Synthesis of Substituted 2-Ethyl-3-(4-hydrazinocarbonylphenyl)-4-quinazolones and 2-Ethyl-3-(4-hydrazinocarbonylmethylphenyl)-4-quinazolones

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Received November 28, 1977

Some substituted 2-ethyl-3-(4-hydrazinocarbonylphenyl)-4-quinazolones and 2-ethyl-3-(4-hydrazinocarbonylmethylphenyl)-4-quinazolones were synthesized and characterized by their sharp melting points, elemental analyses and spectral data.

J. Heterocyclic Chem., 15, 869 (1978)

The ability of 2-methyl-3-*o*-tolyl-4-quinazolone (methaqualone) to possess anticonvulsant (2) and hypnotics (3) properties and several substituted quinazolone hydrazides exhibiting monoamine oxidase inhibitory activity (4-6) led to the synthesis of some hydrazides having quinazolone moiety. The various substituted 2-ethyl-3-(4-hydrazinocarbonyl/hydrazinocarbonylmethylphenyl)-4-quinazolones were prepared according to the steps outlined in Scheme 1.

Table I

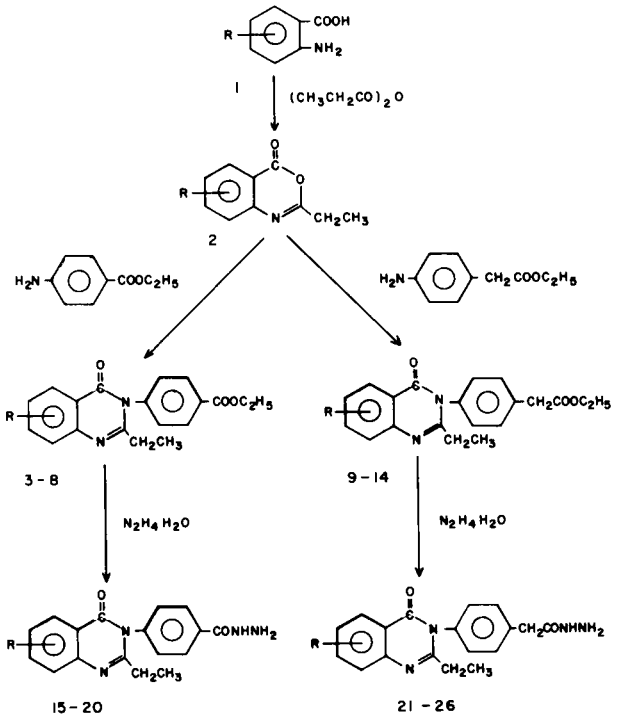
Physical Constants of Substituted 2-Ethyl-3-(4-ethoxycarbonyl/ethoxycarbonylmethylphenyl)-4-quinazolones

Compound	R	M.p. °C	Yield %	Formula	Analysis % Calculated C	Calculated H	Calculated N	Found C	Found H	Found N
3	H	180	55	$C_{19}H_{18}N_2O_3$	70.80	5.59	8.69	70.52	5.60	8.50
4	6-Cl	152-154	55	$C_{19}H_{17}ClN_2O_3$	63.95	4.76	7.85	64.17	4.80	7.60
5	6-Br	156	50	$C_{19}H_{17}BrN_2O_3$	56.85	4.23	6.98	56.64	4.10	6.80
6	6-I	155	60	$C_{19}H_{17}IN_2O_3$	50.89	3.79	6.25	51.20	3.81	6.60
7	6,8-Cl_2	183	42	$C_{19}H_{16}Cl_2N_2O_3$	58.31	4.09	7.16	58.51	4.31	6.90
8	6,8-Br_2	175	55	$C_{19}H_{16}Br_2N_2O_3$	47.50	3.33	5.83	47.82	3.41	6.00
9	H	142-144	50	$C_{20}H_{20}N_2O_3$	71.42	5.98	8.33	71.54	5.78	8.12
10	6-Cl	175	40	$C_{20}H_{19}ClN_2O_3$	64.17	5.12	7.55	64.50	5.23	7.80
11	6-Br	140	55	$C_{20}H_{19}BrN_2O_3$	57.83	4.57	6.74	57.58	4.12	6.45
12	6-I	142	65	$C_{20}H_{19}IN_2O_3$	51.94	4.11	6.06	51.78	4.00	5.82
13	6,8-Cl_2	180	50	$C_{20}H_{18}Cl_2N_2O_3$	58.96	4.42	6.87	58.78	4.38	6.51
14	6,8-Br_2	192	55	$C_{20}H_{18}Br_2N_2O_3$	48.38	3.62	5.64	48.29	3.54	5.30

Table II

Physical Constants of Substituted 2-Ethyl-3-(4-Hydrazinocarbonyl/hydrazinocarbonylmethylphenyl)-4-quinazolones

Compound	R	M.p. °C	Yield %	Formula	Analysis % Calculated C	Calculated H	Calculated N	Found C	Found H	Found N
15	H	170-172	52	$C_{17}H_{16}N_4O_2$	66.23	5.19	18.18	66.54	5.40	18.41
16	6-Cl	178	48	$C_{17}H_{15}ClN_4O_2$	59.56	4.37	16.35	59.54	4.40	16.70
17	6-Br	120-123	53	$C_{17}H_{15}BrN_4O_2$	52.71	3.87	14.47	52.58	3.60	14.70
18	6-I	198	50	$C_{17}H_{15}IN_4O_2$	47.00	3.45	12.90	47.12	3.60	13.20
19	6,8-Cl_2	210	50	$C_{17}H_{14}Cl_2N_4O_2$	54.11	3.71	14.85	54.41	4.20	15.00
20	6,8-Br_2	189	52	$C_{17}H_{14}Br_2N_4O_2$	43.77	3.00	12.01	43.75	3.11	11.90
21	H	115	45	$C_{18}H_{18}N_4O_2$	67.08	5.59	17.39	67.32	6.00	17.12
22	6-Cl	205	45	$C_{18}H_{17}ClN_4O_2$	60.58	4.76	15.70	60.49	4.67	15.60
23	6-Br	225	60	$C_{18}H_{17}BrN_4O_2$	53.86	4.23	13.96	53.68	4.12	13.72
24	6-I	205	60	$C_{18}H_{17}IN_4O_2$	48.21	3.79	12.50	48.37	3.81	12.80
25	6,8-Cl_2	209	50	$C_{18}H_{16}Cl_2N_4O_2$	53.70	4.09	14.32	53.81	4.00	14.00
26	6,8-Br_2	235	50	$C_{18}H_{16}Br_2N_4O_2$	45.00	3.33	11.66	45.12	3.22	11.20



SCHEME 1

Substituted acetanthranils **2** (7) were prepared by refluxing appropriate anthranilic acid **1** (8-10) with propionic anhydride. The condensation of ethyl *p*-aminobenzoate and ethyl *p*-aminophenylacetate with **2** resulted in substituted 2-ethyl-3-(4-ethoxycarbonylphenyl)-4-quinazolones **3-8** and substituted 2-ethyl-3-(4-ethoxycarbonylmethylphenyl)-4-quinazolones **9-14**, respectively. The quinazolone esters **3-8** and **9-14** on refluxing with hydrazine hydrate in absolute ethanol yielded substituted 2-ethyl-3-(4-hydrazinocarbonylphenyl)-4-quinazolones **15-20** and substituted 2-ethyl-3-(4-hydrazinocarbonylmethylphenyl)-4-quinazolones **21-26**, respectively.

EXPERIMENTAL

All compounds were analyzed for their carbon, hydrogen and nitrogen contents. Melting points were taken in an open capillary tubes with an immersion thermometer and are corrected. The infrared and nuclear magnetic resonance spectra of **3**, **9**, **15** and **21** were recorded in the support of their structure.

The infrared spectra were obtained in nujol mull suspension on Beckman IR-33 and nuclear magnetic resonance spectra were recorded in DMSO-d_6 using tetramethylsilane as a standard on EM-390 spectrometer.

Substituted Acetanthranils **2**.

A mixture of **1** (0.1 mole) and propionic anhydride (0.2 mole) was refluxed under anhydrous condition on a free flame for 1 hour. The excess of propionic anhydride was removed by distillation under reduced pressure. The various acetanthranils (9) which separated out as solid mass were used for the preparation of substituted quinazolones **3-14** without further purification.

Substituted 2-Ethyl-3-(4-ethoxycarbonyl/ethoxycarbonylmethylphenyl)-4-quinazolones **3-14**.

Following the method reported earlier (6), equimolar quantities of **2** (0.1 mole) and ethyl *p*-aminobenzoate (0.1 mole) or ethyl *p*-aminophenylacetate (0.1 mole) was refluxed for 1 hour. The jelly-like mass, on work up and recrystallization from ethanol, yielded **3-14**. These compounds were characterized by their sharp melting points and elemental analyses (Table 1). Their structure was further supported by the presence of the characteristic bands in ir and various signals in nmr spectra of **3** and **9**.

2-Ethyl-3-(4-ethoxycarbonylphenyl)-4-quinazolone (**3**).

This compound had ir: $COOC_2H_5$ (1710 cm^{-1}) and *CO*N (1680 cm^{-1}); nmr: δ 1.10 (t, 3H, CH_2CH_3), 2.30 (q, 2H, CH_2CH_3), 1.33 (t, 3H, $COOCH_2CH_3$), 4.33 (q, 2H, $COOCH_2CH_3$) and 7.30-8.30 (m, 8H, aromatic protons).

2-Ethyl-3-(4-ethoxycarbonylmethylphenyl)-4-quinazolone (**9**).

This compound had ir: $COOC_2H_5$ (1730 cm^{-1}) and *CO*N (1680 cm^{-1}); nmr: δ 1.11 (t, 3H, CH_2CH_3), 2.33 (q, 2H, CH_2CH_3), 1.23 (t, 3H, $COOCH_2CH_3$), 4.13 (q, 2H, $COOCH_2CH_3$), 3.70 (s, 2H, CH_2COO) and 7.00-8.00 (m, 8H, aromatic protons).

Substituted 2-Ethyl-3-(4-hydrazinocarbonyl/hydrazinocarbonylmethylphenyl)-4-quinazolones **15-26**.

Appropriate quinazolone esters **3-14** (0.1 mole) and hydrazine hydrate (0.2 mole) in 200 ml. of absolute ethanol were refluxed on a water bath for 8-10 hours (6). The excess of ethanol was removed under reduced pressure and the crude product thus obtained was washed several times with water, dried and recrystallized from ethanol. The physical properties of various quinazolone hydrazides **15-26** are recorded in Table II.

The ir and nmr spectral data of **15** and **21** supported their structural proof.

2-Ethyl-3-(4-hydrazinocarbonylphenyl)-4-quinazolone (**15**).

This compound had ir: *CO*N (1680 cm^{-1}), CON*H* (3310 cm^{-1}) and $CONHNH_2$ (3250 cm^{-1}); nmr: δ 1.33 (t, 3H, CH_2CH_3), 2.60 (q, 2H, CH_2CH_3), 5.70 (s, 2H, $CONH_2$) and 7.30-8.20 (m, 9H, $CONHNH_2$ and aromatic protons).

2-Ethyl-3-(4-hydrazinocarbonylmethylphenyl)-4-quinazolone (**21**).

This compound had ir: CON (1650 cm^{-1}), CO*NH* (3300 cm^{-1}) and $CONHNH_2$ (3230 cm^{-1}); nmr: δ 1.30 (t, 3H, CH_2CH_3), 2.90 (q, 2H, CH_2CH_3), 3.3 (s, 2H, CH_2CONH), 5.70 (s, 2H, $CONHNH_2$), 9.16 (s, 1H, $CONHNH_2$) and 7.00-8.00 (m, 8H, aromatic protons).

Acknowledgment.

This investigation was supported in part by the United States Public Health Service NIDA Grant 7-R01-DA01893-01 and a research grant from the American Parkinson Disease Association. Grateful acknowledgment is made to the Northwest Area Foundation, Saint Paul, Minnesota for providing a Hill Professorship to S. S. Parmar.

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