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Arylcycloalkylamines

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Sympathomimetic amines in which the basic side chain is part of a saturated ring not condensed with their aromatic portion have been the subject of recent studies (*1*). The excellent paper by Gutsche (*3*) concerning ring enlargements with diazomethane and phenyldiazomethane prompts us to record similar reactions used by us for the preparation of intermediates in the synthesis of phenyl- and diphenylcycloalkylamines in an extension of this series.

We prepared 2-phenylcycloheptanone (bp 133°–137°, 1 mm) by the slow methanol catalyzed reaction of cyclohexanone and phenyldiazomethane in a yield of 43%. The ketone yielded 2-phenylcycloheptylamine by the Leuckart reaction, and 5,5-(2′-phenylhexamethylene) hydantoin by the Bucherer method. In a similar way, 2-methylcycloheptanone (*2*) furnished 2-methylcycloheptylamine, and 5,5-(2′-methylhexamethylene) hydantoin, respectively. 4-Methylcycloheptylamine was prepared from 4-methylcycloheptanone (*5*).

Structural analogues of Methadon were obtained by subjecting 2,2-diphenylcyclohexanone (*4*) to the Mannich reaction with secondary amines. The resulting 6-dialkylaminomethyl-2,2-diphenylcyclohexanone derivatives, and the corresponding amino alcohols, are listed in Table 1. 2,2-Diphenyl-6-bromocyclohexanone, obtained from the parent ketone by bromination, has also been converted to 2,2-diphenyl-6-dialkylaminocyclohexanone derivatives.

TABLE 1

PHYSICAL PROPERTIES AND ANALYSES OF SUBSTITUTED CYCLOALKANE DERIVATIVES

Compound	Mp, °C	Formula	Percentage composition	
			Calculated	Found
2-Phenylcycloheptanone semicarbazone	154–156	$C_{14}H_{19}N_3O$	N, 17.13	17.42
2-Phenylcycloheptylamine · HCl	196.5–197.5	$C_{13}H_{20}ClN$	C, 69.16	68.52
			H, 8.93	8.95
			N, 6.20	6.45
5,5-(2′-Phenylhexamethylene) hydantoin	204.5–207.5	$C_{15}H_{18}N_2O_2$	C, 69.74	69.57
			H, 7.02	7.00
			N, 10.85	10.89
2-Methylcycloheptylamine · HCl	225.5–227.5 (dec.)	$C_8H_{18}ClN$	C, 58.70	58.63
			H, 11.08	10.91
			N, 8.56	8.45
5,5-(2′-Methylhexamethylene)hydantoin	216–218.5	$C_{10}H_{16}N_2O_2$	C, 61.20	61.30
			H, 8.22	8.74
			N, 14.28	14.78
4-Methylcycloheptylamine · HCl	207–209	$C_8H_{18}ClN$	C, 58.70	59.24
			H, 11.08	11.21
			N, 8.56	8.27
2,2-Diphenyl-6-dimethylaminomethylcyclohexanone	106–107	$C_{21}H_{25}NO$	C, 82.04	82.18
			H, 8.20	8.18
2,2-Diphenyl-6-dimethylaminomethylcyclohexanol	108.5–109.5	$C_{21}H_{27}NO$	C, 81.51	81.35
			H, 8.80	8.80
2,2-Diphenyl-6-morpholinomethylcyclohexanone · HCl	160	$C_{23}H_{28}ClNO_2$	C, 71.58	71.78
			H, 7.31	7.54
2,2-Diphenyl-6-bromocyclohexanone	117–119.5	$C_{18}H_{17}BrO$	C, 65.66	65.69
			H, 5.21	5.39
2,2-Diphenyl-6-morpholinocyclohexanone	124.5–125	$C_{22}H_{25}NO_2$	C, 78.77	78.98
			H, 7.51	7.71
2,2-Diphenyl-6-piperidinocyclohexanone	121.5–122	$C_{23}H_{27}NO$	C, 82.84	83.12
			H, 8.16	7.63

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