Synthesis of *N,N'*-Diacyl-1,2-di-(4-pyridyl)ethylenediamines

M. F. Braña, María L. Lòpez Rodriguez*

Departmento de Química Orgánica, Facultad de Ciencias Químicas Universidad Complutense
Madrid-3, Spain

J. Garrido and C. M. Roldán

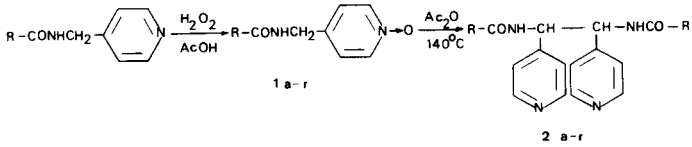
Laboratorios Made, S. A. Avda. de Burgos 91, Madrid-34, Spain

Received March 28, 1981

Reaction of *N*-(4-pyridylmethyl)benzamide *N*-oxides with acetic anhydride yielded dimerization compounds. This dimerization occurs at the atom attached to the pyridine ring. These compounds so obtained were evaluated for analgesic and antiinflammatory activity.

J. Heterocyclic Chem., **18**, 1305 (1981).

Recently (1), we reported the synthesis of *N,N'*-di-(3,5-dimethylbenzoyl)-1,2-di-(4-pyridyl)ethylenediamine by reaction of *N*-(4-pyridylmethyl)-3,5-dimethylbenzamide *N*-oxide with acetic anhydride at 140°. Since this ethylenediamine derivative is a powerful peripheral analgesic (2) agent and in order to confirm the extension of this homolytic dimerization reaction and so as to study the biological action of this series, other *N*-(4-pyridylmethyl)-amide *N*-oxides (**1a-r**) were treated with acetic anhydride under the same conditions to give the corresponding *N,N'*-diacyl-1,2-di-(4-pyridyl)ethylenediamines (**2a-r**) with R = alkyl or aryl groups.



The general method for the synthesis of *N,N'*-diacyl-1,2-di-(4-pyridyl)ethylenediamines (Tables 3 and 4) consists of the reaction of *N*-(4-pyridylmethyl)amide *N*-oxides (Tables 1 and 2) with acetic anhydride under reflux for 1.5 hours.

The synthesis of the *N*-oxides is carried out in good yield by oxidation of the corresponding amides with hydrogen peroxide in acetic acid (3). Amides (4) are obtained by the direct reaction of the corresponding acid with 4-aminomethylpyridine in the presence of dicyclohexylcarbodiimide as condensanting agent in practically quantitative yields. The structures of all compounds were established according to analytical and spectroscopic data (Tables 1-4).

Biological Results.

These compounds were screened for their toxicity. Analgesic activity was assessed by measuring the inhibition of acetic acid induced writhing (5) and were compared with dextropropoxyphene. The antiinflammatory was measured in the carrageenan (6) and ovalbumin (7) induced rat paw edema test and were compared with dexamethasone. Table 5 contains all the biological data.

All these compounds show analgesic action by oral as well as intraperitoneal administration. On the other hand, their toxicity is slight since the LD_{50} is greater than 1 g/Kg for all of them and they are therefore more manageable than the dextropropoxyphene. Although the chemical analgesic with acetic acid is a technique for evaluating analgesics which does not discriminate between their different types, the fact that the majority of the products assayed show antiinflammatory action seems to indicate that antipyretic-antiinflammatory analgesic is being dealt with. To date the compounds **2c** and **2g**, those which show greater analgesic activity by the oral administration, have been chosen for further studies.

EXPERIMENTAL

N-(4-Pyridylmethyl)amides. General Procedure.

A suspension of the carboxylic acid (0.1 mole), 4-aminomethylpyridine (0.05 mole) and dicyclohexylcarbodiimide (0.05 mole) in acetonitrile (150 ml) was stirred at room temperature for 24 hours. The solid product was filtered and the solvent was evaporated *in vacuo*. The residue was acidified with 0.5 normal hydrochloric acid and was then alkalinized with 10% aqueous sodium hydroxide. The amide was isolated by suction, dried and recrystallized.

N-(4-Pyridylmethyl)amide *N*-Oxides (**1a-r**). General Procedure.

To a solution of the corresponding *N*-(4-pyridylmethyl)amide (0.05 mole) in glacial acetic acid (125 ml) was added hydrogen peroxide (20 ml, 40% w/v). The solution was heated at 80° and the completion of the reaction is determined by tlc (silica gel 60 F254, Merck, with benzene:ethanol 9:1 as eluent). The solution was then reduced *in vacuo* to 1/3 of its volume. The residue was alkalinized with 10% sodium hydroxide solution, extracted with chloroform and dried (anhydrous magnesium-sulphate). The solvent was evaporated *in vacuo* to give compounds **1a-r** (except **1c**).

N-(4-Pyridylmethyl)benzamide *N*-Oxide (**1c**).

To a solution (120 g) of acetic anhydride and hydrogen peroxide (90 ml, 40% w/v) was added a solution of *N*-(4-pyridylmethyl)benzamide (30 g, 0.14 mole) in ether (250 ml) with cooling in ice. The mixture was stirred for a week at room temperature. The solution was then reduced *in*

0022-152X/81/071305-04$02.25

Table 1

N-(4-Pyridylmethyl)amide *N*-Oxides **1a-r**

Product	R	Yield %	mp °C (a) (solvent)	Molecular formula	IR (KBr) (b) cm^{-1} NH	C=O	N-O	Found % C	H	N	Calcd. % C	H	N
1a	CH_3	45	165-167 (absolute ethanol)	$C_8H_{10}N_2O_2$ (150.1)	3100	1670	1220	57.58	6.12	16.70	57.82	6.06	16.85
1b	$(CH_3CH_2CH_2)_2$-CH	60	143-145 (chloroform-hexane)	$C_{14}H_{22}N_2O_2$ (250.3)	3260	1630	1240	66.93	8.83	10.98	67.16	8.83	11.99
1c	C_6H_5-CH_2	73	194-195 (ethanol)	$C_{14}H_{14}N_2O_2$ (242.3)	3260	1640	1240	69.68	5.71	11.38	69.40	5.82	11.56
1d	C_6H_5	65	92-94 (ethyl acetate)	$C_{13}H_{12}N_2O_2$ (228.2)	3300	1650	1215	68.27	5.49	12.27	68.08	5.60	12.07
1e	4-CH_3-C_6H_4	55	173-174 (ethyl acetate)	$C_{14}H_{14}N_2O_2$ (242.3)	3300	1640	1230	69.45	5.98	11.85	69.40	5.82	11.56
1f	3-CH_3-C_6H_4	60	138-140 (chloroform-hexane)	$C_{14}H_{14}N_2O_2$ (242.3)	3240	1650	1220	69.16	6.08	11.77	69.40	5.82	11.56
1g	2-CH_3-C_6H_4	65	196-198 (chloroform-hexane)	$C_{14}H_{14}N_2O_2$ (242.3)	3200	1650	1220	69.21	5.89	11.71	69.40	5.82	11.56
1h	4-tC_4H_9-C_6H_4	70	192-193 (ethyl acetate)	$C_{17}H_{20}N_2O_2$ (284.4)	3230	1640	1240	71.67	7.09	9.84	71.80	7.08	9.85
1i	4-CH_3O-C_6H_4	73	172-175 (ethanol)	$C_{14}H_{14}N_2O_3$ (258.3)	3260	1650	1220	64.86	5.23	10.56	65.10	5.46	10.84
1j	4-CH_3SO_2-C_6H_4	60	243-244 (methanol)	$C_{14}H_{14}N_2O_4S$ (306.3)	3100	1650	1230	54.76	4.65	9.40 (S, 10.50)	54.89	4.60	9.14 (S, 10.45)
1k	4-NO_2-C_6H_4	70	245-246 (ethanol)	$C_{13}H_{11}N_3O_4$ (273.2)	3200	1660	1220	57.11	4.19	15.20	57.13	4.06	15.37
1l	4-C_6H_5-C_6H_4	70	220-221 (ethanol)	$C_{19}H_{16}N_2O_2$ (304.3)	3320	1640	1240	74.71	5.13	8.99	74.98	5.29	9.20
1m	4-Cl-C_6H_4	79	166-168 (chloroform-hexane)	$C_{13}H_{11}ClN_2O_2$ (262.7)	3230	1630	1230	59.16	4.27	10.44 (Cl, 13.69)	59.45	4.19	10.67 (Cl, 13.49)
1n	3-Cl-C_6H_4	50	132-135 (dioxane)	$C_{13}H_{11}ClN_2O_2$ (262.7)	3160	1650	1225	59.35	4.37	10.81 (Cl, 13.61)	59.45	4.19	10.67 (Cl, 13.49)
1o	2-Cl-C_6H_4	70	222-225 (ethanol)	$C_{13}H_{11}ClN_2O_2$ (262.7)	3140	1650	1220	59.22	4.27	10.69 (Cl, 13.27)	59.45	4.19	10.67 (Cl, 13.49)
1p	3,5-Cl_2-C_6H_5	69	210-213 (ethanol)	$C_{13}H_{10}Cl_2N_2O_2$ (297.0)	3340	1660	1230	52.70	3.60	9.25 (Cl, 24.13)	52.52	3.36	9.42 (Cl, 23.90)
1q	4-F-C_6H_4	60	168-169 (chloroform-hexane)	$C_{13}H_{11}FN_2O_2$ (246.2)	3230	1640	1240	63.67	4.51	11.38	63.41	4.47	11.38
1r	4-F_3C-C_6H_4	80	192-193 (dioxane)	$C_{14}H_{11}F_3N_2O_2$ (292.2)	3240	1660	1230	56.55	3.91	9.73	56.75	3.71	9.45

(a) The melting points were obtained on a Büchi apparatus and are uncorrected. (b) Measured on a Perkin-Elmer 257 spectrophotometer.

Table 2

^{1}H-NMR (a) Spectra of Products **1a-r**

Product	Solvent	Chemical Shifts δ ppm
1a	CF_3COOH	2.40 (s, 3H, CH_3); 4.80 (d, 2H, CH_2); 7.90 (d, 2H, 2H β-py); 8.40 (d, 2H, 2H α-py)
1b	$CDCl_3$	0.90 (m, 6H, $2CH_3$); 1.15-1.70 (m, 8H, $4CH_2$); 2.20 (m, 1H, CH); 4.30 (d, 2H, CH_2-py); 6.90 (m, 3H, 2H β-py, NH); 7.80 (d, 2H, 2H α-py).
1c	DMSO-d_6	3.40 (s, 2H, CH_2CO); 4.15 (d, 2H, NCH_2); 7.00 (d, 2H, 2H β-py); 7.15 (s, 5H, 5H-ph); 7.95 (d, 2H, 2H α-py); 8.35 (s-broad, 1H, NH).
1d	DMSO-d_6	4.50 (d, 2H, CH_2); 7.40 (d, 2H, 2H β-py); 7.60-8.10 (m, 5H, 5H-ph); 8.30 (d, 2H, 2H α-py); 9.20 (t, 1H, NH).
1e	$CDCl_3$	2.45 (s, 3H, CH_3); 4.60 (d, 2H, CH_2); 7.10-7.50 (m, 4H, 2H β-py, 2H *m*-ph); 7.80-8.20 (m, 5H, 2H, *o*-ph, 2H, α-py, NH).
1f	$CDCl_3$	2.40 (s, 3H, CH_3); 4.60 (d, 2H, CH_2); 7.10-7.50 (m, 4H, 2H β-py, 1H *p*-ph, 1H *m*-ph); 7.70-8.10 (m, 5H, 2H *o*-ph, 2H α-py, NH).
1g	DMSO-d_6	2.35 (s, 3H, CH_3); 4.40 (d, 2H, CH_2); 7.20 (m, 6H, 4H-ph, 2H β-py); 8.10 (d, 2H, 2H α-py); 8.75 (t, 1H, NH).
1h	$CDCl_3$	1.30 (s, 9H, $C(CH_3)_3$); 4.45 (d, 2H, CH_2); 6.80-7.30 (m, 4H, 2H β-py, 2H *m*-ph); 7.60-8.00 (m, 5H, 2H *o*-ph, 2H α-py, NH).
1i	DMSO-d_6	3.75 (s, 3H, OCH_3); 4.40 (d, 2H, CH_2); 6.85 (d, 2H, 2H *m*-ph); 7.15 (d, 2H, 2H β-py); 7.75 (d, 2H, 2H *o*-ph); 8.00 (d, 2H, 2H α-py); 8.80 (t, 1H, NH).
1j	DMSO-d_6	3.30 (s, 3H, CH_3); 4.50 (d, 2H, CH_2); 7.40 (d, 2H, 2H β-py); 8.20 (m, 6H, 4H-ph, 2H α-py); 9.45 (t, 1H, NH).
1k	DMSO-d_6	4.45 (d, 2H, CH_2); 7.30 (d, 2H, 2H β-py); 7.90-8.30 (m, 6H, 4H-ph, 2H α-py); 9.40 (t, 1H, NH).
1l	DMSO-d_6	4.40 (d, 2H, CH_2); 7.15 (d, 2H, 2H β-py); 7.20-7.80 (m, 9H, 9H-ph); 8.00 (d, 2H, 2H α-py); 9.10 (t, 1H, NH).
1m	DMSO-d_6	4.45 (d, 2H, CH_2); 7.20 (d, 2H, 2H β-py); 7.40 (d, 2H, 2H *m*-ph); 7.80 (d, 2H, 2H *o*ph); 8.05 (d, 2H, 2H α-py).
1n	DMSO-d_6	4.40 (d, 2H, CH_2); 7.10-7.50 (m, 4H, 2H β-py, 1H *p*-ph, 1H *m*-ph); 7.80 (m, 2H, 2H *o*-ph); 8.10 (d, 2H, 2H α-py); 9.10 (t, 1H, NH).
1o	CF_3COOH	4.95 (d, 2H, CH_2); 7.30 (s, 4H, 4H-ph); 7.90 (d, 3H, 2H β-py, NH); 8.55 (d, 2H, 2H α-py).
1p	DMSO-d_6	4.35 (d, 2H, CH_2); 7.15 (d, 2H, 2H β-py); 7.65 (m, 3H, 3H-ph); 8.00 (d, 2H, 2H α-py); 9.20 (t, 1H, NH).
1q	DMSO-d_6	4.45 (d, 2H, CH_2); 7.25 (m, 4H, 2H β-py, 2H *m*-ph); 7.90 (m, 2H, 2H *o*-ph); 8.10 (d, 2H, 2H α-py); 9.10 (t, 1H, NH).
1r	DMSO-d_6	4.40 (d, 2H, CH_2); 7.20 (d, 2H, 2H *m*-ph); 7.70 (d, 2H, 2H β-py); 8.00 (m, 4H, 2H *o*-ph, 2H α-py).

(a) Measured on a Varian T-60 A spectrometer.

Table 3

N,N'-Diacyl-1,2-di-(4-pyridyl)ethylenediamines **2a-r**

Product	R	Yield %	mp °C (a) (solvent)	Molecular formula	(M$^+$) (b)	IR (KBr) (c) cm^{-1} NH	IR (KBr) (c) cm^{-1} C=O	Found % C	Found % H	Found % N	Calcd. % C	Calcd. % H	Calcd. % N
2a	CH_3	20	308 (DMF)	$C_{16}H_{18}N_4O_2$	(298)	3300	1650	64.17	6.13	18.63	64.41	6.08	18.78
2b	$(CH_3CH_2CH_2)_2$-CH	43	339 (EtOH)	$C_{28}H_{42}N_4O_2$	(466)	3300	1640	72.31	8.94	11.78	72.06	9.07	12.00
2c	C_6H_5-CH_2	22	312 (DMF)	$C_{28}H_{26}N_4O_2$	(450)	3320	1650	74.59	5.86	12.37	74.64	5.81	12.43
2d	C_6H_5	26	298 (DMF)	$C_{26}H_{22}N_4O_2$	(422)	3340	1635	74.01	5.15	12.97	73.91	5.24	13.26
2e	4-CH_3-C_6H_4	44	291 (DMF)	$C_{28}H_{26}N_4O_2$	(450)	3220	1640	74.39	6.08	12.60	74.64	5.81	12.43
2f	3-CH_3-C_6H_4	41	275 (DMF-H_2O)	$C_{28}H_{26}N_4O_2$	(450)	3300	1640	74.87	5.63	12.60	74.64	5.81	12.43
2g	2-CH_3-C_6H_4	39	339 (DMF)	$C_{28}H_{26}N_4O_2$	(450)	3300	1630	74.80	5.75	12.62	74.64	5.81	12.43
2h	4-tC_4H_9-C_6H_4	70	305 (DMF)	$C_{34}H_{38}N_4O_2$	(534)	3280	1650	76.30	6.89	10.53	76.37	7.16	10.47
2i	4-CH_3O-C_6H_4	44	299 (DMF-H_2O)	$C_{28}H_{26}N_4O_4$	(482)	3260	1640	69.44	5.14	11.41	69.69	5.43	11.61
2j	4-CH_3SO_2-C_6H_4	64	287 (DMF-MeOH)	$C_{28}H_{26}N_4O_6S_2$	(578)	3240	1650	57.93	4.26	9.39 (S, 11.09)	58.12	4.53	9.68 (S, 11.09)
2k	4-NO_2-C_6H_4	54	312 (DMF-H_2O)	$C_{26}H_{20}N_6O_6$	(512)	3340	1650	60.80	4.04	16.11	60.93	3.93	16.40
2l	4-C_6H_5-C_6H_4	40	326 (DMF)	$C_{38}H_{30}N_4O_2$	(574)	3340	1630	79.20	5.44	10.04	79.41	5.26	9.75
2m	4-Cl-C_6H_4	39	323 (DMF)	$C_{26}H_{20}Cl_2N_4O_2$	(491)	3300	1630	63.42	4.24	11.13 (Cl, 14.71)	63.54	4.07	11.40 (Cl, 14.46)
2n	3-Cl-C_6H_4	37	297 (DMF-H_2O)	$C_{26}H_{20}Cl_2N_4O_2$	(491)	3300	1635	63.36	4.30	11.26 (Cl, 14.30)	63.54	4.07	11.40 (Cl, 14.46)
2o	2-Cl-C_6H_4	39	308 (DMF)	$C_{26}H_{20}Cl_2N_4O_2$	(491)	3300	1640	63.42	4.15	11.48 (Cl, 14.66)	63.54	4.07	11.40 (Cl, 14.46)
2p	3,5-Cl_2-C_6H_3	38	275 (DMF)	$C_{26}H_{18}Cl_4N_4O_2$	(560)	3300	1640	55.51	3.50	10.20 (Cl, 25.09)	55.71	3.21	10.00 (Cl, 25.35)
2q	4-F-C_6H_4	33	288 (DMF-MeOH)	$C_{26}H_{20}F_2N_4O_2$	(458)	3300	1650	67.94	4.14	12.44	68.12	4.36	12.22
2r	4-F_3C-C_6H_4	38	316 (DMF)	$C_{28}H_{20}F_6N_4O_2$	(558)	3300	1640	60.03	3.50	9.95	60.21	3.58	10.08

(a) The melting points were obtained on a E. Bühler apparatus and are uncorrected. (b) Measured on a Varian Mat 711 spectrometer. (c) Measured on a Perkin-Elmer 257 spectrophotometer.

Table 4

^{1}H NMR (a) Spectra of Products **2a-r**

Product	Chemical Shifts (CF_3COOH δ ppm)
2a	2.00 (s, 6H, $2CH_3$); 6.20 (s, 2H, 2CH); 8.35 (d, 4H, 4H β-py); 8.90 (d, 4H, 4H α-py).
2b	0.70-1.00 (m, 12H, $4CH_3$); 1.20-1.60 (m, 16H, $8CH_2$); 2.20 (m, 2H, 2CHCO); 6.35 (m, 2H, 2CH); 7.85 (m, 2H, 2NH); 8.20 (d, 4H, 4H β-py); 8.45 (d, 4H, 4H α-py).
2c	3.65 (d, 4H, $2CH_2$); 6.25 (d, 2H, 2CH); 7.10 (m, 4H, 4H *o*-ph); 7.40 (m, 6H, 2H *p*-ph, 4H *m*-ph); 8.25 (m, 4H, 4H β-py); 8.75 (m, 4H, 4H α-py).
2d	6.80 (s, 2H, 2CH); 7.50-7.80 (m, 10H, 10H-ph); 8.70 (d, 4H, 4H β-py); 9.00 (d, 4H, 4H α-py).
2e	(b)
2f	2.00 (s, 6H, $2CH_3$); 6.40 (s, 2H, 2CH); 7.00 (d, 8H, 8H-ph); 8.25 (d, 4H, 4H β-py); 8.65 (d, 4H, 4H α-py).
2g	1.90 (s, 6H, $2CH_3$); 6.40 (s, 2H, 2CH); 6.65-7.20 (m, 8H, 8H, ph); 8.45 (d, 4H, 4H β-py); 8.65 (d, 4H, 4H α-py).
2h	1.35 (s, 18H, $2C(CH_3)_3$); 4.20 (s, 2H, 2CH); 7.75 (q, 8H, 8H, ph); 8.15 (d, 4H, 4H β-py); 8.80 (d, 4H, 4H α-py).
2i	3.97 (s, 6H, $2OCH_3$); 6.70 (s, 2H, 2CH); 7.15 (m, 4H, 4H *m*-ph); 7.70-8.90 (m, 12H, 4H *o*-ph, 8H-py).
2j	3.29 (s, 6H, $2CH_3$); 6.78 (s, 2H, 2CH); 8.00-8.95 (m, 16H, 8H-ph, 8H-py).
2k	6.70 (s, 2H, 2CH); 7.73-8.95 (m, 16H, 8H-ph, 8H-py).
2l	(b)
2m	6.67 (s, 2H, 2CH); 7.50 (q, 8H, 8H-ph); 8.60 (d, 4H, 4H β-py); 8.95 (d, 4H, 4H α-py).
2n	6.20 (s, 2H, 2CH); 6.80-7.10 (m, 8H, 8H-ph); 8.10 (d, 4H, 4H β-py); 8.45 (d, 4H, 4H α-py).
2o	(b)
2p	6.75 (s, 2H, 2CH); 7.55-7.75 (m, 6H, 6H-ph); 8.65 (d, 4H, 4H β-py); 9.00 (d, 4H, 4H α-py).
2q	6.80 (s, 2H, 2CH); 7.00 (d, 4H, 4H *m*-ph); 7.60 (m, 4H, 4H *o*-ph); 7.85 (d, 4H, 4H β-py); 8.50 (d, 4H, 4H α-py).
2r	6.80 (s, 2H, 2CH); 7.80 (s, 8H, 8H-ph); 8.60 (d, 4H, 4H β-py); 8.95 (d, 4H, 4H α-py).

(a) Measured on a Bruker WH 90 MHz spectrometer. (b) Compound very insoluble.

vacuo to 100 ml and alkalinized with 10% aqueous sodium hydroxide to give **1c**.

N,N'-Diacyl-1,2-di-(4-pyridyl)ethylenediamine (**2a-r**). General Procedure.

A solution of *N*-(4-pyridylmethyl)amide *N*-oxide (5 g) in 35 ml of acetic anhydride was refluxed at 140° for 1.5 hours, the precipitate was collected, washed with ethyl acetate and recrystallized to give **2a-r**.

Acknowledgement.

This work was supported by the grants given to one of the authors (M. L. L. R.) from the Ministry of Education and Science of Spain, which is gratefully acknowledged, as well as Professor Dr. A. García Martinez for mass spectra.

REFERENCES AND NOTES

(1) M. F. Braña and M. L. L. Rodriguez, *Tetrahedron Letters*, **21**, 3923 (1980).

(2) C. M. Roldán and J. Garrido, unpublished results.

(3) A. R. Katritzky and J. M. Lagowski, "Chemistry of Heterocyclic *N*-Oxides", Academic Press, London, 1971.

(4) M. F. Braña, M. L. L. Rodriguez and R. L. Arenosa, *An. Quim.*, in press.

(5) E. A. Siegmund, A. Cadmus and G. Lu, *J. Pharmacol. Exp. Ther.*, **119**, 453 (1957).

(6) E. Arrigoni-Martelli and I. Corti, *Farmaco, Ed. Prat.*, **19**, 134 (1964).

(7) C. A. Winter, E. A. Risley and G. V. Nuss, *J. Pharmacol.*, **141**, 369 (1963).

Table 5

Biological Activity of *N,N'*-Diacyl-1,2-di-(4-pyridyl)-ethylenediamines (a)

Product	LD_{50}, mg/Kg (mice, ip) (b)	Analgesic Activity (c) 1 mg/Kg (mice, ip)	Analgesic Activity (c) 5 mg/Kg (mice, po)	Antiinflammatory Activity (d) (rats) Carrageenan 1st h	Carrageenan 3rd h	Carrageenan 24th h	Ovalbumin 1st h	Ovalbumin 3rd h
2a	1124,9	1,01	0,85	0,00	0,59	0,00	NT (e)	NT
2b	>1200	1,43	0.95	NT	NT	NT	0,00	0,00
2c	>1200	0,96	2,13	1,09	0,64	0,55	0,59	0,09
2d	>1200	1,21	1,35	3,00	1,63	0,20	0,60	0,69
2e	>1200	1,04	1,11	1,15	0,60	0,02	0,71	0,77
2f	>1200	1,05	1,64	0,82	0,60	0,31	0,20	0,26
2g	>1200	1,09	1,67	0,72	0,00	0,01	0,54	0,36
2h	>1200	1,11	1,17	1,38	1,84	0,49	1,00	0,90
2i	>1200	1,09	1,23	2,00	0,90	0,11	1,00	1,00
2j	>1200	1,43	1,05	-	1,40	0,21	0,00	0,04
2k	>1200	1,38	1,25	0,98	0,65	0,20	0,00	0,08
2l	>1200	1,08	1,13	0,00	1,09	0,47	0,00	0,00
2m	>1200	1,58	1,29	0,72	0,00	0,01	0,77	0,36
2n	>1200	1,08	1,05	1,09	0,98	0,41	0,78	0,68
2o	1064,3	1,37	1,34	1,14	1,28	0,58	0,40	0,35
2p	>1200	0,84	1,22	1,43	1,04	0,27	0,48	0,42
2q	1107,7	1,17	0,81	2,50	1,19	0,47	1,27	0,81
2r	>1200	1,38	1,19	0,67	0,23	0,00	0,34	0,42
Dextropropoxiphene	98	1,00	1,00					
Dexamethasone	NT			1,00	1,00	1,00	1,00	1,00

(a) All compounds were suspended in a 5% aqueous solution of arabic gum. (b) Albino mice (ICR-Swiss). (c) Effect measured as analgesic effect compound/analgesic effect dextropropoxiphene (dose, 25 mg/Kg). (d) Effect measured as antiinflammatory effect compound/antiinflammatory effect dexamethasone (dose, 5 mg/Kg). (e) NT = Not tested.