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Reactions of *N*- and *C*-Alkenylanilines: IV.* Synthesis of Heterocycles by Oxidation of *N*-Acyl-*o*-(1-alkenyl)anilines with Hydrogen Peroxide

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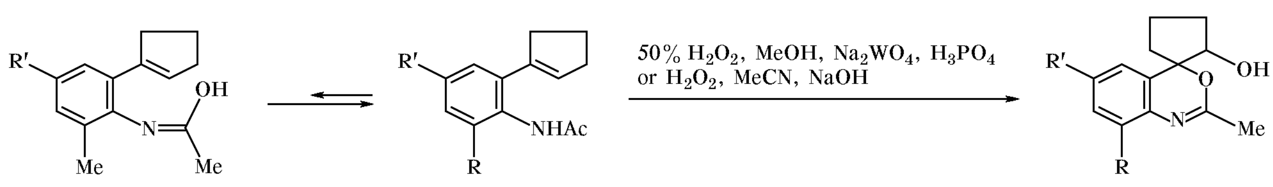
Abstract—Heterocyclic compounds of the 4*H*-3,1-benzoxazine and cyclopenta[*b*]indole series were synthesized by oxydation of *N*-acyl derivatives of 2-(1-alkenyl)anilines with hydrogen peroxide. The structure of the oxidation products is determined by the reaction conditions, substituent in the *ortho*-position of the aromatic ring, protecting group, and alkenyl radical structure.

Some 4*H*-3,1-benzoxazines are known to exhibit a strong biological activity [2]. These compounds are usually synthesized from *o*-aminobenzyl alcohol derivatives [3]. We recently proposed a procedure for preparation of 4*H*-3,1-benzoxazines from *o*-(1-alkenyl)anilides by reaction with bromine, *N*-bromosuccinimide, or hydrogen chloride [4]. In continuation of our studies aimed at developing new methods for selective heterocyclization of alkenyl-substituted arylamines with a view to obtain 3,1-benzoxazine derivatives, in the present work we examined oxidation of acylated *o*-(1-alkenyl)anilines with hydrogen peroxide under various conditions. We found that the result of the reaction of *o*-(1-alkenyl)aniline derivatives with hydrogen peroxide is strongly affected by the substituent in the aromatic ring, protecting group on the nitrogen atom, and structure of the alkenyl fragment.

The reaction of anilides **I** [5], **II** [6], **III** [7], and **IV** with H_2O_2 in acetonitrile in the presence of NaOH afforded, respectively, 3,1-benzoxazines **V**, **VI** [5], **VII** [6], and **VIII** in good yields. Benzoxazines **V**, **VII**, and **VIII** were also obtained by treatment of anilides **I**, **II**, and **IV** with 50% H_2O_2 in methanol in the presence of Na_2WO_4 and H_3PO_4 (Scheme 1). It should be noted that anilides **III** and **IX** did not undergo oxidation under these conditions, and they were recovered from the reaction mixtures. Analysis of the NMR spectra of anilides **III** and **IX** showed that these compounds, unlike their analogs **I**, **II**, and **IV** having no methyl substituent in the *ortho*-position, exist in the enol form (structures **X** and **XI** in Scheme 1).

By reaction of *N*-ethoxycarbonyl derivatives **XII**, **XIII** [5], and **XIV**–**XVI** with H_2O_2 in MeOH in the

Scheme 1.



I, **V**, R = R′ = H; **II**, **VII**, R = H, R′ = Me; **III**, **VI**, **X**, R = Me, R′ = H; **IV**, **VIII**, R = H, R′ = OMe; **IX**, **XI**, R = R′ = Me.

* For communication III, see [1].

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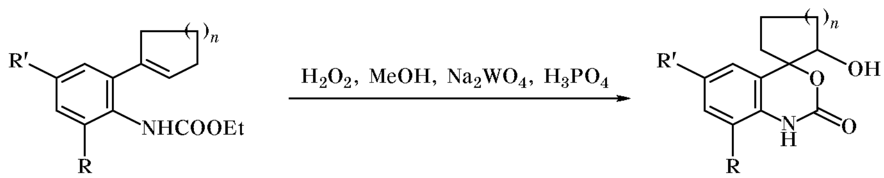
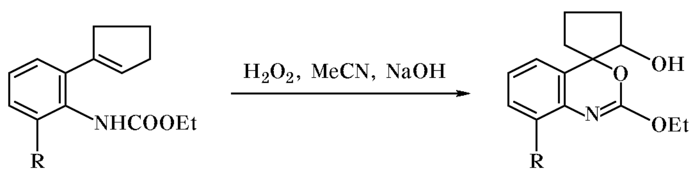
Scheme 2.



XII–XVI **XVII–XXI**

XII, **XVII**, *n* = 1, R = R′ = H; **XIII**, **XVIII**, *n* = 1, R = Me, R′ = H; **XIV**, **XIX**, *n* = 1, R = H, R′ = OMe; **XV**, **XX**, *n* = 1, R = OMe, R′ = H; **XVI**, **XXI**, *n* = 2, R = R′ = H.

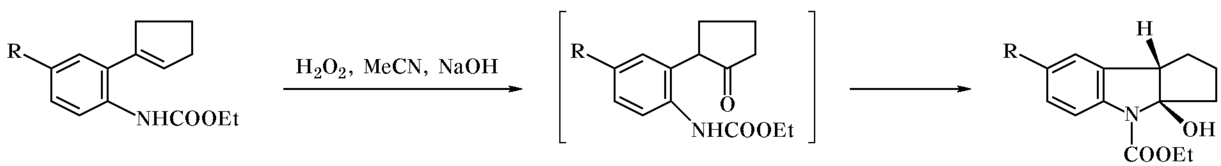
Scheme 3.



XIII, XV **XXII, XXIII**

XIII, **XXII**, R = Me; **XV**, **XXIII**, R = OMe.

Scheme 4.



XII, XXIV **A** **XXV, XXVI**

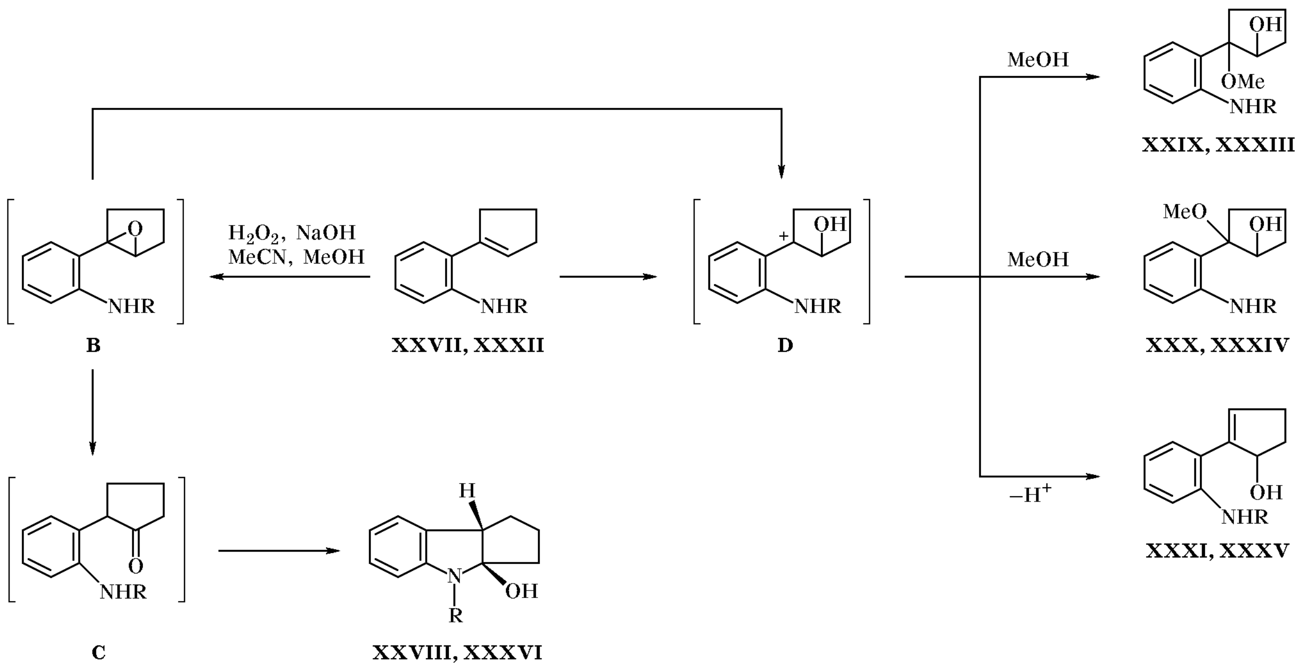
XII, **XXV**, R = H; **XXIV**, **XXVI**, R = Me.

presence of Na_2WO_4 and H_3PO_4 we obtained 3,1-benzoxazin-2-ones **XVII** [5] and **XVIII**–**XXI** (Scheme 2) as the only products.

Both methyl and methoxy group in anilides **XIII** [5] and **XV** exert similar *ortho* effects, and the oxidation of these compounds with H_2O_2 in MeCN in the presence of NaOH gives 3,1-benzoxazines **XXII** [5] and **XXIII** (Scheme 3). By contrast, anilides **XII** and **XXIV** having no *ortho*-substituent give rise to formation of 1,2,3,3a,4,8b-hexahydrocyclopenta[*b*]indoles **XXV** [5] and **XXVI** (Scheme 4) under analogous conditions. Presumably, the oxidation (as with cyclopentenylbenzenes [8]) initially gives ketone **A** which readily undergoes cyclization to indole. In the oxidation of amide **XXVII**, the yield of indole derivatives **XXVIII** is smaller. The reaction leads to formation of a mixture of isomeric methyl ethers **XXIX** and **XXX** and allyl-type alcohol **XXXI** (Scheme 5). Analogous pattern was observed in the oxidation of *N*-tosyl derivative **XXXII** with hydrogen peroxide in acetonitrile in the presence of sodium hydroxide. As a result, a mixture of four compounds **XXXIII**–**XXXVI** was formed, from which methyl ether **XXXIII** and cyclopentaindole **XXXVI** were isolated. In the above reactions, all products are likely to be formed via transformations of intermediate epoxy derivative **B**. Intramolecular cyclization of ketone **C** yields indoles **XXVIII** and **XXXVI**. Ethers **XXIX**, **XXX**, **XXXIII**, and **XXXIV** and alcohols **XXXI** and **XXXV** are products of further transformations of intermediate carbocation **D** (Scheme 5).

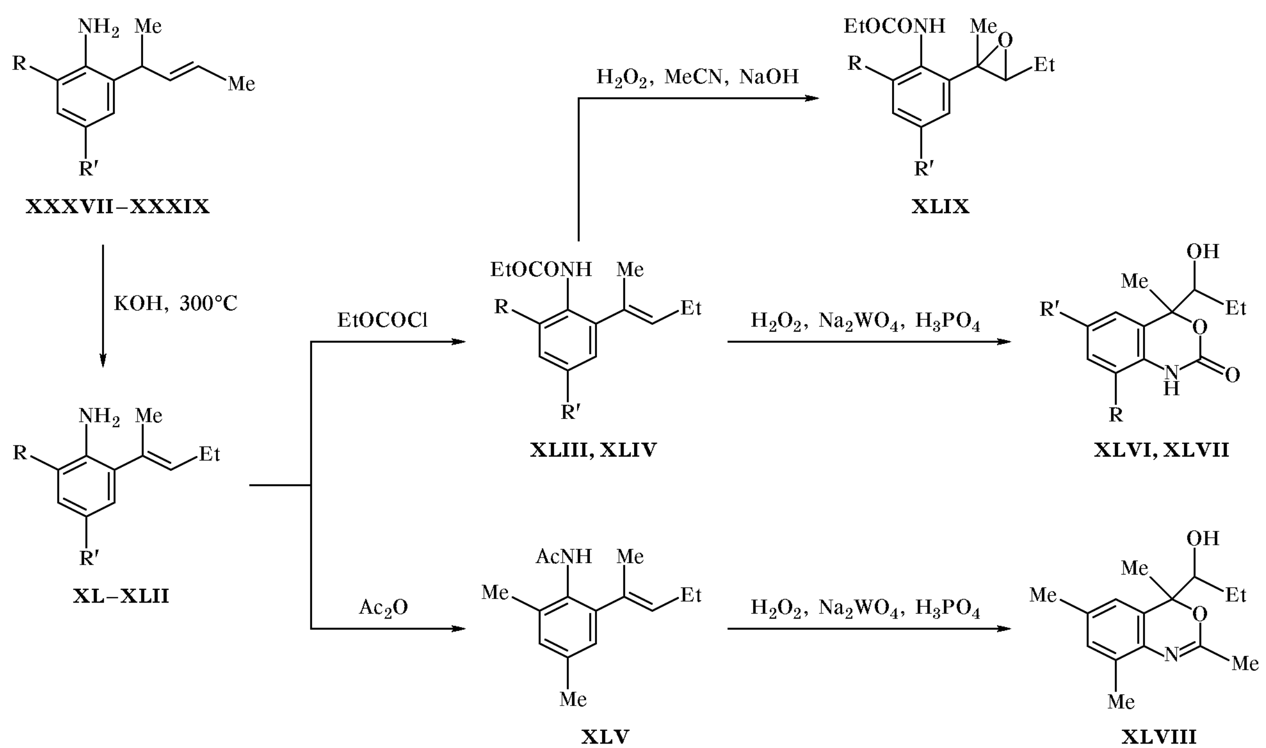
With the goal of obtaining hydroxyalkyl-substituted 3,1-benzoxazines and 3,1-benzoxazin-2-ones, alkenylanilines **XXXVII**–**XXXIX** [9] were subjected to isomerization into the corresponding 2-(1-methyl-1-butenyl)anilines **XL**–**XLII** by the action of potassium hydroxide at 300°C. Compounds **XL**–**XLII** were treated with acetic anhydride and ethyl chloroformate to obtain *N*-acyl derivatives **XLIII**–**XLV**, and the latter were oxidized with hydrogen peroxide in MeOH

Scheme 5.



XXVII–XXXI, R = $MeSO_2$; **XXXII–XXXVI**, R = *p*-$TolSO_2$.

Scheme 6.



XXXVII, **XL**, **XLIII**, R = R′ = H; **XXXVIII**, **XLI**, **XLIV**, **XLVII**, R = Me, R′ = H; **XXXIX**, **XLII**, **XLVI**, R = R′ = Me.

Table 1. Yields, melting points, R_f values, and elemental analyses of compounds **IV**, **VIII**, **XIV–XVI**, **XVIII–XXI**, **XXIII**, **XXIV**, **XXVI–XXVIII**, **XXXII**, **XXXIII**, **XXXVI**, and **XL–XLIX**

Comp. no.	Yield, %	mp, °C, or R_f (eluent)	Found, %			Formula	Calculated, %		
			C	H	N		C	H	N
IV	92	97	72.55	7.50	5.97	$C_{14}H_{17}NO_2$	72.70	7.41	6.06
VIII	73	166	67.70	6.61	5.28	$C_{14}H_{17}NO_3$	68.00	6.93	5.66
XIV	92	0.73 (hexane–EtOAc, 3 : 1)	68.75	7.40	5.27	$C_{15}H_{19}NO_3$	68.94	7.33	5.36
XV	89	0.65 (hexane–EtOAc, 3 : 1)	68.90	7.25	5.35	$C_{15}H_{19}NO_3$	68.94	7.33	5.36
XVI	92	0.7 (hexane–EtOAc, 3 : 1)	73.55	7.80	5.77	$C_{15}H_{19}NO_2$	73.44	7.81	5.71
XVIII	89	142	66.75	6.21	5.78	$C_{13}H_{15}NO_3$	66.94	6.48	6.00
XIX	81	213	62.41	5.79	5.31	$C_{13}H_{15}NO_4$	62.64	6.07	5.62
XX	87	150–152	62.35	5.73	5.40	$C_{13}H_{15}NO_4$	62.64	6.07	5.62
XXI	83	233	66.67	6.20	5.67	$C_{13}H_{15}NO_3$	66.94	6.48	6.00
XXIII	80	90	66.61	6.57	4.87	$C_{15}H_{19}NO_4$	66.97	6.91	5.05
XXIV	90	0.6 (hexane–EtOAc, 3 : 1)	72.98	7.61	5.60	$C_{15}H_{19}NO_2$	73.44	7.81	5.71
XXVI	74	0.6	66.62	7.10	5.07	$C_{15}H_{19}NO_3$	68.94	7.33	5.36
XXVII	84	78–82	60.55	6.45	5.98	$C_{12}H_{15}NO_2S$	60.73	6.37	5.90
XXVIII	35	114	56.67	5.73	5.24	$C_{12}H_{15}NO_3S$	56.90	5.97	5.53
XXXII	90	94–98	69.09	6.16	4.32	$C_{18}H_{19}NO_2S$	68.98	6.11	4.47
XXXIII	27	0.3 (hexane–EtOAc, 3 : 1)	63.08	6.38	3.93	$C_{19}H_{23}NO_4S$	63.13	6.41	3.88
XXXVI	32	0.4 (hexane–EtOAc, 3 : 1)	65.48	5.78	4.43	$C_{18}H_{19}NO_3S$	65.63	5.81	4.25
XL	74	0.7 ($CHCl_3$)	82.08	9.15	8.57	$C_{11}H_{15}N$	81.94	9.38	8.69
XLI	36	0.7 ($CHCl_3$)	82.17	9.69	7.97	$C_{12}H_{17}N$	82.23	9.78	7.99
XLII	48	0.7 ($CHCl_3$)	82.60	10.55	7.35	$C_{13}H_{19}N$	82.48	10.12	7.40
XLIII	93	0.6 (hexane–EtOAc, 4 : 1)	72.18	8.05	5.89	$C_{14}H_{19}NO_2$	72.07	8.21	6.00
XLIV	95	0.6 (hexane–EtOAc, 3 : 1)	72.80	8.66	5.55	$C_{15}H_{21}NO_2$	72.84	8.56	5.66
XLV	88	110	77.92	9.05	6.08	$C_{15}H_{21}NO$	77.88	9.15	6.05
XLVI	74	185–187	67.08	7.26	5.38	$C_{14}H_{19}NO_3$	67.45	7.68	5.62
XLVII	76	123–125	66.11	6.97	5.67	$C_{13}H_{17}NO_3$	66.36	7.28	5.95
XLVIII	77	144–147	72.52	8.27	5.34	$C_{15}H_{21}NO_2$	72.84	8.56	5.66
XLIX	76	0.5 (hexane–EtOAc, 3 : 1)	67.12	7.32	5.37	$C_{14}H_{19}NO_3$	67.45	7.68	5.62

containing Na_2WO_4 and H_3PO_4. As a result, benzoxazinones **XLVI** and **XLVII** and benzoxazine **XLVIII** were isolated (Scheme 6). The oxidation of *N*-ethoxycarbonylaniline **XLIII** with H_2O_2 in acetonitrile in the presence of NaOH gave epoxy derivative **XLIX**.

The structure of the oxidation products was proved by elemental analyses and spectral data (Tables 1–3). The double bond configuration in alkenylanilines **XL**–**XLII** was determined on the basis of our previous data for structurally related compounds [4]. The spectral parameters of previously known benzoxazine and cyclopentaindole derivatives were consistent with those reported in [5]. In the ^1H NMR spectrum of **XLIX**, the CH proton of the oxirane ring appears as a triplet at δ 3.02 ppm (*J* = 5.43 Hz). Signals from the $C^{1'}$ and $C^{2'}$ atoms of the oxirane fragment in **XLIX** are located at δ_C 60.69 (s) and 66.05 ppm (d), respectively.

Table 2. ^{1}H NMR spectra of compounds **IV**, **VIII**, **IX**, **XI**, **XIV–XVI**, **XVIII–XXI**, **XXIII**, **XXIV**, **XXVI–XXXVI**, and **XL–XLIX** in $CDCl_3$

Comp. no.	Chemical shifts δ, ppm (*J*, Hz)
IV	1.92 q (2H, CH_2, *J* = 7.46), 2.02 s (3H, CH_3), 2.43–2.62 m (4H, $2CH_2$), 3.69 s (3H, OCH_3), 5.85 s (1H, =CH), 6.63–6.71 m (3H, H_{arom}), 7.71 s (1H, NH)
VIII	1.72–2.53 m (6H, $3CH_2$), 2.63 s (3H, CH_3), 3.13 br.s (1H, OH), 3.80 s (3H, OCH_3), 4.45 br.s (1H, CHO), 6.70 s (1H, 5-H), 6.77 d (1H, 7-H, *J* = 8.44), 7.49 d (1H, 8-H, *J* = 8.51)
IX, **XI**[a]	1.96 q (2H, CH_2, *J* = 7.40), 2.13 s (1H, CH_3), 2.20 s and 2.24 s (3H, CH_3), 2.28 s and 2.32 s (3H, CH_3), 2.49 d.t (2H, CH_2, J_1 = 1.98, J_2 = 7.35), 2.61 d.t (2H, CH_2, J_1 = 1.84, J_2 = 7.34), 5.82 t (*J* = 2.00), 5.96 t (*J* = 2.04), 6.94 d (1H, 5-H, *J* = 4.20), 7.00 d (1H, 3-H, *J* = 5.83)
XIV	1.90 q (2H, CH_2, *J* = 7.34), 1.23 s (3H, CH_3), 2.41–2.60 m (4H, $2CH_2$), 3.72 s (3H, OCH_3), 4.12 q (2H, OCH_2, *J* = 7.19), 5.78 s (1H, =CH), 6.61–6.72 m (3H, H_{arom}), 7.85 s (1H, NH)
XV	1.20 t (3H, CH_3, *J* = 7.02), 1.92 q (2H, CH_2, *J* = 7.38), 2.44 t.d (2H, CH_2, J_1 = 7.33, J_2 = 2.35), 2.64 t.d (2H, CH_2, J_1 = 7.33, J_2 = 2.60), 3.74 s (3H, CH_3), 4.11 q (2H, OCH_2, *J* = 7.15), 5.94 t (1H, =CH, *J* = 1.95), 6.33 s (1H, NH), 6.74 d (2H, H_{arom}, *J* = 7.27), 6.88 d (1H, H_{arom}, *J* = 7.88), 7.12 t (1H, H_{arom}, *J* = 8.04)
XVI	1.32 t (3H, CH_3, *J* = 7.19), 1.67–1.84 m (4H, $2CH_2$), 2.21 s (4H, $2CH_2$), 4.23 q (2H, OCH_2, *J* = 7.18), 5.74 s (1H, =CH), 6.95–7.08 m (3H, H_{arom}), 7.23 t (1H, H_{arom}, *J* = 6.86), 8.07 s (1H, NH)
XVIII	1.71–2.19 m (4H, $2CH_2$), 2.28 s (3H, CH_3), 2.4–2.6 m (2H, CH_2), 3.31 br.s (1H, OH), 4.19 d (1H, CHO, *J* = 7.17), 6.96 t (1H, H_{arom}, *J* = 7.54), 7.09 d (2H, H_{arom}, *J* = 9.01), 8.70 s (1H, NH)
XIX[b]	1.44–2.12 m (4H, $2CH_2$), 2.20–2.42 m (2H, CH_2), 3.56 br.s (1H, OH), 3.55 s (3H, OCH_3), 3.88 br.s (1H, CHO), 6.62–6.77 m (3H, H_{arom}), 9.69 s (1H, NH)
XX	1.72–2.32 m (4H, $2CH_2$), 2.28–2.51 m (2H, CH_2), 3.03 br.s (1H, OH), 3.78 s (3H, OCH_3), 4.12 d (1H, CHO, *J* = 4.76), 6.78 d (1H, H_{arom}, *J* = 7.99), 6.80 d (1H, H_{arom}, *J* = 7.83), 6.93 t (1H, 6-H, *J* = 7.95), 7.57 s (1H, NH)
XXI[b]	1.01–2.22 m (8H, $4CH_2$), 3.56 s (1H, CHO), 4.66 br.s (1H, OH), 6.64 d (2H, H_{arom}, *J* = 7.51), 6.8–7.0 m (2H, H_{arom}), 9.72 s (1H, NH)
XXIII	1.36 t (3H, CH_3, *J* = 7.12), 1.7–2.3 m (4H, $2CH_2$), 2.4–2.6 m (2H, CH_2), 2.73 br.s (1H, OH), 3.86 s (3H, OCH_3), 4.14 d (1H, CHOH, *J* = 4.62), 4.40 q (2H, OCH_2, *J* = 6.95), 6.82 d (1H, H_{arom}, *J* = 6.57), 6.84 d (1H, H_{arom}, *J* = 7.33), 7.02 t (1H, 6-H, *J* = 8.06)
XXIV	1.20 t (3H, CH_3, *J* = 6.11), 1.93 q (2H, CH_2, *J* = 7.28), 2.12 s (3H, CH_3), 2.42–2.57 m (4H, $2CH_2$), 4.08 q (2H, CH_2O, *J* = 7.01), 5.67 s (1H, =CH), 6.72–7.03 m (3H, H_{arom}), 7.69 br.s (1H, NH)
XXVI	1.38 t (3H, CH_3, *J* = 7.12), 1.54–1.71 m (2H, CH_2), 1.74–1.90 m (2H, CH_2), 2.18–2.39 m (2H, CH_2), 2.32 s (3H, CH_3), 3.52–3.62 m (1H, CH), 4.38 q (2H, CH_2, *J* = 6.7), 6.87–7.20 m (3H, H_{arom}), 7.50 br.s (1H, OH)
XXVII	2.02 q (2H, CH_2, *J* = 7.43), 2.58 br.s (2H, CH_2), 2.66 br.s (2H, CH_2), 2.33 s (3H, CH_3), 5.89 s (1H, =CH), 7.00 s (1H, NH), 7.11 t (1H, 5-H, *J* = 7.64), 7.22–7.28 m (2H, 6-H, 4-H), 7.56 d (1H, 3-H, *J* = 8.02)
XXVIII	1.55–1.86 m (2H, CH_2), 2.12–2.57 m (4H, $2CH_2$), 3.06 s (3H, CH_3), 3.59 d.d (1H, CH, J_1 = 4.24, J_2 = 8.85), 4.34 s (1H, OH), 7.02 t (1H, H_{arom}, *J* = 7.38), 7.14–7.27 m (3H, H_{arom})
XXIX, **XXX**, **XXXI**[a]	1.55–2.76 m (CH_2), 2.89 s (CH_3), 3.04 s (CH_3), 3.06 s (CH_3), 3.12 s (CH_3), 3.15 s (CH_3), 3.58 s (OCH), 4.42 d (OCH, *J* = 6.09), 3.93 s (OCH), 6.06 d (=CH, *J* = 2.45), 7.05–7.66 m (H_{arom}), 8.83 s (NH), 9.12 s (NH), 9.38 s (NH)
XXXII	1.92 q (2H, CH_2, *J* = 7.32), 2.29 t.d (2H, CH_2, J_1 = 7.53, J_2 = 2.12), 2.36 s (3H, CH_3), 2.50 t.d (2H, CH_2, CH_2, J_1 = 7.56, J_2 = 2.30), 5.57 t (1H, =CH, *J* = 1.98), 7.04–7.22 m (7H, H_{arom}, NH), 7.62 d (2H, H_{arom}, *J* = 8.27)
XXXIII	1.50–1.72 m (2H, CH_2), 1.97–2.31 m (4H, $2CH_2$), 2.38 s (3H, CH_3), 2.97 s (1H, OH), 3.09 s (3H, OCH_3), 3.81 s (1H, CHO), 7.00–7.14 m (2H, H_{arom}), 7.26 d (2H, H_{arom}, Ts, *J* = 8.01), 7.56–7.68 m (2H, H_{arom}), 7.83 d (2H, H_{arom}, Ts, *J* = 8.05), 9.20 br.s (1H, NH)

Table 2. (Contd.)

Comp. no.	Chemical shifts δ, ppm (*J*, Hz)
XXXIV, **XXXV**[a]	1.53–2.52 m (CH_2), 2.36 s (CH_3), 2.41 s (CH_3), 3.01 s (OCH_3), 4.27 d (OCH, *J* = 6.26), 4.80 d (OCH, *J* = 6.37), 5.38 t (=CH, *J* = 2.50), 7.00–7.82 m (H_{arom}), 8.98 s (NH), 9.44 s (NH)
XXXVI	1.51–2.47 m (6H, $3CH_2$), 2.40 s (3H, CH_3), 3.61 d.d (1H, CH, J_1 = 5.10, J_2 = 9.16), 4.32 s (1H, OH), 7.08–7.40 m (4H, H_{arom}), 7.38 d (2H, H_{arom}, Ts, *J* = 8.41), 7.92 d (2H, H_{arom}, Ts, *J* = 8.37)
XL	1.01 t (3H, CH_3, *J* = 7.5), 1.91 q (2H, CH_2, *J* = 7.40), 1.95 s (3H, CH_3), 3.80 br.s (2H, NH_2), 5.56 t (1H, =CH, *J* = 7.12), 6.73 d (1H, 6-H, *J* = 8.04), 6.82 t (1H, 4-H, *J* = 7.67), 7.01 d (1H, 3-H, *J* = 7.38), 7.11 t (1H, 5-H, *J* = 7.74)
XLI	1.01 d.t (3H, CH_3, J_1 = 1.44, J_2 = 7.39), 1.92 t (2H, CH_2, *J* = 7.02), 2.06 s (3H, CH_3), 2.28 s (3H, CH_3), 3.71 br.s (2H, NH_2), 5.68 t (1H, =CH, *J* = 7.06), 6.79 t (1H, 5-H, *J* = 7.34), 6.92 d (1H, 4-H, *J* = 7.39), 7.07 d (1H, 3-H, *J* = 7.38)
XLII	1.07 t (3H, CH_3, *J* = 7.40), 1.07 q (2H, CH_2, *J* = 7.29), 2.11 s (3H, CH_3), 2.30 s (3H, CH_3), 2.38 s (3H, CH_3), 3.64 br.s (2H, NH_2), 5.72 t.d (1H, =CH, J_1 = 7.23, J_2 = 1.51), 6.80 s (1H, 3-H), 6.95 s (1H, 5-H)
XLIII	0.92 t (3H, CH_3, *J* = 6.30), 1.32 t (3H, CH_3, *J* = 6.09), 1.80 q (2H, CH_2, *J* = 7.18), 2.02 s (3H, CH_3), 4.17 q (2H, CH_2O, *J* = 7.14), 5.70 t (1H, =CH, *J* = 7.42), 6.84 br.s (1H, NH), 7.03–7.32 m (3H, H_{arom}), 8.10 d (1H, H_{arom}, *J* = 8.13)
XLIV	0.94 t (3H, CH_3, *J* = 7.37), 1.07 t (3H, CH_3, *J* = 7.23), 1.80 q (2H, CH_2, *J* = 7.30), 1.92 s (3H, CH_3), 2.29 s (3H, CH_3), 4.19 q (2H, CH_2, *J* = 7.13), 5.47 t (1H, =CH, *J* = 7.05), 6.09 br.s (1H, NH), 6.82 t (1H, 5-H, *J* = 7.22), 6.92 d (1H, 4-H, *J* = 7.25), 7.09 d (1H, 3-H, *J* = 7.30)
XLV	1.08 t (3H, CH_3, *J* = 7.38), 1.10 q (2H, CH_2, *J* = 7.25), 2.10 s (3H, CH_3), 2.15 s (3H, CH_3), 2.32 s (3H, CH_3), 2.36 s (3H, CH_3), 5.68 t.d (1H, =CH, J_1 = 7.19, J_2 = 1.47), 6.83 s (1H, 3-H), 6.94 s (1H, 5-H), 8.10 s (1H, NH)
XLVI	0.97 t (3H, CH_3, *J* = 7.42), 1.4–1.7 m (2H, CH_2), 1.71 s (3H, CH_3), 2.26 s (3H, CH_3), 2.30 s (3H, CH_3), 2.52 br.s (1H, OH), 3.77 d.d (1H, CHO, J_1 = 2.60, J_2 = 10.05), 6.84 s (1H, 5-H), 6.93 s (1H, 7-H), 8.39 s (1H, NH)
XLVII	0.94 t (3H, CH_3, *J* = 7.29), 1.4–1.6 m (2H, CH_2), 1.71 s (3H, CH_3), 2.26 s (3H, CH_3), 3.11 br.s (1H, OH), 3.78 d.d (1H, CHO, J_1 = 2.58, J_2 = 9.40), 6.95 t (1H, 6-H, *J* = 7.51), 7.03 d (1H, 5-H, *J* = 7.38), 7.07 d (1H, 7-H, *J* = 7.24), 7.39 s (1H, NH)
XLVIII	0.62 t (3H, CH_3, *J* = 7.40), 1.57 s (3H, CH_3), 2.08 s (3H, CH_3), 1.9–2.1 m (2H, CH_2), 2.33 s (3H, CH_3), 2.68 s (3H, CH_3), 3.50 d (1H, CHO, *J* = 6.02), 5.0 br.s (1H, OH), 6.64 s (1H, 5-H), 7.03 s (1H, 7-H), 7.62 s (1H, NH)
XLIX	0.97 t (3H, CH_3, *J* = 7.04), 1.0–1.2 m (2H, CH_2O), 1.29 t (3H, CH_3, *J* = 6.98), 1.56 s (3H, CH_3), 3.02 t (1H, CHO, *J* = 5.43), 4.19 q (2H, CH_2, *J* = 6.88), 6.96 t (1H, 5-H, *J* = 7.01), 7.04 d (1H, 3-H, *J* = 6.34), 7.23 t (1H, 4-H, *J* = 7.00), 8.10 d (1H, 6-H, *J* = 7.84), 8.38 s (1H, NH)

[a] Mixture of isomers.
[b] In DMF-d_7.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded on a Bruker AM-300 spectrometer at 300.13 MHz for ^1H and 75.47 MHz for ^{13}C using TMS as internal reference. The purity of the products was checked by GLC on a Chrom-5 chromatograph equipped with a flame-ionization detector (1200 × 3.5-mm column, stationary phase SE-30 on Chromaton, carrier gas helium, oven temperature programming at 12°C/min) and by TLC on Silufol UV-254 plates.

Oxidation of anilides with the system H_2O_2–MeOH–Na_2WO_4–H_3PO_4 (*typical procedure*). To a mixture of 0.5 g (2.48 mmol) of appropriate anilide, 50 mg (0.17 mmol) of Na_2WO_4 in 0.2 ml of water, and 1 drop of concentrated phosphoric acid in 5 ml of methanol we added 0.34 g (4.98 mmol) of 50% hydrogen peroxide. The mixture was kept for 24 h at 30°C, 50 ml of methylene chloride was added, and the organic phase was washed with saturated solutions of Na_2CO_3 and $Na_2S_2O_3$ and with water and dried over $MgSO_4$.

Table 3. ^{13}C NMR spectra of compounds **IV**, **VIII**, **IX**, **XI**, **XIV–XVI**, **XVIII–XXI**, **XXIII**, **XXIV**, **XXVI–XXXVI**, and **XL–XLIX** in $CDCl_3$

Comp. no.	Chemical shifts δ_C, ppm
IV	23.14, 33.46, 35.97 ($3CH_2$), 23.75 (CH_3), 55.06 (OCH_3), 111.99 (C^3), 113.44 (C^5), 124.93 (C^6), 127.39 (C^2), 130.16 ($C^{2'}$), 131.81 ($C^{1'}$), 140.41 (C^1), 156.24 (C^4), 168.48 (C=O)
VIII	19.86 (CH_3), 19.33, 31.17, 36.87 ($3CH_2$), 55.79 (OCH_3), 79.64 (CHOH), 97.85 (C^4), 112.40 (C^7), 113.87 (C^5), 119.68 (C^8), 121.84 (C^{4a}), 123.69 (C^{8a}), 159.97 (C^6), 168.62 (C=N)
IX, **XI**[a]	18.24 (CH_3), 20.79, 20.85 (CH_3), 22.87 (CH_3), 23.64, 23.70 ($C^{4'}$), 33.36 ($C^{3'}$), 35.66, 35.91 ($C^{5'}$); singlets: 129.93, 130.87, 135.69, 136.06, 136.19, 136.29, 136.83, 137.50; doublets: 127.47, 130.01 (Ar), 126.71 (C^3), 129.85 (C^5), 129.18, 130.91 ($C^{2'}$), 141.13, 141.56 (C^1), 169.12, 173.44 (C=O)
XIV	23.19, 34.05, 36.17 ($3CH_2$), 14.35 (CH_3), 55.54 (OCH_3), 60.23 (OCH_2), 111.90 (C^3), 114.32 (C^5), 124.62 (C^6), 126.99 (C^2), 129.86 ($C^{2'}$), 131.65 ($C^{1'}$), 140.56 (C^1), 155.44 (C^4), 154.38 (C=O)
XV	14.31 (CH_3), 23.40, 33.11, 35.05 ($3CH_2$), 55.36 (OCH_3), 60.78 (OCH_2), 109.02 (C^5), 120.02 (C^3), 122.73 (C^2), 126.66 (C^4), 129.18 ($C^{2'}$), 136.48 (C^1), 140.96 ($C^{1'}$), 141.03 (C^6), 154.51 (C=O)
XVI	14.35 (CH_3), 21.68, 22.72, 25.10, 29.68 ($4CH_2$), 60.86 (OCH_2), 118.79 (C^6), 122.58 ($C^{2'}$), 127.20 (C^4), 128.01 (C^3), 128.16 (C^5), 133.49 ($C^{1'}$), 134.17 (C^2), 135.43 (C^1), 153.40 (C=O)
XVIII	16.82 (CH_3), 20.19, 31.50, 33.43 ($3CH_2$), 75.94 (CHOH), 93.85 (C^4), 119.47 (C^{4a}), 122.56 (C^5), 122.82 (C^8), 123.72 (C^6), 131.11 (C^7), 133.77 (C^{8a}), 152.51 (C=O)
XIX[b]	20.52, 32.88, 34.04 ($3CH_2$), 55.79 (OCH_3), 75.81 (CHOH), 93.77 (C^4), 113.30 (C^7), 114.25 (C^5), 115.03 (C^8), 123.04 (C^{4a}), 130.83 (C^{8a}), 151.60 (C^6), 155.51 (C=O)
XX	20.20, 31.56, 33.53 ($3CH_2$), 55.89 (OCH_3), 76.09 (CHOH), 94.12 (C^4), 110.71 (C^7), 117.90 (C^5), 120.09 (C^{4a}), 122.66 (C^6), 124.71 (C^{8a}), 145.14 (C^8), 151.20 (C=O)
XXI[b]	19.29, 21.16, 29.28, 30.12 ($4CH_2$), 67.57 (CHOH), 84.12 (C^4), 114.71 (C^8), 122.86 (C^6), 125.45 (C^{4a}), 127.53 (C^5), 129.30 (C^7), 136.64 (C^{8a}), 151.74 (C=O)
XXIII	14.28 (CH_3), 20.59, 31.36, 34.00 ($3CH_2$), 56.13 (OCH_3), 64.56 (OCH_2), 75.23 (CHOH), 93.42 (C^4), 111.97 (C^7), 117.31 (C^5), 123.81 (C^{4a}), 124.10 (C^6), 130.94 (C^{8a}), 151.77 (C^8), 155.43 (C=N)
XXIV	14.4, 20.4 ($2CH_3$), 23.1, 33.6, 36.4 ($3CH_2$), 60.8 (CH_2O), 122.4 ($C^{1'}$), 128.0 (C^6), 128.1 ($C^{2'}$), 129.1 (C^3), 129.8 (C^5), 132.1 (C^2), 132.3 (C^4), 140.5 (C^1), 153.7 (C=O)
XXVI	14.6, 20.9 (CH_3), 25.5 (C^2), 34.0 (C^1), 42.2 (C^3), 53.2 C(^{8b}), 61.8 (OCH_2), 103.7 (C^{3a}), 114.2 (C^5), 125.0 (C^8), 128.2 (C^6), 129.5 (C^7), 132.7 (C^{8a}), 141.8 (C^{4a}), 153.1 (C=O)
XXVII	23.05, 33.65, 36.85 ($3CH_2$), 39.30 (CH_3), 119.28 (C^6), 124.25 (C^4), 127.87 (C^3), 128.39 (C^5), 129.27 (C^2), 131.10 ($C^{2'}$), 133.50 (C^1), 139.70 ($C^{1'}$)
XXVIII	25.07 (C^2), 33.67 (C^1), 39.71 (CH_3), 43.29 (C^3), 54.12 (C^{8b}), 106.96 (C^{3a}), 111.75 (C^7), 123.27 (C^5), 124.93 (C^8), 127.87 (C^6), 132.08 (C^{8a}), 140.71 (C^{4a})
XXIX, **XXX**, **XXXI**[a]	19.37, 20.24, 28.10, 30.56, 31.42, 31.80, 32.38, 34.45 ($8CH_2$), 39.25, 39.45, 40.57 ($3CH_3SO_2$), 50.10, 51.58 ($2CH_3O$), 76.23, 78.20, 79.23 (3HCO), 88.87, 92.34 (2CO), 118.1–143.12 (Ar)
XXXII	21.30 (CH_3), 23.02, 33.59, 36.76 ($3CH_2$); doublets: 121.04, 124.42, 126.91, 127.52, 127.92, 129.34, 130.58; singlets: 130.17, 133.18, 136.15, 139.76, 143.63
XXXIII	20.50 (CH_3), 21.45, 31.13, 31.54 ($3CH_2$), 52.01 (OCH_3), 77.32 (CHOH), 89.48 ($C^{1'}$), 118.62, 122.96, 124.83, 127.23, 128.21, 129.19, 129.59, 136.84, 137.08, 143.75 (Ar)
XXXIV, **XXXV**[a]	19.49, 27.93, 30.47, 32.00, 34.38 ($5CH_2$), 21.43, 21.51 ($2CH_3$), 50.07 (CH_3O), 76.33, 79.42 (2HCO), 92.45 (CO), 120.07–144.10 (Ar)
XXXVI	21.10 (CH_3), 25.30 (C^2), 33.56 (C^1), 43.65 (C^3), 53.80 (C^{8b}), 107.05 (C^{3a}), 112.20, 122.43, 124.58, 126.73, 127.68, 129.73, 131.69, 136.95, 140.44, 143.97 (arom.)
XL	14.3 (CH_3), 22.5, (CH_2), 24.5 (CH_3), 114.9 (C^6), 118.5 (C^4), 127.6 (C^3), 127.8 (C^2), 128.9 (C^5), 131.2 ($C^{2'}$), 133.0 ($C^{1'}$), 142.7 (C^1)

Table 3. (Contd.)

Comp. no.	Chemical shifts δ_C, ppm
XLI	14.17, 17.73, 24.48 (CH_3), 22.44 (CH_2), 117.70 (C^4), 121.85 (C^6), 126.33 (C^3), 127.43 (C^2), 128.64 ($C^{2'}$), 131.13 (C^5), 133.23 ($C^{1'}$), 140.72 (C^1)
XLII	14.23, 17.72, 20.42, 24.63 (4CH_3), 22.51 (CH_2), 120.04 (C^6), 126.74 ($C^{2'}$), 127.65 (C^4), 129.47 (C^3), 130.96 (C^5), 133.45 (C^2), 138.25 ($C^{1'}$), 142.20 (C^1)
XLIII	14.1, 14.5 (2CH_3), 22.4, (CH_2), 24.8 (CH_3), 61.0 (CH_2O), 118.2 (C^4), 122.7 (C^2), 127.5 (C^5), 128.0 ($C^{2'}$), 130.6 (C^6), 131.6 ($C^{1'}$), 132.7 (C^3), 134.3 (C^1), 153.5 (C=O)
XLIV	13.98, 15.00, 18.55, 20.50, 23.89 (4CH_3), 22.72 (CH_2), 60.43 (OCH_2), 118.02 (C^4), 121.79 (C^6), 126.22 (C^3), 128.11 (C^2), 128.74 ($C^{2'}$), 131.50 (C^5), 133.34 ($C^{1'}$), 140.62 (C^1), 152.00 (C=O)
XLV	14.57, 18.02, 20.22, 23.17, 24.93 (5CH_3), 24.41 (CH_2), 119.14 (C^6), 126.33 ($C^{2'}$), 127.25 (C^4), 129.23 (C^3), 131.04 (C^5), 133.05 (C^2), 138.85 ($C^{1'}$), 141.04 (C^1), 165.03 (C=O)
XLVI	10.87, 16.81, 20.92, 21.61 (4CH_3), 23.59 (CH_2), 77.39 (CHOH), 87.85 (C^4), 122.50 (C^8), 122.65 (C^{4a}), 123.41 (C^5), 130.68 (C^6), 131.40 (C^7), 132.30 (C^{8a}), 152.20 (C=N)
XLVII	10.75, 16.85, 21.21 (3CH_3), 23.51 (CH_2), 77.17 (CHOH), 87.87 (C^4), 122.61 (C^8), 122.73 (C^5), 122.87 (C^{4a}), 122.98 (C^6), 130.57 (C^7), 133.00 (C^{8a}), 152.45 (C=N)
XLVIII	9.91, 18.37, 19.20, 20.56, 23.27 (5CH_3), 22.49 (CH_2), 77.64 (CHOH), 91.67 (C^4), 122.43 (C^5), 123.66 (C^8), 124.94 (C^{4a}), 126.99 (C^6), 131.65 (C^7), 138.63 (C^{8a}), 171.59 (C=N)
XLIX	9.86, 14.35, 24.92 (3CH_3), 23.37 (CH_2), 60.69 ($C^{1'}$), 63.40 (OCH_2), 66.05 (CHO), 119.99 (C^6), 122.13 (C^4), 125.69 (C^2), 127.08 (C^3), 127.92 (C^5), 137.30 (C^1), 153.62 (C=O)

[a] Mixture of isomers.
[b] In DMF-d_7.

Oxidation of anilides with the system H_2O_2–NaOH–MeOH–MeCN. A solution of 0.2 g of NaOH in a mixture of 5 g of methanol and 5 g of acetonitrile was added to 8.66 mmol of appropriate anilide, and 1 g (29.4 mmol) of 50% hydrogen peroxide (excess) was added dropwise. The reaction was accompanied by evolution of oxygen and by a slight exothermic effect. The mixture was kept for 2 h, 10 ml of a saturated solution of $Na_2S_2O_3$ was added, and the mixture was extracted with methylene chloride. The extract was dried over $MgSO_4$ and evaporated under reduced pressure. To remove tar-like impurities, the yellow oily residue was passed through a column charged with 5 g of silica gel using hexane–ethyl acetate (2 : 1) as eluent.

Compounds **XL**–**XLII** were synthesized by heating a mixture of amine **XXXVII**–**XXXIX** and an equal amount (by weight) of potassium hydroxide for 1 h at 300°C. The products were isolated by fractional distillation under reduced pressure.

Compound **XLV** was obtained by mixing 10 mmol of amine **XLII** with 12 mmol of acetic anhydride on cooling, followed by evaporation of acetic acid and recrystallization of the product from benzene.

Compounds **XLIII** and **XLIV** were synthesized as follows. Ethyl chloroformate, 1.3 g (12 mmol), was added dropwise under vigorous stirring at 20°C to a suspension of 10 mmol of amine **XL** or **XLI** and 2.76 g (20 mmol) of K_2CO_3 in 20 ml of methylene chloride. After 1 h, 2 ml of water was added, the mixture was stirred, the precipitate was filtered off, and the filtrate was washed with water and dried over $MgSO_4$. The solvent was removed under reduced pressure to obtain compounds **XLIII** and **XLIV** as yellow oily substances.

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