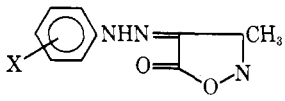
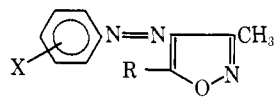


I



IIa, R = CH_3
b, R = C_6H_5

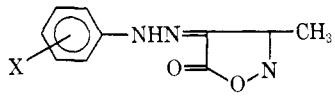
(IIa) produced essentially no hypoglycemic activity as compared to chloropropamide. After a predetermined time of peak effect the blood was analyzed for glucose with the aid of a Technician auto-analyzing unit using the modified method of Hoffman.[7]

Experimental Section

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

Arylhydrazono Derivatives. General Procedure.—These were obtained by adapting the route of Garg, *et al.*[1-3]

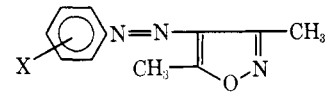
Table I
Characteristics of
3-Methyl-4-arylhydrazono-2-isoxazolin-5-ones



No.	X	Yield, %	Mp, °C	Color[a]	Formula	Analyses
1	H	70	186	YF	$C_{10}H_9N_3O_2$	N
2	2-NO_2	65	158	YN	$C_{10}H_8N_4O_4$	N
3	3-NO_2	60	192	PeYN	$C_{10}H_8N_4O_4$	N
4	4-NO_2	70	210	OY	$C_{10}H_8N_4O_4$	N
5	2-Me	65	155	YN	$C_{11}H_{11}N_3O_2$	N
6	3-Me	60	150	PeY	$C_{11}H_{11}N_3O_2$	N
7	4-Me	50	189-191	PeYN	$C_{11}H_{11}N_3O_2$	N
8	2-MeO	45	163	ON	$C_{11}H_{11}N_3O_3$	N
9	3-MeO	50	167-169	YN	$C_{11}H_{11}N_3O_3$	N
10	4-MeO	55	180-181	YON	$C_{11}H_{11}N_3O_3$	N
11	2-EtO	50	130	ON	$C_{12}H_{13}N_2O_3$	N
12	4-EtO	60	141	YON	$C_{12}H_{13}N_3O_3$	N
13	2,4-Me_2	50	110	ON	$C_{12}H_{13}N_3O_2$	N
14	2,5-Me_2	55	149-150	DR	$C_{12}H_{13}N_3O_4$	N
15	2,5-Cl_2	70	180	OYN	$C_{10}H_7Cl_2N_3O_2$	Cl

[a] B, brown; D, dark; F, fibres; G, golden; N, needles; O, orange; P, plates; Pe, pale; R, red; V, violet; Y, yellow.

Table II
Characteristics of 3,5-Dimethyl-4-arylazoisoxazoles



No.	X	Yield, %	Mp, °C	Color[a]	Formula	Analyses
1	H	60	46	PeYN	$C_{11}H_{11}N_3O$	N
2	2-NO_2	65	150-152	ON	$C_{11}H_{10}N_4O_3$	N
3	3-NO_2	60	147	GYN	$C_{11}H_{10}N_4O_3$	N
4	2-MeO	55	120	OYN	$C_{12}H_{13}N_3O_2$	N
5	3-MeO	55	58	YP	$C_{12}H_{13}N_3O_2$	N
6	4-MeO	65	100-101	PeY	$C_{12}H_{13}N_3O_2$	N
7	2-EtO	50	98	OYN	$C_{13}H_{15}N_3O_2$	N
8	4-EtO	60	76	PeYN	$C_{13}H_{15}N_3O_2$	N
9	2,4-Me_2	65	104	YN	$C_{13}H_{15}N_3O$	N
10	2,5-Me_2	60	64	YN	$C_{13}H_{15}N_3O$	N
11	2,6-Me_2	60	66	YON	$C_{13}H_{15}N_3O$	N
12	2,5-Cl_2	70	130-132	YN	$C_{11}H_9Cl_2N_3O$	Cl
13	2,5-$(MeO)_2$	55	104-105	BRN	$C_{13}H_{15}N_3O_3$	N
14	2-Cl-6-Me	65	102	ON	$C_{12}H_{12}ClN_3O$	Cl

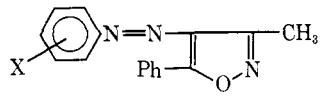
[a] See footnote *a* of Table I.

(7) W. S. Hoffman, *J. Biochem.*, **120**, 51 (1937).

3-Methyl-4-arylhydrazono-2-isoxazolin-5-ones (I).—$NH_2OH \cdot HCl$ (0.005 mole) in H_2O (5 ml) and NaOAc (1.0 g) was added to an appropriate ethyl 2,3-dioxobutyrate 2-phenylhydrazone (0.005 mole) in EtOH (20 ml). It was refluxed for 2 hr. On cooling shining crystals separated and was recrystallized from EtOH (Table I).

3,5-Dimethyl-3-methyl-5-phenyl-4-arylazoisoxazoles were prepared from 3-arylhydrazono derivatives of 1,3-diketones and $NH_2OH \cdot HCl$ as described for I analogs (see Tables II and III).

Table III
Characteristics of 3-Methyl-5-phenyl-4-arylazoisoxazoles



No.	X	Yield, %	Mp, °C	Color[a]	Formula	Analyses
1	H	60	97	YN	$C_{16}H_{13}N_3O$	N
2	2-NO_2	50	166-168	YF	$C_{16}H_{12}N_4O_3$	N
3	3-NO_2	60	132	OYN	$C_{16}H_{12}N_4O_3$	N
4	2-Me	55	90-91	OYN	$C_{17}H_{15}N_3O$	N
5	2-MeO	45	117	OYN	$C_{17}H_{15}N_3O_2$	N
6	3-MeO	50	88	BYN	$C_{17}H_{15}N_3O_2$	N
7	4-EtO	55	107-108	YN	$C_{18}H_{17}N_3O_2$	N
8	2,4-Me_2	65	104-105	YN	$C_{18}H_{17}N_3O$	N
9	2,5-Me_2	60	100	OYN	$C_{18}H_{17}N_3O$	N
10	2,5-Cl_2	70	174	OYN	$C_{16}H_{11}Cl_2N_3O$	Cl
11	2,6-Cl_2	65	121	OY	$C_{16}H_{11}Cl_2N_3O$	Cl
12	2,5-$(MeO)_2$	55	122-124	B	$C_{18}H_{17}N_3O_3$	N

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

Acknowledgment.—We thank Dr. Maxwell Gordon, Smith Kline and French Laboratories, Philadelphia, Pa., for the supply of some rare chemicals, Professor W. U. Malik, Head of this Department, for the facilities for work, and the C.S.I.R., New Delhi, for a junior Research Fellowship (to P. P. S.).

Pyrolysis of 1-Adamantyl Azidomethyl Ketone

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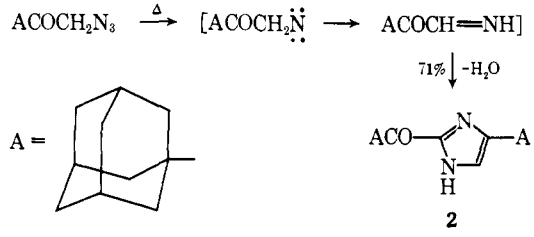
Our search for new structures in the adamantane series for testing as medicinals[1] led us to investigate the pyrolysis of the title compound **1**. A good yield



of the imidazole **2** was obtained. The mode of formation of **2** undoubtedly parallels that of the pyrolysis of phenacyl azides.[2]

* To whom correspondence should be addressed.

(1) See for instance: (a) W. L. Davies, R. R. Grunert, R. F. Haff, J. W. McGahen, E. M. Neumayer, M. Paulshock, J. C. Watts, T. R. Wood, E. C. Hermann, and C. E. Hoffmann, *Science*, **144**, 862 (1964); (b) K. Gerzon, D. J. Tobias, Sr., R. E. Holmes, R. E. Rathbun, and R. W. Kattau, *J. Med. Chem.*, **10**, 603 (1967).

(2) J. H. Boyer and D. Straw, *J. Amer. Chem. Soc.*, **74**, 4506 (1952).

Experimental Section[a]

1-Adamantyl Azidomethyl Ketone (1).—A mixture of 5.14 g (20 mmoles) of 1-adamantyl bromomethyl ketone (Aldrich Chemical Co., mp 76–79°), 2.6 g (40 mmoles) of NaN_3, and 200 ml of MeOH was boiled gently on the steam bath for 20 min. MeOH was evapd *in vacuo*. The remaining mixture was stirred with 100 ml of pet ether (bp 30–60°) and filtered. Evaporation of the filtrate gave 4.11 g (94%) of essentially pure 1 as a light yellow oil which was used in the pyrolysis. This oil could be purified by solution in a small vol of pet ether and chilling in Dry Ice bath: colorless needles; mp 24–25.5°; ir (CCl_4) 2105 (N_3). *Anal.* ($C_{12}H_{17}N_3O$) C, H, N.

2-(1-Adamantanoyl)-4(or 5)-(1-adamantyl)imidazole (2).—A soln of 13.2 g (60 mmoles) of crude 1 in 200 ml of xylene was heated to a slow reflux for 15 hr. Upon partial concn and cooling of the mixture, 8.0 g (73%) of 2 pptd as a colorless amorphous solid, mp 267.5–269.5°. After recrystn from PhMe, colorless needles were obtained: mp 267.5–269.5°; ir (KBr) 3320 (NH) and 1645 cm^{-1} (CO); uv (EtOH) 296 nm (ϵ 16,200); mass spectra (low resol) *m/e* 79, 93, 135, 149, 202, 216, 229, 307, 336 and 364. *Anal.* ($C_{24}H_{32}N_2O$) C, H N.

Acknowledgments.—We thank the Physical Chemistry Section of our laboratories headed by Dr. P. Bommer for the spectra and Mr. Steve Grunberg for technical assistance.

(3) Melting points were taken in a Thomas-Hoover melting point apparatus, and are corrected. Ir spectra were determined using a Beckmann IR-9 spectrophotometer, mass spectra with a CEC-21-110 spectrometer, nmr spectra with a Varian A-60 spectrometer (Me_4Si), and uv spectrum with a Cary 15 recording spectrophotometer.

Book Reviews

Lithium in the Treatment of Mood Disorders. By ANTOINETTE A. GATTOZZI. National Clearinghouse for Mental Health Information, Publication No. 5033. U. S. Government Printing Office, Washington, D. C. 20402. 1970. vi + 99 pp. 15 × 23 cm. Paperback. 60 cents.

Lithium is used in light-weight alloys, in the fusion–fusion reaction of thermonuclear explosions, and now in psychiatry. The story of the discovery of the therapeutic effect of Li^+ in manic states by John F. J. Cade in Australia in 1949 provides one of the most instructive examples of serendipity and ensuing logical development in medicinal chemistry. Even more interesting is the subsequent assignment of Li^+ therapy to the differential diagnosis of severe mood disturbances. The little book at hand recounts these events in the form of an easily understood documented story, and places Li^+ therapy in the total framework of medical findings and patient care. It is a stimulating and amazing story to read.

UNIVERSITY OF VIRGINIA ALFRED BURGER
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Progress in Drug Research. Volume 13. Edited by E. JUCKER. Birkhäuser Verlag. Basel and Stuttgart. 1969. 413 pp. 24 × 17.5 cm. Fr. 118.

The collection of periodic reviews presented in this volume contains the following articles: Biological activity of the terpenoids and their derivatives (M. Martin-Smith, W. E. Sneader); Antihypertensive agents, 1962–1968 (O. Schier, A. Marxer); Comparative drug metabolism (L. B. Mellett); Repository antimalarial drugs (E. F. Elslager); Hypolipidemic agents (W. L. Bencze, R. Hess, G. deStevens); Quinuclidine derivatives (M. D. Mashkovsky, L. N. Yakhontov); and Reactivity of rat and man to egg-white (S. I. Ankier). Some of these reviews constitute broad surveys of multiple structural types while others (such as that on quinuclidines) concentrate on a narrower structural field. The largest scope is covered in the terpenoid article; it includes innumerable indole alkaloids whose biogenetic derivation from more traditional terpenes justifies their incorporation in this review. But the compounds in this chapter have been chosen frankly with biological activity in mind, and the author has achieved this goal with skill and in depth, both in discussing the very complex chemistry and the therapeutic applications of the products.

The other systematic reviews of structure–activity relationships will be valuable reference articles, especially since they have been written by acknowledged experts in each field. The survey of comparative drug metabolism leans, and quite rightly so, toward the physiological significance of biochemical metabolic reactions. The most "far-out" article concerns immunochemical aspects of egg-white, and again the right mixture of chemical and biological balance has been attained in this review. Altogether, this is one of the best collections of articles in this series, and its high quality should presage equally good selections in future volumes.

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The Chemistry of Cyclic Enaminonitriles and *o*-Aminonitriles. By EDWARD C. TAYLOR and ALEXANDER MCKILLOP. Interscience. New York, N. Y. 1970. xii + 415 pp. 15 × 23 cm. $29.59

The first chapter of this book is devoted to cyclic enaminonitriles. The emphasis in this chapter is on the scope of the Thorpe–Ziegler reaction in the preparation of enaminonitriles from dinitriles. Shorter sections are devoted to review of physical evidence for the structure of enaminonitriles and to a summary of the hydrolysis of enaminonitriles. An attempt to review the literature comprehensively has been made and nearly 30 of the 60 pages in this chapter are devoted to tables showing starting materials, cyclization conditions, yield, and product structure for numerous Thorpe–Ziegler cyclizations. There are also extensive tables summarizing the literature regrading hydrolysis of enaminonitriles. The second chapter of the book is devoted to the synthesis and reactions of aromatic *o*-aminonitriles, both heterocyclic and homocyclic. The section on reactions emphasizes the important area of using *o*-aminonitriles for construction of new fused rings, particularly substituted pyrimidines. Again much of the chapter (over 200 pages) is devoted to tables summarizing preparation and reactions of *o*-aminonitriles. Generous use of structural formulas has been been made in the tables. Particularly impressive is Table XXX which lists all known cyclic enaminonitriles and *o*-aminonitriles in order of increasing complexity of molecular formula. For each entry literature references to preparation and, where applicable, its subsequent use as a synthetic intermediate are given. Needless to say the effort required for compilation of this table must have been enormous. As a result this book gives, to chemists interested in synthesis or use of aminonitriles, very ready access to the extensive prior literature in the field. Workers in the field of synthesis and reactions of nitrogen heterocyclic compounds will want to have the vast amount of information in the volume easily available.

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