Experimental Section[2]

5,6-Dihydro-7*H*,12*H*-6-carbamyldibenz[*c*,*f*]azocine (1).—A soln of KCNO (3.57 g, 0.044 mole) in H_2O (55 ml) was added to a soln of 5,6-dihydro-7*H*,12*H*-dibenz[*c*,*f*]azocine·HCl[3] (10.8 g, 0.044 mole) in H_2O (6500 ml). After 15 days stirring at room temp, the reaction mixture afforded, when concd, a solid which was recrystd from EtOH to give **1** (6.6 g, 59.4%) as colorless crystals, mp 237–239°. *Anal.* ($C_{16}H_{16}N_2O$) C, H, N.

5,7,12,13-Tetrahydro-6-carbamyldibenz[*c*,*g*]azonine (2).—Compound **2** was obtained similarly in 73.2% yield from 5,7,12,13-tetrahydro-6*H*-dibenz[*c*,*g*]azonine·HCl[4] (12 g, 0.046 mole) and KCNO (3.75 g, 0.046 mole) in H_2O (2000 ml). Colorless crystals from 95% EtOH, mp 194–196°. *Anal.* ($C_{17}H_{18}N_2O$) C, H, N.

1-Cyano-2,3-diphenylaziridine (3).—A soln of BrCN (20.36 g, 0.19 mole) in Et_2O (80 ml) was dropped at 0–5° for 20 min into a soln of *cis*-2,3-diphenylaziridine[5] (31.2 g, 0.16 mole) and Et_3N (19.4 g, 0.19 mole) in Et_2O (400 ml). The mixture was stirred for 4 hr at room temp and then filtered, the cake was repeatedly washed with Et_2O, and the combined filtrates were evapd to dryness. The residue was taken up with hexane and filtered to give **3** (33 g, 94%) as a colorless solid, mp 116–117°. *Anal.* ($C_{15}H_{12}N_2$) C, H, N.

1-Carbamyl-2,3-diphenylaziridine (4).—A mixture of **3** (41.3 g, 0.187 mole), NaOH (75 g), H_2O (130 ml), and dioxane (950 ml) was stirred for 7 days at room temp and then for 24 hr at 50°. The resulting cloudy soln was evapd to dryness under reduced pressure, and the residue was taken up with H_2O and little Et_2O and then recrystd from C_6H_6 to give **4** (11.2 g, 25%) as colorless crystals, mp 158–160°. *Anal.* ($C_{15}H_{14}N_2O$) C, H, N.

(2) Melting points are corrected and were taken on a Büchi capillary melting point apparatus. All compounds were analyzed for C, H, N and anal. results were within ±0.4% of the theoretical values.

(3) G. Pala, A. Mantegani, and E. Zugna, *Tetrahedron*, **26**, 1275 (1970).

(4) G. Pala, E. Crescenzi, and G. Bietti, *ibid.*, in press.

(5) A. Weissberger and H. Bach, *Chem. Ber.*, **64B**, 1095 (1931).

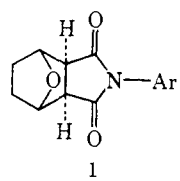
Some Derivatives of 7-Oxabicyclo[2.2.1]heptane-*exo*-*cis*-2,3-dicarboxylic Acid

Samuel J. Dominianni* and Ronald L. Young

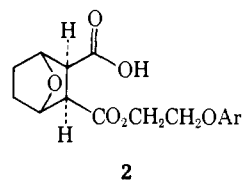
The Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, Indiana 46206

Received August 15, 1970

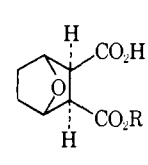
Recently some 7-oxabicyclo[2.2.1]heptane-2,3-dicarboximides (**1**) with anticonvulsant activity were described.[1] Some aryloxyethyl esters **2** were also reported[2] as plant growth regulators. We record herein the preparation of additional examples of **1** and of some mono esters **3**, all of which proved to be highly toxic CNS depressants (Table I).



1



2



3

Experimental Section

***N*-Fluoroarylimides. 1.**—A mixture of equimolar amts of 7-oxabicyclo[2.2.1]heptane-*exo*-*cis*-2,3-dicarboxylic anhydride and the appropriate fluoroaniline was heated without solvent at 150° for 1–2 hr. The cooled residue was then recrystd from EtOH.

Monoesters. 3.—A mixture of anhydride and the appropriate alcohol was heated at 125° for 1–2 hr. The cooled residue was extd with aq Na_2CO_3 and the aq extracts were acidified with HCl. The ppt was collected, washed with H_2O, dried, and recrystd from an appropriate solvent, usually C_6H_6–Skelly B.

The *i*-Pr deriv **3a** was prepared by refluxing the anhydride in *i*-PrOH containing pyridine.

Table I

Compd	R or Ar	Formula[a]	Mp,[b] °C	Approx[c] LD, mg/kg
1a	*o*-FC_6H_4	$C_{14}H_{12}FNO_3$	135–137	1000
1b	*m*-FC_6H_4	$C_{14}H_{12}FNO_3$	136–138	300
1c	*p*-FC_6H_4	$C_{14}H_{12}FNO_3$	168–169	300
3a	$(CH_3)_2CH$	$C_{11}H_{16}O_5$	127–129	300
3b	*o*-$CH_3OC_6H_4CH_2$	$C_{16}H_{18}O_6$	98–100	30
3c	*m*-$CH_3OC_6H_4CH_2$	$C_{16}H_{18}O_6$	127–128	30
3d	*p*-$CH_3OC_6H_4CH_2$	$C_{16}H_{18}O_6$	110–112	10
3e	$C_6H_5CH_2$	$C_{15}H_{16}O_5$	122–124	30
3f	*m*-$ClC_6H_4CH_2$	$C_{15}H_{15}ClO_5$	143–145	30
3g	*p*-$ClC_6H_4CH_2$	$C_{15}H_{15}ClO_5$	158–160	30
3h	*p*-$FC_6H_4CH_2$	$C_{15}H_{15}FO_5$	135–136	10
3i	3,4-$(OCH_2O)C_6H_3CH_2$	$C_{16}H_{16}O_7$	145–147	10

[a] All new compounds described gave elemental analyses for C and H within ±0.4% of the calculated values. Ir and nmr spectra were also in agreement with the assigned structures; in particular, the nmr spectra confirmed the assignment of exo-cis stereochemistry.[1] [b] Uncorr; recorded on a Mel-Temp apparatus. [c] Dose at which fatalities occurred; compds were administered ip to mice.

* To whom correspondence should be addressed.

(1) E. R. Bockstahler, L. C. Weaver, and D. L. Wright, *J. Med. Chem.*, **11**, 603 (1968).

(2) V. A. Kraft and N. N. Mel'nikov, *Biol. Aktivn. Soedin.*, 255 (1965); *Chem. Abstr.*, **64**, 673*g* (1966).

Potential Antidiabetics. 7. N^1-(β-Hydroxybenzylmethyl)-3-methyl-4-arylhydrazono-2-pyrazolin-5-ones and N^1-(β-Hydroxybenzylmethyl)-3-methyl-4-arylazo-5-methyl- or -phenylpyrazoles

H. G. Garg and Chandra Prakash

Department of Chemistry, University of Roorkee, Roorkee, India

Received August 4, 1970

A few pyrazoles and related compounds appear to give promising results in antidiabetic tests[1,2] and, therefore, further combinations seem worthwhile studying. This paper describes the synthesis of N^1-(β-hydroxybenzylmethyl)-3-methyl-4-arylhydrazono-2-pyrazolin-5-ones and N^1-(β-hydroxybenzylmethyl)-3-methyl-4-arylazo-5-methyl- or -phenylpyrazoles and also includes the hypoglycemic activity of 3-methyl-4-arylazo-5-phenylisoxazoles.[2]

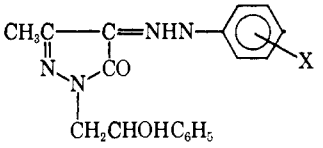
Biological Results.—On oral administration at various doses (25–100 mg/kg) in fasted guinea pigs for 18 hr prior to and during testing, 4-phenylazo-, 4-(2-nitrophenylazo)-, 4-(3-nitrophenylazo)-, 4-(2-methylphenylazo)-, 4-(2-methoxyphenylazo)-, 4-(3-methoxyphenylazo)-, 4-(4-ethoxyphenylazo)-, 4-(2,5-dichlorophenylazo)-, and 4-(2,6-dichlorophenylazo)-3-methyl-5-phenylisoxazoles essentially displayed no hypoglycemic activity as compared with chloropropamide. After a predetermined time of peak effect the blood was ana-

(1) H. G. Garg, D.Sc. Thesis, Agra University, India (1969).

(2) H. G. Garg and P. P. Singh, *J. Med. Chem.*, **13**, 1250 (1970), and ref cited therein.

TABLE I

N^1-(β-HYDROXYBENZYLMETHYL)-3-METHYL-4-ARYLHYDRAZONO-5-PYRAZOLIN-2-ONES

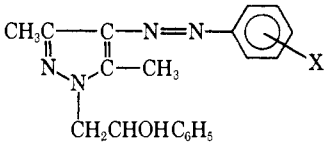


No.	X	Yield, %	Mp, °C	Color[a]	Formula	*Anal.*
1	H	55	133	YN	$C_{18}H_{18}N_4O_2$	C, H, N
2	3-Cl	50	89	OP	$C_{18}H_{17}ClN_4O_2$	N, Cl
3	4-Cl	52	139	ON	$C_{18}H_{17}ClN_4O_2$	N, Cl
4	2-MeO	55	157	OP	$C_{19}H_{20}N_4O_3$	C, H, N
5	2-NO_2	55	178	RP	$C_{18}H_{17}N_5O_4$	C, H, N
6	4-Me	50	98	DON	$C_{19}H_{20}N_4O_2$	C, H, N
7	4-SO_2NH_2	65	227	ON	$C_{18}H_{19}SN_5O_4$	N, S
8	2,4-Br_2	58	143	DYP	$C_{18}H_{16}Br_2N_4O_2$	Br, N

[a] B, Brown; D, dark; N, Needles; O, orange; P, plates; Pe, pale; R, red; Y, yellow.

TABLE II

N^1-(β-HYDROXYBENZYLMETHYL)-3,5-DIMETHYL-4-ARYLAZOPYRAZOLES



No.	X	Yield, %	Mp, °C	Color[a]	Formula	*Anal.*
1	H	50	129	DYN	$C_{19}H_{20}N_4O$	C, H, N
2	2-Me	52	131	PeYN	$C_{20}H_{22}N_4O$	C, H, N
3	4-Me	56	139	DYN	$C_{20}H_{22}N_4O$	C, H, N
4	3-Cl	60	170	YP	$C_{19}H_{19}ClN_4O$	Cl, N
5	4-Cl	62	164	YN	$C_{19}H_{19}ClN_4O$	Cl, N
6	2-Br	65	161	OP	$C_{19}H_{19}BrN_4O$	Br, N
7	3-NO_2	50	147	ON	$C_{19}H_{19}N_5O_3$	C, H, N
8	4-EtO	55	103	YN	$C_{21}H_{24}N_4O_2$	C, H, N
9	2,3-Cl_2	52	118	PeYN	$C_{19}H_{18}Cl_2N_4O$	Cl, N
10	2,3-Me_2	56	126	YN	$C_{21}H_{24}N_4O$	C, H, N
11	2,4-Me_2	56	114	YN	$C_{21}H_{24}N_4O$	C, H, N
12	2,4-$(MeO)_2$	55	159	YN	$C_{21}H_{24}N_4O_3$	C, H, N
13	2-Cl-6-Me	60	97	YN	$C_{20}H_{21}ClN_4O$	Cl, N
14	2-Cl-4-NO_2	62	181	ORP	$C_{19}H_{18}ClN_5O_3$	Cl, N

[a] See footnote *a*, Table I.

lyzed for glucose with the aid of a Technician AutoAnalyzer using the modified method of Hoffman.[3]

Experimental Section

Melting points were taken with a Kofler hot-stage apparatus and are uncorrected.

(3) W. S. Hoffman, *J. Biol. Chem.*, **120**, 51 (1937).

α-(Hydrazinomethyl)benzyl alcohol,[4] ethyl 2,3-dioxobutyra 2-arylhydrazones,[5] 2,3,4-pentanetrione 3-arylhydrazones,[6] an 1-phenyl-2-arylhydrazono-1,2,3-butanetriones[7] were prepared previously described.

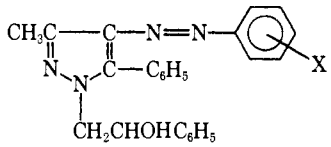
N^1-(β-Hydroxybenzylmethyl)-3-methyl-4-arylhydrazono-pyrazolin-5-one.—A hot solution of α-(hydrazinomethyl)benz alcohol (2 mmoles) in EtOH (10 ml) was added to ethyl 2,3-diox butyrate-2-arylhydrazone (2 mmoles) in EtOH (15 ml). Tl mixture was refluxed on a steam bath for 3 hr, followed by tl addition of glacial AcOH (4 ml). It was refluxed for another hr and allowed to stand overnight at 5–10°, when a cryst su' stance sepd. This was recrystd from EtOH (see Table I).

N^1-(β-Hydroxybenzylmethyl)-3,5-dimethyl-4-arylazopyrazol were obtained by using the same procedure as for I (see Tab II).

N^1-(β-Hydroxybenzylmethyl)-3-methyl-4-arylazo-5-pheny pyrazoles were also prepared by the same method (see Tab III).

TABLE III

N^1-(β-HYDROXYBENZYLMETHYL)-3-METHYL-4-ARYLAZO-5-PHENYLPYRAZOLES



No.	X	Yield, %	Mp, °C	Color[a]	Formula	*Anal.*
1	H	54	140	DYP	$C_{24}H_{22}N_4O$	C, H, N
2	2-NO_2	50	123	DYP	$C_{24}H_{21}N_5O_3$	C, H, N
3	2-Br	57	101	OP	$C_{24}H_{21}BrN_4O$	Br, N
4	2-MeO	55	157	DYN	$C_{25}H_{24}N_4O_2$	C, H, N
5	2,3-Cl_2	55	141	YP	$C_{24}H_{20}Cl_2N_4O$	Cl, N
6	2,4-Cl_2	55	160	YP	$C_{24}H_{20}Cl_2N_4O$	Cl, N
7	2,4-$(MeO)_2$	50	167	BP	$C_{26}H_{26}N_4O_3$	C, H, N
8	2,3-Me_2	58	178	YP	$C_{26}H_{26}N_4O$	C, H, N

[a] See footnote *a*, Table I.

3-Methyl-4-arylazo-5-phenylisoxazoles had been synthesize in our laboratories earlier.[2]

Acknowledgments.—We thank Professor W. U Malik, Head of this Department, for the facilities fc the work, and the State C.S.I.R., Lucknow, for a Junic Research Assistantship (to C.P.). A 15-g sample c α-(hydrazinomethyl)benzyl alcohol was kindly supplie by Dr. D. T. Manning of the Research and Develoj ment Department, Union Carbide Corporation, Sout Charleston, W. Va. 25303.

(4) D. T. Manning and H. A. Coleman, *J. Org. Chem.*, **34**, 2746 (1969).
(5) H. G. Garg and P. P. Singh, *J. Med. Chem.*, **11**, 1104 (1968).
(6) H. G. Garg and P. P. Singh, *ibid.*, **11**, 1103 (1968).
(7) H. G. Garg and P. P. Singh, *J. Chem. Soc. C*, 1141 (1969).