

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF TEXAS]

## 5,5-Dimethylhydantoin Containing a —NRR' Substituent. II

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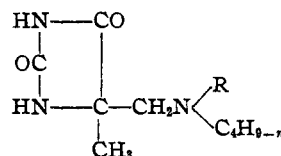
About four years ago there was reported<sup>3</sup> from this Laboratory the synthesis of a series of 5,5-dimethylhydantoin containing a dialkylamino substituent in which the two alkyls were alike. More recently,<sup>4</sup> was recorded the preparation of another series of 5,5-dimethylhydantoin, these, however, containing a —NRR' substituent in which R represented a normal alkyl group or phenyl and R' phenyl or benzyl. Intermediate between these two series would be that containing a —NRR' substituent in which R and R' represent different alkyl groups.

As a result of another investigation<sup>5</sup> there were available eight N-alkyl-*n*-butylaminoacetones. Each of these has been converted into the corresponding hydantoin derivative by reaction with ammonium carbonate and potassium cyanide. Through the courtesy of Parke, Davis and Company, six of these hydantoin have received preliminary testing on mice intraperitoneally for toxicity and possible hypnotic action. The N-methyl and N-ethyl members of the series

verted into substituted hydantoin by the Bucherer<sup>5</sup> procedure. In general, 0.1 mole of the N-alkyl-*n*-butylaminoacetone was dissolved in 75 cc. of ethyl alcohol; then a solution of 0.11 mole of potassium cyanide dissolved in 60 cc. of water was added. Ammonium carbonate (0.3 mole) was crushed to a coarse powder and added to the ketone-cyanide mixture. Now, 60% alcohol solution was added until only one liquid phase existed in the reaction mixture at 55–60°; the ammonium carbonate was completely in solution after a few hours. The warming continued at 55–60° under a reflux condenser for ten to twelve hours. The light yellow solution was chilled causing virtually complete separation of the hydantoin. The latter was recrystallized from diluted alcohol; in some instances addition of petroleum ether to a benzene solution of the hydantoin proved to be an efficacious method for purification. Data concerning certain physical properties for and analyses of the eight hydantoin have been placed in Table I.

TABLE I

—R	M. p., °C. (cor.)	Yield, %	Carbon, %		Hydrogen, %		Nitrogen, %	
			Calcd.	Found	Calcd.	Found	Calcd.	Found
Methyl	137–138	63	56.30	56.04	8.98	9.08	19.71	19.67
Ethyl	136–137	59	58.12	57.95	9.31	9.56	18.49	18.75
<i>n</i> -Propyl	146–147	57	59.72	59.34	9.61	9.67	17.42	17.96
Isopropyl	160–162	56	59.72	59.97	9.61	9.89	17.42	17.22
Isobutyl	177.5–178	79	61.14	61.16	9.87	10.10	16.46	16.62
<i>s</i> -Butyl	188–189	43	61.14	61.15	9.87	9.99	16.46	16.31
<i>n</i> -Amyl	165–166	46	62.41	62.44	10.11	10.13	15.60	15.81
Isoamyl	181.5–182	49	62.41	62.04	10.11	10.13	15.60	15.90

5-[N-ALKYL-*n*-BUTYLAMINOMETHYL]-5-METHYLHYDANTOINS

produced slight analgesia in nearly fatal doses. None exhibited any appreciable hypnotic activity.

## Experimental

The dialkylaminoacetones were readily con-

- (1) From the Ph.D. Dissertation of D. D. Humphreys, June, 1941.
- (2) Present address, Sharples Chemicals Inc., Wyandotte, Mich.
- (3) Magee with Henze, *THIS JOURNAL*, **60**, 2148 (1938).
- (4) Henze and Magee, *ibid.*, **62**, 912 (1940).
- (5) Henze and Humphreys, *ibid.*, **64**, 2878 (1942).

## Summary

Eight new 5-[N-alkyl-*n*-butylaminomethyl]-5-methylhydantoin have been prepared. These compounds appear to be devoid of hypnotic activity but some are slightly analgesic in nearly fatal doses.

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(6) Bucherer and Lieb, *J. prakt. Chem.*, [2] **141**, 5 (1934).