

the same intense ether band in the 8.5–8.9  $\mu$  region as was evident in the spectrum of V and the starting material. The 2,4-dinitrophenylhydrazone of VIII was prepared from VII by the customary procedure, and was recrystallized from ethanol; yellow-orange crystals, m.p. 178–180°. The infrared spectrum of this derivative (chf.) had sharp peaks at 3.01, 5.75, and 6.16  $\mu$ .

Anal. Calcd. for  $C_{20}H_{20}O_6N_4$ : C, 58.25; H, 4.89. Found: C, 58.09; H, 4.76.

As with V, attempts to hydrolyze VII in warm, dilute

acids resulted in formation of dark gum, and partial recovery of the starting material. Alkaline hydrolysis of VII gave a polymeric substance.

*Acknowledgments.* I am indebted to Dr. William C. Alford and his staff for analytical data and to Mrs. H. Franklin Byers for infrared spectra.

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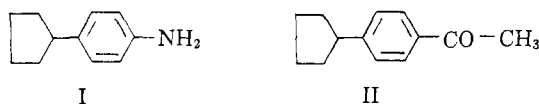
## *p*-Cyclopentylacetophenone and Its Derivatives

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The preparation of cyclopentylbenzene, and of *p*-cyclopentylacetophenone obtained therefrom, has been investigated, and the use of the latter ketone as an intermediate for the synthesis of various aromatic and heterocyclic cyclopentyl compounds, especially *p*-cyclopentylaniline, is described. In the course of this work, a large number of derivatives of *p*-cyclohexylaniline have been prepared for evaluation of their tuberculostatic activity.

As part of a general investigation on the relationship between tuberculostatic properties and chemical structure,<sup>1</sup> several derivatives of *p*-cyclopentylaniline were required for comparison of their activity with that of similar derivatives of *p*-cyclohexylaniline. The most promising method for preparing *p*-cyclopentylaniline (I) free from position isomers seemed to be *via* Beckmann rearrangement of the oxime of *p*-cyclopentylacetophenone (II), a ketone which had already been briefly described<sup>2</sup> but which was now more thoroughly investigated. This in turn led us to examine the various procedures for the preparation of the main intermediate, *viz.* cyclopentylbenzene.



Since its discovery by Kursanoff,<sup>3</sup> cyclopentylbenzene has been synthesized by several methods: (1) by Friedel-Crafts reaction of chloro- or bromocyclopentane and benzene;<sup>4</sup> (2) by direct condensation of cyclopentanol with benzene in the presence of Lewis acids;<sup>5</sup> and (3) by addition of cyclopentene

to benzene in the presence of aluminum chloride.<sup>6</sup> A reinvestigation of these various methods showed the condensation of cyclopentanol with benzene to be the most satisfactory, as regards both simplicity and yields; a study of the influence of the various factors of the reaction on the yield of cyclopentylbenzene showed the temperature to be the only important variable, and that the best yield was attained at a temperature of 50°. All the methods furnished from 10–20% of dicyclopentylbenzene (probably a mixture of the three position isomers).

Friedel-Crafts acetylation of cyclopentylbenzene furnished an excellent yield of *p*-cyclopentylacetophenone, giving a semicarbazone, m.p. 232°, at variance with von Braun<sup>7</sup> who recorded a very poor yield for this ketone, and m.p. 212–215° for the semicarbazone. Table I lists some chalcones prepared by condensation of ketone II with various aromatic and heterocyclic aldehydes; oxidation of the same ketone with sodium hypobromite afforded *p*-cyclopentylbenzoic acid, identical with the acid which Kleene prepared by carbonation of cyclopentylphenylmagnesium bromide.<sup>2</sup> Beckmann rearrangement of *p*-cyclopentylacetophenone oxime to *p*-cyclopentylacetanilide was effected, in excellent yields, with phosphorus pentachloride in ether, and subsequent hydrolysis furnished *p*-cyclopentylaniline (I), a liquid amine which was characterized by several solid derivatives: 1-*p*-cyclopentylphenyl-2,5-dimethylpyrrole (III) (by condensation with acetonylacetone), 2-chloro-3-(*p*-cyclopentylanilino)-1,4-naphthoquinone (by condensation with 2,3-dichloro-1,4-naphthoquinone), 2,5-dichloro-3,6-bis(*p*-cyclopentyl-

(1) For tuberculostatic activity of thiocarbanilides, see N. P. Buu-Hoï and N. D. Xuong, *Compt. rend.*, **237**, 498 (1953); N. P. Buu-Hoï, N. D. Xuong, and N. H. Nam, *J. Chem. Soc.*, 1573 (1955); N. P. Buu-Hoï, N. D. Xuong, N. H. Nam, J. M. Gazave, J. Pillot, and L. Schembri, *Experientia*, **11**, 97 (1955); M. Welsch, N. P. Buu-Hoï, P. Danthinne, and N. D. Xuong, *Experientia*, **12**, 102 (1956); N. P. Buu-Hoï, N. D. Xuong, J. M. Gazave, J. Pillot, and G. Dufraisse, *Experientia*, **12**, 474 (1956).

(2) R. D. Kleene, *J. Am. Chem. Soc.*, **71**, 1893 (1949).

(3) N. Kursanoff, *Ann.*, **318**, 309 (1901).

(4) J. von Braun, *Ber.*, **60**, 1080 (1927).

(5) R. C. Huston and K. Goodmoot, *J. Am. Chem. Soc.*, **56**, 2432 (1934).

(6) P. Cagniant, A. Deluzarche, and G. Chatelus, *Compt. rend.*, **224**, 1064 (1947).

(7) J. von Braun and M. Kühn, *Ber.*, **60**, 2562 (1927).

anilino)-1,4-benzoquinone (by reaction with chloranil), and *N*-(*p*-cyclopentylphenyl)tetrachlorophthalimide (by condensation with tetrachlorophthalic anhydride).

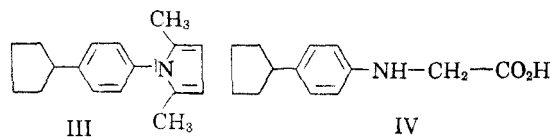


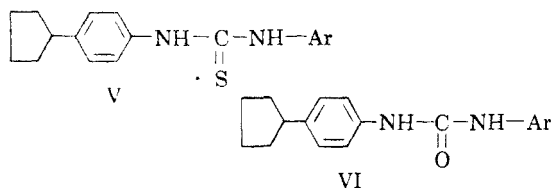
TABLE I

CHALCONES<sup>a</sup> DERIVED FROM *p*-CYCLOPENTYLACETOPHENONE

R	Formula	M.P., °C	Analyses			
			Calcd.		Found	
			C	H	C	H
2-Furyl	C <sub>18</sub> H <sub>18</sub> O <sub>2</sub>	99	81.2	6.8	81.4	6.7
2-Thenyl	C <sub>18</sub> H <sub>18</sub> OS	105	76.6	6.4	76.9	6.5
1-Naphthyl	C <sub>24</sub> H <sub>22</sub> O	98	88.3	6.7	88.4	6.7
3-Chlorophenyl	C <sub>20</sub> H <sub>19</sub> ClO	106	77.4	6.1	77.6	6.1
3-Methoxyphenyl	C <sub>21</sub> H <sub>22</sub> O <sub>2</sub>	84	82.3	7.2	82.5	7.2

<sup>a</sup> Prepared by shaking a solution of equimolar amounts of *p*-cyclopentylacetophenone and the appropriate aldehyde in warm ethanol with a few drops of 20% aqueous sodium hydroxide; the precipitate formed was recrystallized from ethanol, giving in all cases shiny pale yellow needles.

In view of the pronounced *in vitro* tuberculostatic activity of various *N*-arylglycines,<sup>8</sup> *N*-(*p*-cyclopentylphenyl)glycine (IV) was prepared by condensation of amine I with chloroacetic acid; the corresponding ethyl ether reacted with hydrazine hydrate to give *N*-(*p*-cyclopentylphenyl)glycine hydrazide. The condensation of *p*-cyclopentylaniline with various aryl isothiocyanates Ar—N=C=S yielded a series of substituted *p*-cyclopentylthiocarbonylides (V), listed in Table II. These thiocarbonylides, with the exception of the *p*'-bromo and *o*'-phenyl derivatives, showed considerable *in vitro* tuberculostatic



activity against *Mycobacterium tuberculosis* var. *hominis* (strain H 37 RvD) at a concentration of 10  $\gamma$  per ml. Dubos culture medium; a number of substituted *p*-cyclopentylcarbamoylides (VI), similarly synthesized from various aryl isocyanates Ar—N=C=O, and listed in Table III, were found inactive in that respect.

(8) H. W. Bersch and W. Döpp, *Arzneimittel-Forsch.*, **5**, 183, 335 (1955); N. P. Buu-Hoi, N. D. Xuong, N. B. Tien, J. M. Gazave, J. Pillot, and G. Dufraisse, *Experientia*, **13**, 234 (1957).

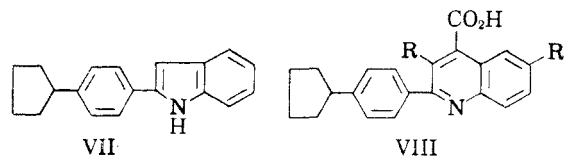
TABLE II  
SUBSTITUTED 4-CYCLOPENTYLTHIOCARBANILIDES (V)

Substituent	Formula	M.P., °C.	Analyses			
			Calcd.		Found	
			C	H	C	H
4'-Fluoro	C <sub>18</sub> H <sub>20</sub> N <sub>2</sub> S	142	73.0	6.7	72.9	6.7
	C <sub>18</sub> H <sub>17</sub> FN <sub>2</sub> S	177	68.8	6.0	68.8	5.9
4'-Chloro	C <sub>19</sub> H <sub>19</sub> ClN <sub>2</sub> S	208	65.3	5.7	65.1	5.7
4'-Bromo	C <sub>18</sub> H <sub>19</sub> BrN <sub>2</sub> S	215	57.6	5.0	57.5	5.1
4'-Methyl	C <sub>19</sub> H <sub>22</sub> N <sub>2</sub> S	158	73.5	7.1	73.3	7.0
2',4'-Dimethyl	C <sub>20</sub> H <sub>24</sub> N <sub>2</sub> S	145	74.1	7.4	73.9	7.3
4'-Ethyl	C <sub>20</sub> H <sub>24</sub> N <sub>2</sub> S	130	74.1	7.4	74.3	7.5
4'-Ethoxy	C <sub>20</sub> H <sub>24</sub> N <sub>2</sub> OS	167	70.6	7.0	70.5	7.2
4'-Isoamylxy	C <sub>23</sub> H <sub>30</sub> N <sub>2</sub> OS	128	72.2	7.8	72.2	7.8
2'-Phenyl	C <sub>24</sub> H <sub>24</sub> N <sub>2</sub> S	187	77.4	6.4	77.1	6.1
4'-Cyclopentyl	C <sub>23</sub> H <sub>28</sub> N <sub>2</sub> S	203	75.8	7.7	75.7	7.6

TABLE III  
SUBSTITUTED *N*-(*p*-CYCLOPENTYLPHENYL)UREAS

N'-Substituent	Formula	M.P., °C.	Analyses			
			Calcd.		Found	
			C	H	C	H
Phenyl	C <sub>18</sub> H <sub>20</sub> N <sub>2</sub> O	195	77.1	7.1	77.0	7.3
<i>p</i> -Chlorophenyl	C <sub>18</sub> H <sub>17</sub> ClN <sub>2</sub> O	229	68.7	6.0	68.3	6.0
<i>o</i> -Xenyl	C <sub>24</sub> H <sub>24</sub> N <sub>2</sub> O	169	80.9	6.7	80.7	6.5
$\beta$ -Naphthyl	C <sub>22</sub> H <sub>22</sub> N <sub>2</sub> O	220	80.0	6.6	79.9	6.5

Several nitrogen-containing heterocyclic derivatives of cyclopentylbenzene were prepared in the course of this work. Thus, Fischer indolization of *p*-cyclopentylacetophenone phenylhydrazone readily afforded 2-(*p*-cyclopentylphenyl)indole (VII), and Pfitzinger reaction of ketone II and its higher homologs, *p*-cyclopentylpropiophenone and *p*-cyclopentylbutyrophenone, yielded a number of 2-(*p*-cyclopentylphenyl)cinchoninic acids (VIII), listed in Table IV; thermal decarboxylation of these



acids led to the corresponding quinoline bases.

## EXPERIMENTAL

*Preparation of intermediates.* Bromocyclopentane, b.p. 135–136°, was prepared by the reaction of phosphorus tribromide and cyclopentanol according to the Noller and Adams procedure;<sup>9</sup> cyclopentene was obtained by dehydration of cyclopentanol, using either phosphorus pentoxide (75% yield) or hydrogen potassium sulfate (68–70% yield).

*Cyclopentylation of benzene.* (a) *With bromocyclopentane.*

(9) C. Noller and R. Adams, *J. Am. Chem. Soc.*, **48**, 1084 (1926).

TABLE IV  
QUINOLINE DERIVATIVES

Substance	Formula	M.P., °C.	Analyses			
			Calcd.		Found	
			C	H	C	H
2-( <i>p</i> -Cyclopentylphenyl)-cinchoninic acid	C <sub>21</sub> H <sub>19</sub> NO <sub>2</sub>	248	79.5	6.0	79.8	6.0
2-( <i>p</i> -Cyclopentylphenyl)-quinoline	C <sub>20</sub> H <sub>19</sub> N	110	87.9	7.0	88.1	6.9
6-Bromo-2-( <i>p</i> -cyclopentylphenyl)cinchoninic acid	C <sub>21</sub> H <sub>18</sub> BrNO <sub>2</sub>	254 (dec.)	63.6	4.5	63.9	4.7
6-Methyl-2-( <i>p</i> -cyclopentylphenyl)cinchoninic acid	C <sub>22</sub> H <sub>21</sub> NO <sub>2</sub>	230	79.7	6.3	80.0	6.4
6-Methyl-2-( <i>p</i> -cyclopentylphenyl)quinoline	C <sub>21</sub> H <sub>21</sub> N	142	87.8	7.3	87.6	7.4
3-Methyl-2-( <i>p</i> -cyclopentylphenyl)cinchoninic acid	C <sub>22</sub> H <sub>21</sub> NO <sub>2</sub>	315	79.7	6.3	79.6	6.5
3-Ethyl-2-( <i>p</i> -cyclopentylphenyl)cinchoninic acid	C <sub>23</sub> H <sub>23</sub> NO <sub>2</sub>	288	80.0	6.7	80.2	6.5

To a well stirred mixture of 100 ml. of dry, thiophene-free benzene, 50 ml. of carbon disulfide, and 1 g. of finely powdered aluminum chloride, 25 g. of bromocyclopentane was added dropwise, the temperature remaining at 45–50°. One more gram of catalyst was then added, followed by a further 25 g. of bromocyclopentane, and the mixture heated on a water bath until hydrogen bromide ceased to evolve. After cooling, ice water was added, the organic layer separated and washed first with 10% aqueous sodium hydroxide, then with water, and dried over calcium chloride. The solvent was removed, and the residue was distilled to yield 54% of cyclopentylbenzene, b.p. 215–217°,  $n_D^{20}$  1.5230, and 20% of dicyclopentylbenzene, b.p. 178–180°/15 mm.,  $n_D^{20}$  1.5427.

(b) *With chlorocyclopentane.* The same procedure, applied to 30 g. of chlorocyclopentane, furnished a 54% yield.

(c) *With cyclopentene.* The reaction was performed by adding dropwise 15 g. of cyclopentene to a well stirred mixture of 70 ml. of benzene and 2 g. of aluminum chloride, the temperature rising from 0° to 25° in 10 minutes. The yield was 53%.

(d) *With cyclopentanol.* A well stirred mixture of 120 ml. of benzene and 17 g. of aluminum chloride was treated dropwise with 23 g. of cyclopentanol, 17 g. more of aluminum chloride was then added, followed by a further 20 g. of cyclopentanol. The reaction mixture was then poured on ice, and the organic layer washed several times with 10% aqueous sodium hydroxide, then with water, dried over calcium chloride, and distilled. The yield was 54% of cyclopentylbenzene, and 15–20% of dicyclopentylbenzene.

*Acetylation of cyclopentylbenzene.* Into a solution of 14.6 g. of cyclopentylbenzene and 8.5 g. of acetyl chloride in 60 ml. of dry carbon disulfide, 14.8 g. of aluminum chloride was stirred portionwise, and the reaction mixture left overnight at room temperature, then heated on a water bath until hydrogen chloride ceased to evolve. After decomposition with ice, the product was taken up in chloroform and worked up in the usual way, to give a 79% yield of *p*-cyclopentylacetophenone, b.p. 170°/15 mm.,  $n_D^{20}$  1.5509; Kleene<sup>2</sup> gave b.p. 140–145°/2.5 mm. The corresponding semicarbazone crystallized from ethanol in shiny colorless prisms, m.p. 233°.

*Anal.* Calcd. for C<sub>14</sub>H<sub>19</sub>N<sub>3</sub>O: C, 68.6; H, 7.7; N, 17.1. Found: C, 68.5; H, 7.6; N, 17.1.

The *oxime* crystallized from ethanol in shiny colorless needles, m.p. 104°.

*Anal.* Calcd. for C<sub>13</sub>H<sub>17</sub>NO: C, 76.8; H, 8.30; N, 6.9. Found: C, 76.7; H, 8.2; N, 6.9.

Degradation of 3.8 g. of this ketone with aqueous sodium hypobromite (prepared from 6.4 g. of sodium hydroxide and 9.6 g. of bromine) at 60–70° afforded *p*-cyclopentylbenzoic

*acid*, crystallizing from benzene in colorless prisms, m.p. 200°. Yield: 42%.

*p*-Cyclopentylpropiofenone. Prepared as for the lower homolog, from 14.8 g. of cyclopentylbenzene, 9.2 g. of propionyl chloride, and 14.8 g. of aluminum chloride in carbon disulfide, this ketone was obtained in 80% yield as a pale yellow liquid, b.p. 182°/17 mm.,  $n_D^{19}$  1.5439.

*Anal.* Calcd. for C<sub>14</sub>H<sub>18</sub>O: C, 83.1; H, 9.0. Found: C, 83.0; H, 9.1.

*p*-Cyclopentylbutyrophenone. This ketone, obtained in 80% yield from 14.8 g. of cyclopentylbenzene, 10.6 g. of butyryl chloride, and 14.8 g. of aluminum chloride in carbon disulfide, was a pale yellow oil, b.p. 204–206°/27 mm.,  $n_D^{19}$  1.5437.

*Anal.* Calcd. for C<sub>15</sub>H<sub>20</sub>O: C, 83.3; H, 9.3. Found: C, 83.2; H, 9.5.

*p*-Cyclopentylaniline (I). To an ice-cooled solution of 20.3 g. of *p*-cyclopentylacetophenone oxime in 100 ml. of dry ether, 31 g. of finely powdered phosphorus pentachloride was added portionwise with stirring. After evaporation of the solvent, the residue was treated with ice, and the precipitate which formed was recrystallized from ethanol. Yield: 16 g. of *p*-cyclopentylacetanilide, shiny colorless prisms, m.p. 136°.

*Anal.* Calcd. for C<sub>13</sub>H<sub>17</sub>NO: C, 76.8; H, 8.3. Found: C, 76.7; H, 8.3.

Hydrolysis of 20.3 g. of the foregoing amide, effected by refluxing for 2 hr. with 30 ml. of hydrochloric acid in 100 ml. of ethanol, followed by the usual treatment, yielded 12 g. of *p*-cyclopentylaniline, a colorless liquid, b.p. 165–167°/22 mm.,  $n_D^{19}$  1.5710.

*Anal.* Calcd. for C<sub>11</sub>H<sub>15</sub>N: C, 81.9; H, 9.3; N, 8.7. Found: C, 81.7; H, 9.2; N, 8.8.

1-*p*-Cyclopentyl-2,5-dimethylpyrrole (III). A mixture of 3.3 g. of *p*-cyclopentylaniline and 4 g. of acetylacetone was refluxed for 30 min., then vacuum distilled. Yield: 3 g. of a pyrrole, b.p. 207°/25 mm., crystallizing from methanol in shiny colorless prisms, m.p. 42°.

*Anal.* Calcd. for C<sub>17</sub>H<sub>21</sub>N: C, 85.3; H, 8.8. Found: C, 85.2; H, 8.7.

2-Chloro-3-(*p*-cyclopentylanilino)-1,4-naphthoquinone. An ethanolic solution of 1.2 g. of 2,3-dichloro-1,4-naphthoquinone, 0.8 g. of *p*-cyclopentylaniline, and 1.2 g. of sodium acetate was refluxed for one hour, and the precipitate formed on cooling was recrystallized from a mixture of ethanol and benzene, giving shiny violet needles, m.p. 158°.

*Anal.* Calcd. for C<sub>21</sub>H<sub>19</sub>ClNO<sub>2</sub>: C, 71.7; H, 5.1. Found: C, 71.5; H, 5.0.

2,5-Dichloro-3,6-bis(*p*-cyclopentylanilino)-1,4-benzoquinone. Prepared as above from 1 g. of *p*-cyclopentylaniline, 0.9 g. of chloranil, and 2 g. of sodium acetate, this compound

crystallized from toluene in shiny brown leaflets, m.p. 309°.

*Anal.* Calcd. for  $C_{23}H_{23}Cl_2N_2O_2$ : C, 67.9; H, 5.6. Found: C, 67.5; H, 5.7.

*N-(p-Cyclopentylphenyl)tetrachlorophthalimide.* To a boiling solution of 1 g. of tetrachlorophthalic anhydride in 15 ml. of acetic acid, 0.6 g. of *p*-cyclopentylaniline was added dropwise, and the mixture refluxed for a few minutes. The solid formed after cooling was recrystallized from acetic acid, giving shiny colorless needles, m.p. 242°.

*Anal.* Calcd. for  $C_{19}H_{13}Cl_4NO_2$ : C, 53.2; H, 3.0. Found: C, 53.4; H, 2.9.

*N-(p-Cyclopentylphenyl)glycine (IV).* A mixture of 3.2 g. of *p*-cyclopentylaniline, 2 g. of chloroacetic acid, and 6 g. of sodium acetate in aqueous solution was heated on a water bath for 1 hr. After cooling, and dilution with water, the precipitate formed was collected, redissolved in 10% aqueous ammonium carbonate, and the filtrate acidified with acetic acid; the precipitate, obtained in 50% yield, crystallized from water in shiny colorless prisms, m.p. 199°.

*Anal.* Calcd. for  $C_{13}H_{17}NO_2$ : C, 71.2; H, 7.8. Found: C, 71.1; H, 7.8.

The corresponding *ethyl ester* was prepared by heating for 3 hr. on a water bath a mixture of 6.4 g. of *p*-cyclopentylaniline, 8 g. of ethyl bromoacetate, and 15 g. of sodium acetate. 50 ml. of water was then added, the reaction product taken up in chloroform, the chloroform solution washed with water and dried over sodium sulfate, the solvent removed, and the residue fractionated to yield 77% of an ester, b.p. 219–221°/15 mm., crystallizing from petroleum ether in colorless prisms, m.p. 42°.

*Anal.* Calcd. for  $C_{15}H_{21}NO_2$ : C, 72.9; H, 8.5. Found: C, 72.7; H, 8.4.

The corresponding *hydrazide* was prepared by refluxing for 2 hr. a solution of 2.5 g. of the foregoing ester and 1.5 g. of 98% hydrazine hydrate in 20 ml. of ethanol; the precipitate obtained in 98% yield after cooling, was recrystallized from ethanol, giving shiny colorless prisms, m.p. 153°.

*Anal.* Calcd. for  $C_{13}H_{19}N_3O$ : C, 66.9; H, 8.1. Found: C, 66.8; H, 8.0.

*Preparation of thiocarbanilides derived from I.* Equimolar amounts of *p*-cyclopentylaniline and the appropriate aryl isothiocyanate were heated at 50–60° for 30 min. in ethanol medium; the precipitate formed on cooling was re-

crystallized from ethanol, giving in every instance shiny colorless prisms, with a bitter taste.

*Preparation of N,N'-diaryltureas derived from I.* *p*-Cyclopentylaniline was allowed to react with an equimolar quantity of the appropriate aryl isocyanate in benzene medium in the cold; the urea obtained was recrystallized from ethanol or an ethanol-benzene mixture.

*2-(p-Cyclopentylphenyl)indole (VII).* A mixture of 3 g. of *p*-cyclopentylacetophenone and 2 g. of phenylhydrazine was heated for a few minutes at 140–150° with removal of water; to this crude phenylhydrazone, 7 g. of finely powdered, fused zinc chloride was added, and the mixture heated for 15 min. at 185–195°. After cooling, aqueous acetic acid was added, the reaction product taken up in benzene, and the benzene solution washed with water and dried over sodium sulfate. The residue from evaporation of the solvent was vacuum distilled, and the fraction, b.p. 270–272°/13 mm., recrystallized from a benzene-ethanol mixture. Yield: 70% of shiny colorless prisms, m.p. 236°, giving a deep violet picrate.

*Anal.* Calcd. for  $C_{19}H_{19}N$ : C, 87.3; H, 7.3. Found: C, 87.0; H, 7.4.

*Pfitzinger reactions with 4-acylcyclopentylbenzenes.* A mixture of 1 mole of isatin and 1 mole of the appropriate ketone with a 20% ethanol solution of 3 moles of potassium hydroxide was gently refluxed on a water bath for 72 hr.; after dilution with water and ether-extraction of the neutral impurities, the aqueous layer was acidified with acetic acid, and the precipitated *cinchoninic acid* was washed with water, dried, and recrystallized from ethanol, giving yellowish needles in every instance. The yields ranged from 30% for *p*-cyclopentylbutyrylphenone, to 80–85% of *p*-cyclopentylacetophenone. For the preparation of the corresponding quinolines, the appropriate cinchoninic acid was heated above its melting point, and the decarboxylation product was vacuum-distilled and recrystallized from ethanol, to give shiny colorless prisms.

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[CONTRIBUTION FROM THE RADIUM INSTITUTE OF THE UNIVERSITY OF PARIS]

## $\alpha,\alpha$ -Dimethyl- $\beta$ -arylethylamines, and Their Behavior in the Bischler-Napieralski Reaction

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Several new *p*-substituted  $\alpha,\alpha$ -dimethyl- $\beta$ -phenethylamines have been synthesized for biological testing as potential sympathomimetic amines, and their amides found to resist the Bischler-Napieralski cyclization to dihydroisoquinolines. This failure is accounted for on the grounds of steric hindrance.

$\alpha,\alpha$ -Dialkyl- $\beta$ -arylethylamines (I), investigated first by Mentzer,<sup>1</sup> and then by Mentzer, Buu-Hoï, and Cagniant,<sup>2</sup> possess interesting sympathomimetic activity, and recently one of the compounds of this group, *N*-methyl- $\alpha,\alpha$ -dimethyl- $\beta$ -phenethylamine, has found therapeutic application<sup>3</sup> under the

name of "Mephentermine," as a vasoconstrictor with no cerebral-stimulating effects. It was of interest to examine the biological properties of a number of hitherto unknown *p*-substituted  $\alpha,\alpha$ -dimethyl- $\beta$ -phenethylamines, and the synthesis of several of these new compounds is now described.

(1) C. Mentzer, *Compt. rend.*, **213**, 581 (1941).

(2) C. Mentzer, N. P. Buu-Hoï, and P. Cagniant, *Bull. soc. chim., France*, **9** [5], 813 (1942).

(3) cf. A. Burger, *Medicinal Chemistry*, Interscience Publishers Inc., New York, 1951, p. 311.