cyclization takes place, in the course of which the N-phenyltetrahydrooxazin-2-one derivatives 5-8 are formed. The *cis* isomers 5, 8 and 8a-e are thermodynamically stable endproducts, while the *trans* derivatives 6 and 7, formed in a kinetically controlled process, undergo ring cleavage on methanolysis to yield the 16-(N-phenyl,N-methoxycarbonylaminomethyl) derivatives 9 and 11. The cyclization takes place with (N-6) neighboring group participation.

Urethanes attached to the estrane skeleton and also certain  $\alpha,\beta$ substituted halourethane derivatives exhibit contraceptive effects.<sup>2,3</sup> In the solvolysis of vicinal halourethanes, oxazolidinone derivatives condensed to the sterane skeleton are formed, which are likewise potential pharmacons.<sup>4</sup> The cyclization of unsubstituted  $\alpha$ , -tosylurethanes on the androstane skeleton has already been investigated.<sup>5</sup> The present work extends these studies to compounds with estrane skeleton.

The investigation has two aims: a study of the neighboring group participation in N-phenylurethanes, and the synthesis of new estrane derivatives with variously annelated N-phenyl groups and with various substituents on the phenyl group.

In selective tosyl ester formation and subsequent reaction with phenyl isocyanate, the four stereoisomers of 16-hydroxymethyl-3-methoxy-estra-1,3,5(10)-trien-17-ol<sup>6,7</sup> were converted into 3-methoxy-16-*p*-tolyl-sulfonyloxymethylestra-1,3,5(10)-triene-17-phenylurethanes 1-4. The substi-

tuted phenylurethane derivatives 4a-f were obtained by reaction of the O(17)-chlorocarbonic acid ester of 3-methoxy-16 $\beta$ -p-tolylsulfonyloxymethyl-estra-1,3,5(10)-trien-17 $\beta$ -ol and the appropriately substituted aniline. Compounds 1-4 and 4a-f were subjected to methanolysis in the presence of four equivalents of NaOCH<sub>3</sub>.

Under these experimental conditions, in a rapid reaction the  $16\alpha$ , $17\alpha$  stereoisomer 1 yields a single product, the *N*-phenyltetrahydrooxazin-2-one 5. The cyclization can be explained by the nucleophilic attack of the nitrogen atom of the deprotonated acid amide. In the notation proposed by Winstein<sup>8</sup>, this process can be characterized by the symbol (N<sup>-</sup>-6).

The  $16\beta,17\beta$  stereoisomer 4 is transformed into the  $16\beta,17\beta$ -condensed heterocycle 8 in a rapid reaction. The ring system obtained here is sterically more hindered than in the case of 5, since the heterocycle is situated on the same side as the 13-methyl group. In spite of this, neither 5 nor 8 decomposed on the action of a large excess of NaOCH<sub>3</sub> under refluxing conditions for 24 h (Scheme 1).





 $g: R = p - F_i$   $b: R = p - C_i$   $c: R = p - Me_i$   $d: R = p - OMe_i$   $g: R = m - OMe_i$   $f: R = p - NO_2$ 



The N-aryltetrahydrooxazin-2-one derivatives 8a-e, substituted in the para or meta position, are similarly stable. The p-nitrophenyltosylurethane 4f is an exception, since its cyclized product 8f undergoes ring cleavage

under the conditions of the solvolysis to yield 3-methoxy- $16\beta$ -(N-p-nitro-phenylaminomethyl)estra-1,3,5(10)-trien-17 $\beta$ -ol (13a).

The cis ring-annelated N-aryl- and N-substituted-aryltetrahydrooxazin-2-ones 5, 8 and 8a-e exhibit high stability, thereby differing significantly from the simple N-aryltetrahydrooxazin-2-one derivatives, which decompose into the corresponding N-arylaminoalcohols under similar conditions.<sup>9,10</sup>

The two trans isomers 2  $(16\alpha, 17\beta)$  and 3  $(16\beta, 17\alpha)$  also undergo cyclization, and the corresponding trans-annelated N-phenyltetrahydrooxazin-2-ones 6 and 7 are formed. The cyclization is surprising, since cyclic products were not obtained from trans isomers in our earlier studies on reactions involving neighboring group participation.<sup>1,6</sup> Compounds 6 and 7 are not stable, however: the hetero ring is split off under the conditions of solvolysis and the corresponding 3-methoxy-16-(N-phenyl,Nmethoxycarbonylaminomethyl)estra-1,3,5(10)-trien-17-ols 9a and 11a are formed. These compounds can be acetylated to the 17-acetoxy derivatives 9b and 11b. Jones oxidation yields the 17-keto compounds 10 and 12, respectively (Scheme 2).





Scheme 2

This type of ring cleavage is also unusual in *trans*-annelated *N*-phenyltetrahydrooxazin-2-ones, but similar reactions leading to an *N*-phenylcarbaminic acid ester have already been observed in the case of another *N*-phenyloxazolidin-2-one condensed to a carbocycle.<sup>11</sup>

With N-arylurethane stereoisomers attached to the sterane skeleton, the reaction involving participation of a neighboring group is not stereospecific. For the *cis* isomers 1, 4 and 4a-e, the intramolecular reaction of the strongly nucleophilic acid amide nitrogen leads to the thermodynamically stable end-products 5, 8 and 8a-e. The *trans* isomers 2 and 3 also yield the cyclic products 6 and 7 in a kinetically controlled process, but these undergo ring cleavage under the conditions of solvolysis.

Spectral data on compounds 1-13 are given in Tables 1 and 2. Their structure-confirming character is evident, and only the following facts need be emphasized here:

The diastereomers 1-4 are characterized primarily by the coupling constant  ${}^{3}J(\text{H-16},\text{H-17})$ , which indicates also the preferred conformation of ring D<sup>1</sup>. Splittings of about 5.5, 7.5, < 2 and 10 Hz, respectively, are due to the 16a,17a, 16a,17ß, 16ß,17a and 16ß,17ß configurations. Additionally, 17ß-substituted isomers are characterized by an upfield shift (field effect<sup>12</sup>) of the 13-methyl signal in the  ${}^{13}\text{C-NMR}$  spectrum, due to the steric hindrance between the 17-substituent and the methyl group. In the 17a-substituted and 17-oxo compounds, the steric hindrance between the 17-substituent and the 12-methylene group causes a field effect of about 6.5 ppm for the C-12 line, as compared with the other compounds. These spectral data support the structures assumed for compounds 1-5, 8, 9, 11 and 13. The two D/E trans-annelated isomers 6 and 7 are exceptions. Because of the condensed oxazinone ring, ring D here is forced into a conformation where the dihedral angle H-C<sub>18</sub>-C<sub>17</sub>-H is nearly 180<sup>o</sup>, and thus the corresponding coupling is higher (10.2 and 9.5 Hz).

The conformation change caused in compound 7 by the condensed oxazinone ring is reflected in the ca. 6 ppm downfield shift of the C-14 signal. The  $17\alpha$ -oxygen here is farther from H-14, and hence the steric hindrance that causes the field effect in the other compounds does not occur between them.

The shift of the H-17 signal is sensitive to the D/E ring annelation: it is about 0.5 ppm smaller in the spectra of the *trans*-annelated 2, 3, 6 and 7 than in the spectra of the corresponding *cis* compounds 1, 4, 5 and 8.

In compound 7, the condensed ring E forces the 16-methylene group away from the 13-methyl substituent, and thus the field effect observable in precursor 3 disappears and the methyl  $^{13}$ C-NMR signal of 7 shows a 5.7 ppm downfield shift as compared with 3.

The high downfield shift of the C-17 line in 10 and 12, characteristic of ketones,<sup>13</sup> should be mentioned, as should the field effect (4.0 ppm) for the C-16 and  $CH_2(16)$  signals of the more crowded  $16\alpha$ -substituted isomer 10 as compared with the analogous compound 12. The vicinity of the carbonyl causes a ca. 5 ppm downfield shift of the C-13 signal in 10 and 12. For the

same signal, an upfield shift is observed for 5, 7 and, to a lesser extent, 6, which can be explained by the more strained skeleton.

Table 1.	Characteristic ir-bands (in KBr discs, $cm^{-1}$ ) and <sup>1</sup> H-nmr signals (in CDCl <sub>3</sub> ,
	δ <sub>TMS</sub> = 0 ppm, coupling constants in Hz) for compounds 1, 2, 3, 4a-f, 5, 6, 7,
	8a-f, 9a,b, 10, 11a,b, 12 and 13a,b at 250 MHz.

Com <del>-</del> pound	Me(18) s(3H)	OMe(3) s(3H)	H-17 d(1H) <sup>a</sup>	CH <sub>2</sub> 2xdd or d	(16)  d+t(2x1H) <sup>b</sup>	) C=( uretha)	) ane <sup>c</sup> )	
1	0.83	3.77	5.00	4.1	17	17	34	
2	0.84	3.77	4.56	4.04	4.18	17	22	
3	0.76	3.77	4.50	4.16	4.28	17	32	
4a	0.84	3.77	4.90	4.05	4.22	17	44	
4b	0.84	3.77	4.90	4.05	4.22	17	40	
4c	0.83	3.77	4.88	4.07	4.20	17	30	
4d	0.83	3.77	4.88	4.05 <sup>d</sup>	4.20 <sup>d</sup>	17	25	
4e	0.84	3.77	4.89	4.07	4.20	17	35	
4f	0.87	3.77	4.94	4.04	4.27	17	40	
5	0.87	3.78	4.44	3.50	4.00	1700	1715	
6	0.99	3.78 <sup>e</sup>	3.92	3.59	~3.80 <sup>e</sup>	1700	1690	
7	1.02	3.78 <sup>e</sup>	4.08	3.62	3.76 <sup>e</sup>	17	03	
8	0.98	3.78	4.04	3.59	3.74	1718	1700	
8a	0.99	3.78	4.04	3.57	3.68	17	10	
8Ъ	0.98	3.78	4.39	3.56	3.70	1722	1702	
8c	0.99	3.78	4.38	3.56	3.68	1708	1700	
8d	0.99	3.78	4.39	3.56	3.65	17	00	
8e	0.99	3.78	4.38	3.56	3.72	17	10	
8f	1.00	3.78	4.43	3.63	3.84	1718	1707	
9a	0.75	3.77	3.47	~3.8	35 <sup>f</sup>	16	90	
9Ъ	0.77	3.77	4.68	3.8	30	17	10	
10	0.88	3.78 <sup>e</sup>	-	3.80 <sup>e</sup>	3.97	170	08	
11a	0.81	3.76 <sup>e</sup>	3.658	3.77 <sup>e</sup>	3.94	16	86	
11b	0.90	3.76	4.71	3.88	4.00	17	10 <sup>h</sup>	
12	0.93	3.78	-	3.92	4.05	17	00	
13a	0.85	3.78	3.92	3.25	3.45		-	
13b	0.91	3.77	4.86	3.10	3.25		_	

Further ir-bands and <sup>1</sup>H-nmr signals:  $\forall$  NH: 3340-3380 (1-3, 4a-f), 3412 (13b),  $\forall$ OH: 3480 (9a),  $\forall$  NH +  $\forall$ OH: 3500, 3420 (13a), NO<sub>2</sub>: 1540, 1330, 855 (4f), 1510, 1320, 849 (8f), 1501, 1302, 1288, 839 (13a), 1599, 1323, 854 (13b),  $\forall$ C=0(17-OAc): 1740 (9b), 1710<sup>g</sup> (11b), 1723 (13b),  $\forall$ C=0(17): 1730 (10), 1742 (12), CH<sub>3</sub>(Ac)<sup>1</sup>: 2.04 (9b), 2.00 (11b, 13b), CH<sub>3</sub>(Ar)<sup>1</sup>: 2.32 (4c, 8c), CH<sub>3</sub>(Ts)<sup>1</sup>: 2.38 ± 0.04 (1-3, 4a-f), OCH<sub>3</sub>(Ar)<sup>1</sup>: 3.80 (4d,e, 8d,e), OCH<sub>3</sub> (urethane)<sup>1</sup>: 3.68 (9a,b, 10, 11a,<sup>g</sup> b, 12). <sup>a</sup> J: 5.8 (1), 7.7 (2, 9a,b), 2.0 (3), 10.1 ± 0.1 (4a-f, 6, 8, 8a-f), 6.3 (5), 9.5 (7), 1.4 (11b), 9.8 (13b), for 13a dd (J: ~10 and ~5 Hz). <sup>D</sup> A and B part of an ABX spin-system <sup>2</sup>(A,B): 9.6 (2, 3, 4a-f, 7), 12.1 (5, 8, 8a-f), 13.8 (10, 11a,b, 12), <sup>3</sup>(A,X): 5.2 ± 0.1 (2), 6.1 ± 0.1 (3, 4a,c), 7.2 ± 0.2 (4e,f, 8, 8a-f), 4.6 (5), 7.8 (9b, 11b), 11.2 (10), 8.5 (11a), 10.6 (12), <sup>3</sup>(B,X): 7.5 ± 0.2 (2, 3, 4a-c), 5.9 (4e), 4.4 ± 0.2 (4f, 5), 10.8 (8, 8a-f), 5.5 (10); d for 1 and 9b (J: 7.7), 2xddd for 13a,b (unresolved lines due to coupling with NH group); <sup>c</sup> Splitted band pair for 5, 8, 8b,c,f; <sup>d</sup> Unresolved lines; <sup>e,g</sup> Overlapping signals; <sup>I</sup> Coalesced lines of a spin-system near to the A<sub>2</sub>X limiting case; <sup>h</sup>Coalesced with the  $\forall$ C=0(Ac) band; <sup>i</sup> s(3H).

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Table 2. <sup>13</sup>C-nmr chemical shifts (6<sub>TMS</sub> = 0 ppm) of compounds 1-3, 4a-f, 5-8, 8a-f, 9a,b, 10, 11a,b, 12 and 13a,b in CDCl<sub>3</sub> solution of 20 or 63 MHz.<sup>a</sup>

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#### Experimental

The melting points were measured on a Kofler block and are uncorrected. Specific rotation was measured with a Polamat-A polarimeter in chloroform, c=1. The TLC tests were performed on Kieselgel-G (Merck) layers of 0.5 mm layer thickness. Developing solvent: benzene/methanol (a) (99:1); (b) (98:2). Detection: spraying with 50% aqueous phosphoric acid and subsequent heating at 100-120  $^{\rm OC}$  for 15 min. The R<sub>f</sub> values were determined in UV light at 365 nm. The column chromatographic separations were performed on Al<sub>2</sub>O<sub>3</sub> columns of activity III-IV, standardized according to Brockmann. The IR spectra were recorded in KBr pellets with a Bruker IFS-113v vacuum optic FT spectrometer equipped with an Aspect 2000 computer. <sup>1</sup>H- and <sup>13</sup>C-NMR spectra were recorded in CDCl<sub>3</sub> solution in 5 or 10 mm (<sup>13</sup>C) tubes, at room temperature, on a Bruker WM-250 and/or WP-80-SY FT spectrometer controlled by an Aspect 2000 computer at 250.13 MHz (<sup>1</sup>H) and 62.89 or 20.14 MHz (<sup>13</sup>C), respectively, and using the deuterium signal of the solvent as the lock and SiMe<sub>4</sub> as internal standard.

DEPT spectra were recorded in the usual way, using only the  $\Theta$ =135<sup>o</sup> pulse to separate CH/CH<sub>3</sub> and CH<sub>2</sub> lines phased "up" and "down", respectively. Physical constants of the compounds are given in Table 3.

## 3-Methoxy-17-N-phenylcarbamoyloxy-16-p-tolylsulfonyloxymethylestra-

## 1,3,5(10)-triene 1-4

## <u>General method</u>

3-Methoxy-16a-p-tolylsulfonyloxymethylestra-1,3,5(10)-trien-17a-o1<sup>7</sup>, 3-methoxy-16a-p-tolylsulfonyloxymethylestra-1,3,5(10)-trien-17a-o1<sup>6</sup>, 3methoxy-16β-p-tolylsulfonyloxymethylestra-1,3,5(10)-trien-17a-o1<sup>6</sup>, or 3methoxy-16β-p-tolylsulfonyloxymethylestra-1,3,5(10)-trien-17β-o1<sup>6</sup> (2.32 g, 5 mmol) was dissolved in dichloromethane (30 ml), and phenyl isocyanate (2.4 g, 20 mmol) and triethylamine (0.5 ml) were added to it. The reaction mixture was refluxed at the boiling point for 6 h, and was then poured into 10% NaHCO<sub>3</sub> solution. The dichloromethane fraction was washed thoroughly with water, dried and evaporated to dryness. The residue was subjected to chromatographic separation in benzene/light petroleum (1:1).

# 3-Methoxyestra-1,3,5(10)-triene-N-phenyl(16,17-e)-4H-oxazin-2'-one 5-8 and 8a-f

## <u>General method</u>

Compound 1, 2, 3, 4 (1.178 g, 2 mmol) or 4a-f (2 mmol) was dissolved in methanol (30 ml) and then kept at the boiling point together with NaOCH<sub>3</sub> (432 mg, 8 mmol). The progress of the reaction was monitored by TLC. In the preparation of 5, 8 and 8a-e, refluxing was continued until consumption of the starting material, about 120 minutes. In the preparation of 6 7 and 8f, the conversion was continued until the appearance of 9a, 11a or 13a. The reaction mixture was neutralized with dilute hydrochloric acid, and diluted with water, and the crystals that separated out were filtered off, dried, and then crystallized from chloroform/light petroleum.

Products 6 and 7 were subjected to chromatograpic separation in chloroform/benzene (1:1).

Compound		Yield	M.p./°C	$/\alpha/20$	R <sub>f</sub>	Fc	ound (	(%)	Re	quired	(%)
(Fo	ormula)	(%)			_	С	н	N	С	Н	N
1	(C34H30NO6S)	92	152-154	+74	0.85ª	69.45	6.71	2.40	69.24	6.66	2.37
2	$(C_{3/H_{30}NO_{6}S})$	95	187-189	+16	0.82ª	69.31	6.72	2.45	69.24	6.66	2.37
3	$(C_{24}H_{20}NO_{\epsilon}S)$	82	93-95	+25	0.80 <sup>a</sup>	69.15	6.72	2.48	69.24	6.66	2.37
4	$(C_{3/H_{30}NO_{6}S})$	90	181-183	+36	0.85 <sup>a</sup>	69.30	6.51	2.30	69.24	6.66	2.37
4a	$(C_{2}/H_{2}FNO_{2}S)$	85	196-200	+23	0.95ª	67.28	6.50	2.47	67.19	6.30	2:30
4Ъ	$(C_{3/H_{38}}CINO_{6}S)$	78	141-144	+2	0.90 <sup>a</sup>	65.55	6.32	2.41	65.42	6.13	2.24
4c	$(C_{35}H_{41}NO_{4}S)$	65	oil	-7	0.90ª	69.50	6.78	2.40	69.62	6.84	2.32
4d	$(C_{35}H_{41}NO_{7}S)$	68	oil	+22	0.80ª	67.75	6.50	2.30	67.82	6.66	2.26
4e	(C <sub>35</sub> H <sub>41</sub> NO <sub>7</sub> S)	75	151-153	+43	0.80 <sup>a</sup>	67.85	6.72	2,41	67.82	6.66	2.26
4f	(C <sub>34</sub> H <sub>38</sub> N <sub>2</sub> O <sub>8</sub> S)	62	190-193	-18	0.80 <sup>a</sup>	64.48	6.17	4.65	64.33	6.03	4.41
5	(C <sub>27</sub> H <sub>31</sub> NO <sub>3</sub> )	96	167-170	+22	0.80 <sup>b</sup>	77.50	7.52	3.14	77.66	7.48	3.35
6	(C <sub>27</sub> H <sub>31</sub> NO <sub>3</sub> )	98	188-191	+152	0.75 <sup>b</sup>	77.82	7.30	3.42	77.66	7.48	3.35
7	(C <sub>27</sub> H <sub>31</sub> NO <sub>3</sub> )	87	183-185	-34	0.70 <sup>b</sup>	77.45	7.31	3.45	77.66	7.48	3.35
8	(C <sub>27</sub> H <sub>31</sub> NO <sub>3</sub> )	95	182-184	+117	0.75 <sup>b</sup>	77.72	7.40	3.50	77.66	7.48	3.35
8a	(C <sub>27</sub> H <sub>30</sub> FNO <sub>3</sub> )	90	273-275	+109	0.50 <sup>a</sup>	74.55	6.73	3.40	74.45	6.94	3.21
8b	(C <sub>27</sub> H <sub>30</sub> CINO <sub>3</sub> )	92	255~258	+110	0.65 <sup>a</sup>	71.50	6.78	3.21	71.74	6.69	3.09
8c	(C <sub>28</sub> H <sub>33</sub> NO <sub>3</sub> )	91	229-231	+87	0.50ª	78.05	7.53	3.40	77.92	7.70	3.24
<b>8</b> d	(C <sub>28</sub> H <sub>33</sub> NO <sub>4</sub> )	92	215-218	+108	0.40 <sup>a</sup>	75.25	7.50	3.05	75.13	7.43	3.12
8e	(C <sub>28</sub> H <sub>33</sub> NO <sub>4</sub> )	87	183-185	+108	0.45 <sup>a</sup>	73.35	7.30	3.20	75.13	7.43	3.12
8f	(C <sub>27</sub> H <sub>30</sub> N <sub>2</sub> O <sub>5</sub> )	56	298~302	+169	0.65 <sup>a</sup>	70.25	6.32	5.90	70.11	6.53	6.05
9a	(C <sub>28</sub> H <sub>35</sub> NO <sub>4</sub> )	95	163~165	+37	0.35 <sup>b</sup>	74.95	7.66	3.05	74.80	7.84	3.11
9Ъ	(C <sub>30</sub> H <sub>37</sub> NO <sub>5</sub> )	98	170-171	+3	0.45 <sup>a</sup>	73.35	7.65	2.51	73.29	7.58	2.84
10	(C <sub>28</sub> H <sub>33</sub> NO <sub>4</sub> )	96	154~157	+106	0.40 <sup>a</sup>	75.31	7.50	3.06	75.13	7.43	3.12
11a	(C <sub>28</sub> H <sub>35</sub> NO <sub>4</sub> )	96	153~154	+60	0.35 <sup>b</sup>	74.72	7.95	3.00	74.80	7.84	3.11
116	(C <sub>30</sub> H <sub>37</sub> NO <sub>5</sub> )	92	oil	+43	0.45 <sup>a</sup>	73.05	7.63	2.95	73.29	7.58	2.84
12	(C28H33NO4)	90	132-133	+98	0.45 <sup>a</sup>	75.30	7.25	3.20	75.13	7.43	3.12
13a	(C <sub>26</sub> H <sub>32</sub> N <sub>2</sub> O <sub>4</sub> )	80	198-200	+73	0.40 <sup>a</sup>	71.32	7.20	6.53	71.53	7.38	6.41
13b	(C28H34N2O5)	97	186~188	+83	0.80 <sup>a</sup>	70.33	7.05	6.00	70.26	7.16	5.85

Table 3. Characterization data for compounds 1-4, 4a-f, 5-8, 8a-f, 9a,b, 10, 11a,b, 12, 13a,b

## <u>3-Methoxy-16-(N-phenyl,N-methoxycarbonylaminomethyl)estra-1,3,5(10)-trien-</u> <u>17-ol</u> 9a and 11a

## <u>General method</u>

Compound 2 or 3 (1.179 g, 2 mmol) was dissolved in methanol (30 ml),  $NaOCH_3$  (432 mg, 8 mmol) was added, and the mixture was refluxed at the boiling point for 3 h. At the end of the conversion, the reaction mixture was neutralized with dilute hydrochloric acid, diluted with water and filtered. The separated product was dried and crystallized from chloroform/light petroleum.

17-Acetoxy-3-methoxy-16-(N-phenyl, N-methoxycarbonylaminomethyl)estra-

## 1,3,5(10)-triene 9b and 11b

## General method

Compound 9a or 11a (449 mg, 1 mmol) was dissolved in a mixture of pyridine and acetic anhydride (1:1, 3 ml), which was then allowed to stand for 24 h, and subsequently diluted with water. The precipitate that separated out was filtered off, washed thoroughly with water, and then crystallized from methanol.

<u>3-Methoxy-16-(N-phenyl,N-methoxycarbonylaminomethyl)estra-1,3,5(10)-trien-17-one</u> 10 and 12

## General method

Compound 9a or 11a (449 mg, 1 mmol) was dissolved in acetone (5 ml), and Jones reagent (1 ml) was added under cooling with ice. After standing for 1 h, the mixture was diluted with water, and the precipitate was filtered off, washed with water and crystallized from methanol.

3-Methoxy-16B-(N-p-nitrophenylaminomethyl)estra-1,3,5(10)-trien-17B-ol 13a

Compound 4f (634 mg, 1 mmol) was dissolved in methanol (30 ml) and the mixture was refluxed with  $NaOCH_3$  (216 mg, 4 mmol). The conversion was complete after 180 min. The reaction mixture was diluted with water, and the precipitate of 13a was filtered off, washed, dried and recrystallized from chloroform.

<u>17β-Acetoxy-3-methoxy-16β-(N-p-nitrophenylaminomethyl)estra-1,3,5(10)-</u> triene 13b

Compound 13a (218 mg, 0.5 mmol) was dissolved in a mixture of pyridine and acetic anhydride (1:1, 2 ml), which was then allowed to stand for 24 h. After this, it was diluted with water, and the precipitate was filtered off, dried and crystallized from methanol.

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