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

Oxidative Reactions of Hydrazines. V. Synthesis of Monobenzyl 1,1-Disubstituted Hydrazines and 2-Amino-2,3-dihydro-1H-benz[de]isoquinoline[1,2]

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A series of 1,1-disubstituted hydrazines has been prepared. Reduction of the corresponding nitrosamines by aluminum amalgam yielded 1-*t*-butyl-, 1-*n*-butyl- and 1-allyl-1-benzylhydrazines. Benzoylation of *t*-butyl 2-benzylcarbazate followed by removal of the carbo-*t*-butoxy group gave 1-benzoyl-1-benzylhydrazine. 2-Amino-2,3-dihydro-1-*H*-benz[de]isoquinoline was obtained by reduction of N-aminonaphthalimide. Preliminary oxidation studies of 1-*n*-butyl- and 1-*t*-butyl-1-benzylhydrazine are reported.

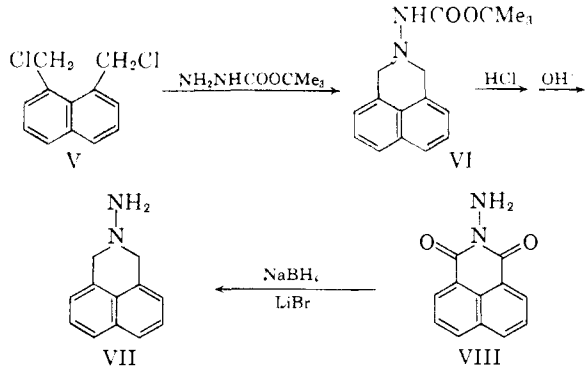
It was reported recently[3] that 1,1-dibenzyl-2-arenesulfonhydrazides upon treatment with aqueous alkali underwent conversion to bibenzyls. It had been reported earlier that mercuric oxide oxidation of the corresponding free hydrazines also yielded bibenzyls.[4,5] To date the only 1,1-disubstituted hydrazines which have been observed to undergo these two reactions with the formation of coupling products are those having two benzyl, benzyl-like or α-cyanoalkyl substituents. In the present work a number of monobenzyl derivatives has been prepared in order to provide for further study of the scope of the reaction. The synthesis of 1-allyl-, 1-*n*-butyl- and 1-*t*-butyl-1-benzylhydrazine proceeded by reduction of the corresponding nitrosamine by means of aluminum amalgam in wet ether. Of the methods previously used most commonly in the reduction of nitrosamines such as those involving zinc–acetic acid, lithium aluminum hydride or sodium in ethanol,[6] only the last-named gave consistent reduction to the hydrazine.[7] However, the yields were lower and the reaction less convenient to carry out than reductions involving aluminum amalgam.

1-Benzyl-1-benzoylhydrazine (I) was prepared by benzoylation of *t*-butyl 2-benzylcarbazate (III) and removal of the carbo-*t*-butoxy group.[8]

$C_6H_5CH{=}NNHCOOCMe_3$ (II) $\qquad$ $C_6H_5CH_2NHNHCOOCMe_3$ (III)

$C_6H_5CH_2NNHCOOCMe_3$
$\quad\quad|$
$\quad COC_6H_5$
IV

The cyclic hydrazine VII was first prepared in a similar manner from 1,8-dichloromethylnaphthalene and *t*-butyl carbazate. A more convenient method involved reduction of N-aminonaphthalimide (VIII) by means of sodium borohydride and lithium bromide in diglyme solution.[9] Attempted application of this procedure to the reduction of

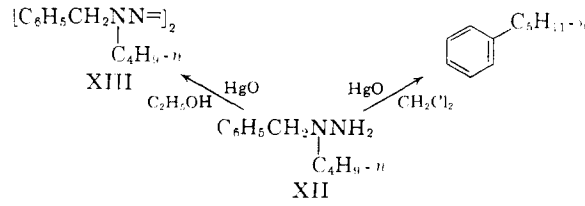


N-aminophthalimide[10] was unsuccessful. Most of the new hydrazines prepared in the course of this work were characterized as their arenesulfonyl derivatives. These were prepared in the usual manner by acylation in dimethylformamide in the presence of triethylamine.[3] The hydrazides prepared are listed in Table I. Generally *p*-toluene and β-naphthalene sulfonhydrazides have been used in this work.

Oxidation of 1-*t*-butyl-1-benzylhydrazine (IX) by mercuric oxide in methylene dichloride gave a low yield (23.6%) of the corresponding hydrocarbon, 1-phenyl-2,2-dimethylpropane (X), accompanied by dibenzylmercury (XI). Similarly oxi-

$$\underset{\text{IX}}{C_6H_5CH_2\underset{\displaystyle NH_2}{\underset{|}{N}}CMe_3} \xrightarrow[CH_2Cl_2]{HgO} \underset{\text{X}}{C_6H_5CH_2CMe_3} + \underset{\text{XI}}{(C_6H_5CH_2)_2Hg}$$

dation of 1-*n*-butyl-1-benzylhydrazine (XII) by mercuric oxide in methylene dichloride solution gave a low yield (20%) of *n*-amylbenzene. Oxida-



tion by mercuric oxide in 95% ethanol gave a compound to which the tetrazene structure XIII is assigned on the basis of its infrared spectrum and the observation that warming with dilute sulfuric acid causes gas evolution and the development of a strong odor of benzaldehyde. Oxidation by silver-

(1) Supported by the United States Air Force under Contract No. AF 18(603)-114. Reproduction in whole or in part is permitted for any purpose of the United States Government.

(2) Taken in part from the M.S. Thesis (1959) of R. W. M.

(3) L. A. Carpino, THIS JOURNAL, **79**, 4427 (1957).

(4) M. Busch and B. Weiss, *Ber.*, **33**, 270 (1900); see also C. G. Overberger and B. S. Marks, THIS JOURNAL, **77**, 4104 (1955).

(5) R. L. Hinman and K. L. Hamm, *ibid.*, **81**, 3294 (1959).

(6) H. Zimmer, L. F. Audrieth, M. Zimmer and R. A. Rowe, *ibid.*, **77**, 790 (1955).

(7) For example in the case of *t*-butylbenzylnitrosamine zinc-acetic acid regenerated the *sec*-amine and lithium aluminum hydride gave a mixture of substances not completely identified.

(8) L. A. Carpino, THIS JOURNAL, **79**, 98 (1957).

(9) H. C. Brown and B. C. Subba Rao, *ibid.*, **78**, 2582 (1956).

(10) H. D. K. Drew and H. H. Hatt, *J. Chem. Soc.*, 16 (1937).

TABLE I

1,1-DISUBSTITUTED-2-ARENESULFONHYDRAZIDES, $\begin{matrix} R' \\ R \end{matrix}\!\!>\!NNHSO_2R''$

R	R'	R''	M.p., °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
C_6H_5	$C_6H_5CH_2$	p-C_7H_7	142–143.5[a]	$C_{20}H_{20}N_2SO_2$	68.15	68.25	5.72	5.71
C_6H_5	CH_2=$CHCH_2$	p-C_7H_7	101[b]	$C_{16}H_{18}N_2SO_2$	63.55	63.23	6.00	6.02
$C_6H_5CH_2$	CH_2=$CHCH_2$	β-$C_{10}H_7$	115.5–116[c]	$C_{20}H_{20}N_2SO_2$	68.15	67.80	5.72	6.01
C_6H_{11}	C_6H_{11}	p-C_7H_7	133–133.5[d]	$C_{19}H_{30}N_2SO_2$	65.10	65.20	8.63	8.51
$C_6H_5CH_2$	n-C_4H_9	β-$C_{10}H_7$	72.5–73.5[e]	$C_{21}H_{24}N_2SO_2$	68.45	68.38	6.55	6.31
R—R' =	$(CH_2)_5$	p-C_7H_7	122.5–123[f]	$C_{12}H_{18}N_2SO_2$	56.66	56.62	7.13	6.94

[a] Recrystallized from nitromethane. The hydrazine was obtained from the Eastman Kodak Co. [b] Recrystallized from 60–90° ligroin. The hydrazine was prepared by the method of A. Michaelis and C. Claessen, *Ber.*, **22**, 2233 (1889). [c] Recrystallized from 60–90° ligroin. [d] Recrystallized from ethanol–water. The hydrazine was prepared by the method of C. Hannah and F. W. Shuler, THIS JOURNAL, **74**, 3693 (1952). [e] Recrystallized from methanol–water. [f] Recrystallized from nitromethane. The hydrazine was prepared by lithium aluminum hydride reduction of the corresponding nitramine; see Experimental section.

(I) oxide[11] yielded *n*-butylbenzylamine as the primary product. A more detailed study of the effect of solvent and oxidizing agent on the oxidation of 1-*t*-butyl- and 1-*n*-butyl-1-benzylhydrazine is being made prior to a study of the oxidation of VII and the other monobenzyl hydrazines reported herein.

Experimental[12,13]

Allylbenzylamine and Allylbenzylnitrosamine.—A mixture of 40 g. of sodium hydroxide, 300 ml. of water, 107.1 g. of benzylamine and 76.5 g. of allyl chloride was stirred under gentle reflux for 15 hours. The organic layer was separated from the cooled reaction mixture and the aqueous layer was extracted twice with 50-ml. portions of methylene dichloride. The combined organic layers were dried (magnesium sulfate) and fractionated through a 30-cm. helices-packed column. There was obtained 62.7 g. (42.6%) of allylbenzylamine, b.p. 105–110.5° (11 mm.), lit.[14] b.p. 205–208°.[15] A solution of 27 g. of benzylallylamine in 37 ml. of water and 37 ml. of glacial acetic acid was cooled in an ice-bath and with stirring 14.2 g. of sodium nitrite was added in small portions over a period of 8–10 minutes. The mixture was then heated on a steam-bath (internal temperature 75–80°) for 0.5 hour and the oily layer extracted with two 50-ml. portions of methylene dichloride. The solvent was removed from the dried (magnesium sulfate) solution and the nitrosamine distilled through a 30-cm. helices packed column; b.p. 107–109° (1.2 mm.), 53.2 g. (82.2%).

Anal. Calcd. for $C_{10}H_{12}N_2O$: C, 68.15; H, 6.87. Found: C, 68.24; H, 6.90.

1-Allyl-1-benzylhydrazine.—To a slowly stirred mixture of 68.2 g. of aluminum amalgam[16] and 1300 ml. of ordinary ether was added in one portion 148.4 g. of allylbenzylnitrosamine. It was necessary to cool the mixture in an ice-bath for about 0.5 hour in order to moderate the vigorous reaction. When the spontaneous refluxing began to slow down, the ice-bath was removed and 45.5 g. of water was added dropwise with vigorous stirring at a rate to maintain steady refluxing (1.5 hours). The mixture was stirred at room temperature for an additional 4 hours and the ether and aluminum oxide sludge decanted from the unreacted aluminum into a stirred solution of 318 g. of sodium hydroxide dissolved in 1300 ml. of water at room temperature. The mixture was stirred for 10–15 min. to ensure complete solution of the oxide, the layers separated and the ether layer combined with a 75-ml. portion of fresh ether used to extract the aqueous layer. After removal of the ether from the combined and dried (magnesium sulfate) solution, the residue was distilled through a Claisen head and then fractionated through a 30-cm. helices packed column. There was obtained 80 g. (62.3%) of the hydrazine, b.p. 74–79° (0.3 mm.). Redistillation through the same column gave 69.5 g. (51%), b.p. 73–75° (0.3 mm.).[17]

Anal. Calcd. for $C_{10}H_{14}N_2$: C, 74.03; H, 8.70. Found: C, 74.44; H, 8.76.

1-Benzyl-1-*n*-butylhydrazine.—Reduction of 190 g. of *n*-butylbenzylnitrosamine in 1500 ml. of ether by means of 67.5 g. of aluminum amalgam was carried out by the method indicated for the corresponding allyl derivative except that the nitroso compound was added dropwise, after the addition of a 50-g. charge, to the reaction mixture at a rate to maintain steady refluxing (1–1.5 hr.). Dropwise addition of 45 g. of water required another 1.5 hr. after which stirring was continued at room temperature for 4 hours and the mixture decomposed as before. There was obtained 110.5 g. (62.7%) of the hydrazine, b.p. 78–81° (0.2 mm.).[18]

Anal. Calcd. for $C_{11}H_{18}N_2$: C, 74.11; H, 10.18. Found: C, 74.18; H, 10.03.

1-Benzyl-1-*t*-butylhydrazine.—*t*-Butylbenzylamine[19] (from benzyl chloride and *t*-butylamine, 75–80%) was nitrosated by the method described above for allylbenzylnitrosamine. The yield was 88–93%, m.p. 44.5–46° (ligroin, b.p. 60–90°), lit.[20] m.p. 45–46°. Into a stirred mixture of 101 g. of the nitrosamine, 42.5 g. of aluminum amalgam and 1100 ml. of ether there was allowed to drop 28.4 g. of water at a rate to maintain spontaneous refluxing (2 hours). The mixture was stirred at room temperature for an additional 8 hours and worked up as given for the corresponding allyl compound. Fractionation through a 30-cm. helices-packed column gave 34.5 g. (40%) of *t*-butylbenzylamine, b.p. 81–85° (3.4 mm.), and 35.5 g. (38%) of 1-benzyl-1-*t*-butylhydrazine,[21] b.p. 96–99° (3.0 mm.).

Anal. Calcd. for $C_{11}H_{18}N_2$: C, 74.11; H, 10.18. Found: C, 74.42; H, 10.23.

The benzal derivative had m.p. 84–86° (ethanol).

Anal. Calcd. for $C_{18}H_{22}N_2$: C, 81.16; H, 8.33. Found: C, 80.93; H, 8.46.

(11) Silver(I) oxide has been used as a substitute for mercuric oxide in the oxidation of hydrazones to diazo compounds; see W. Schroeder and L. Katz, *J. Org. Chem.*, **19**, 718 (1954).

(12) Melting points and boiling points are uncorrected.

(13) Analyses are by Weiler and Strauss, Oxford, England.

(14) C. Paal and H. Apitzsch, *Ber.*, **32**, 78 (1899).

(15) Benzylallylamine also was prepared by treatment of N-benzylacetamide with sodium hydride in refluxing xylene (18 hours) followed by addition of allyl chloride (8-hour reflux) and hydrolysis of the resulting crude, distilled amide [79%, b.p. 126–129° (1.5 mm.)] by 30-hour refluxing with concentrated hydrochloric acid. The yield was 45%.

(16) Aluminum (8–20 mesh) was amalgamated by the method of I. Vogel, *J. Chem. Soc.*, 594 (1927).

(17) Reduction by means of zinc dust and dilute acetic acid at 10–20° gave only 18% of the hydrazine accompanied by an equal weight of the secondary amine.

(18) Reduction of 80.1 g. of the nitrosamine by means of 40 g. of sodium in 400 ml. of commercial absolute ethanol by the method of Audrieth, *et al.*,[8] gave 31.3 g. (42%) of the hydrazine. Approximately 25% of the unreacted nitrosamine was recovered.

(19) N. Bortnick, L. S. Luskin, M. D. Hurwitz, W. E. Craig, L. J. Exner and J. Mirza, THIS JOURNAL, **78**, 4039 (1956).

(20) R. Labriola, I. Dorronsoro and O. Verruno, *Anales asoc. quim. argentina*, **37**, 79 (1949).

(21) Reduction of the nitrosamine by means of sodium and ethanol gave a 31% yield of the hydrazine.

N-Aminopiperidine from N-Nitropiperidine.[22]—To a stirred suspension of 19.8 g. of lithium aluminum hydride in 350 ml. of dry ether there was added 27 g. of N-nitropiperidine dropwise at a rate to maintain gentle refluxing. The mixture was stirred for an additional hour and then decomposed by the addition of 50 ml. of wet ether followed by 30–40 ml. of water. The solution was filtered to remove the aluminum salts, dried (magnesium sulfate) and the ether removed by distillation from a water-bath with the aid of a water aspirator.

The hydrazine was distilled at 81–87° (21 mm.) and amounted to 19.2 g. (92%), lit.[23] b.p. 145–146° (728 mm.).

2-*t*-Butyloxycarbonylamino-2,3-dihydro-1-*H*-benz[de]-isoquinoline (VI).—A solution of 44.5 g. of 1,8-bis-(chloromethyl)-naphthalene[24] and 26 g. of *t*-butyl carbazate in 200 ml. of dimethylformamide was warmed to 50° and 39.8 g. of triethylamine was added in small portions while keeping the temperature below 60°. After the mixture had stood for several hours at 25°, 500 ml. of water was added and the mixture extracted with three 100-ml. portions of methylene dichloride. Removal of the solvent gave 22 g. (38%) of the substituted carbazate, m.p. 200–250° dec. An analytical sample was prepared by recrystallization from nitromethane; m.p. 240–250° dec.

Anal. Calcd. for $C_{17}H_{20}N_2O_2$: C, 71.80; H, 7.08. Found: C, 72.32; H, 6.97.

N-Aminonaphthalimide (VIII).—A suspension of 39.7 g. of naphthalic anhydride in 200 ml. of dimethylformamide was heated nearly to boiling and 9.1 ml. of 64% hydrazine added slowly. The solid gradually dissolved and was replaced by yellow-gray needles which were filtered when cool giving 38 g. (89.7%) of VIII, m.p. 260–262°. Recrystallization from nitromethane gave 32.5 g. (76.7%) of golden needles, m.p. 265–266° (softening at 260°) (lit.[25] m.p. 262°).

The benzal derivative crystallized from dimethylformamide as yellow needles, m.p. 208–210° (lit.[25] m.p. 206°).

2-Amino-2,3-dihydro-1*H*-benz[de]isoquinoline Hydrochloride (VII·HCl).—A reducing solution was prepared by addition of 3.6 g. of sodium borohydride and 8.26 g. of lithium bromide to 40 ml. of well-stirred diglyme.[8] The mixture was cooled in a water-bath at 10–15° and 8.48 g. of N-aminonaphthalimide was added during 15 min. The cooling bath was removed and the mixture stirred at room temperature for 6 hours and decomposed by the addition of 50 ml. of water followed by solid potassium hydroxide until phase separation occurred. After adding 40 ml. of ether, the layers were separated and the aqueous layer extracted with three additional 25-ml. portions of ether. The combined and dried (magnesium sulfate) extracts were treated with hydrogen chloride which precipitated 4.4 g. (50%) of cream-white powder, m.p. 231–235° dec. Dissolution in hot ethanol and then precipitation with an excess of ether gave 4 g. (45.3%) of small cream-white crystals, m.p. 233–237° dec. The same substance (m.p. and mixed m.p.) was obtained by cleavage of VI in the usual manner.[8]

Anal. Calcd. for $C_{12}H_{13}N_2Cl$: C, 65.30; H, 5.93. Found: C, 65.50; H, 6.15.

2-*p*-Toluenesulfonylamino-2,3-dihydro-1*H*-benz[de]isoquinoline.—A solution of 6.6 g. of the hydrochloride of VII in 80 ml. of hot dimethylformamide was treated with 8.35 ml. of triethylamine. The mixture was cooled well in an ice bath and 5.71 g. of *p*-toluenesulfonyl chloride added during 15 min. After standing for 1 hour in the ice-bath and 6 hours at room temperature, the mixture was slowly and carefully diluted with 175 ml. of water which caused the separation of 7 g. (69%) of the crude hydrazide. Recrystallization from nitromethane gave 5.5 g. (54%) of tan-cream crystals, m.p. 159–163° dec. An analytical sample was prepared by recrystallization from nitromethane which gave small white crystals, m.p. 164–166° dec.

Anal. Calcd. for $C_{19}H_{18}N_2SO_2$: C, 67.42; H, 5.37. Found: C, 67.66; H, 5.50.

2-Amino-2,3-dihydro-1*H*-benz[de]isoquinoline.—A solution of 7 g. of the hydrochloride of VII dissolved in 125 ml. of warm water was treated with an excess of solid potassium hydroxide and the floating oil extracted with methylene chloride. Evaporation of the solvent from a water-bath with a water aspirator gave 5 g. (85.5%) of cream-tan solid, m.p. 65–71°. Recrystallization from ligroin (b.p. 60–90°) gave 4.3 g. (73.5%) of white needles, m.p. 70–72°.

Anal. Calcd. for $C_{12}H_{12}N_2$: C, 78.22; H, 6.57. Found: C, 78.40; H, 6.79.

The benzal derivative of VII, prepared in the usual manner, crystallized from ethanol as small white needles, m.p. 118.5–120.5°.

Anal. Calcd. for $C_{19}H_{16}N_2$: C, 83.79; H, 5.92. Found: C, 83.60; H, 5.92.

***t*-Butyl Benzalcarbazate.**[8]—A solution of 66 g. of *t*-butyl carbazate in 250 ml. of ethyl alcohol was treated slowly with a stream of 53 g. of benzaldehyde. In a short time a cream colored solid precipitated. After allowing the mixture to stand for two hours the solid was filtered giving 103 g. (94%), m.p. 179–180°, of the benzal derivative. Recrystallization from ethyl alcohol gave 91 g. (83%) of II, m.p. 185–187°.

***t*-Butyl 2-Benzylcarbazate (III).**—To a stirred suspension of 10 g. of lithium aluminum hydride in 250 ml. of dry ether there was added 52.5 g. of the benzal derivative of *t*-butyl carbazate (finely powdered) during 1 hour. The mixture was refluxed for 3 hours and the excess hydride destroyed by the dropwise addition of 50 ml. of wet ether followed by about 40 ml. of water. An excess of water should be avoided in order to avoid emulsification of the aluminum salts. The precipitate was filtered and washed with 200 ml. of ether. The combined filtrates were dried (magnesium sulfate), the ether removed and the residual oil distilled from a Claisen flask which gave 32.5 g. (62%) of the carbazate, b.p. 120–126° (0.8 mm.). An analytical sample had b.p. 121° (0.8 mm.).

Anal. Calcd. for $C_{12}H_{18}N_2O_2$: C, 64.83; H, 8.16. Found: C, 65.38; H, 8.50.

***t*-Butyl 2-Benzoyl-2-benzylcarbazate (IV).**—A solution of 6.5 g. of *t*-butyl 2-benzylcarbazate in 17 ml. of dimethylformamide and 4.1 ml. of triethylamine was cooled in an ice-bath and with stirring there was added during 10 min. a solution of 3.41 g. of benzoyl chloride in 10 ml. of dimethylformamide. The mixture was allowed to stand in the ice-bath for 30 min., diluted to 100 ml. with water and allowed to stand for several hours until the oil solidified. The white solid amounted to 8 g. (84%), m.p. 107–115° (softening at 100°). Recrystallization from nitromethane gave 6 g. (63%) of small white crystals, m.p. 119–124°. The analytical sample (nitromethane) had m.p. 125–126.5°.

Anal. Calcd. for $C_{19}H_{22}N_2O_3$: C, 69.91; H, 6.80. Found: C, 69.96; H, 6.62.

1-Benzoyl-1-benzylhydrazine.[26]—A solution of 2 g. of *t*-butyl 2-benzoyl-2-benzylcarbazate dissolved in 12 ml. of nitromethane was treated with a stream of hydrogen chloride gas for 5 min. The cloudy solution was diluted with 30 ml. of ether and cooled in an ice-bath which caused the separation of 1.4 g. (87%) of the hydrochloride, m.p. 155–161°. Recrystallization by dissolution in ethanol and dilution with ether gave 1.1 g. (68.5%) of white flocky crystals, m.p. 159–163°. This crude material was added to 10 ml. of water and the resulting mixture made basic with sodium bicarbonate solution. An oil separated which crystallized on cooling in an ice-bath to a white solid; 0.6 g. (63.6%), m.p. 66–70°. The analytical sample was recrystallized from ligroin (b.p. 60–90°)–benzene; m.p. 69–71°.

Anal. Calcd. for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24. Found: C, 74.37; H, 6.18.

Mercuric Oxide Oxidation of 1-Benzyl-1-*t*-butylhydrazine.—A suspension of 21.7 g. of mercuric oxide[27] in 120 g. of methylene dichloride was treated slowly (5–8 min.) with 17.8 g. of 1-benzyl-1-*t*-butylhydrazine allowing the vigorous

(22) Lithium aluminum hydride reduction of nitrosamines often is accompanied by a dangerous induction period. This was not observed when the nitramine was used.

(23) L. Knorr, *Ann.*, **221**, 297 (1883).

(24) V. Boekelheide and G. K. Vick, THIS JOURNAL, **78**, 653 (1956).

(25) A. Bistrzycki and J. Risi, *Helv. Chim. Acta*, **8**, 810 (1925).

(26) The isomeric 1-benzyl-2-benzoylhydrazine, m.p. 115°, has been prepared by reduction of the corresponding hydrazone; see J. S. Aggarwal, N. L. Darbari and J. N. Ray, *J. Chem. Soc.*, 1941 (1929).

(27) The mercuric oxide was prepared by adding a warm solution of 22.4 g. of potassium hydroxide in 200 ml. of water to a solution of 54.3 g. of mercuric chloride in 500 ml. of hot water. When prepared in this way the oxide has a brown color. Inverse addition of the reagents yields an oxide of yellow color.

reaction to subside between additions. The oxide was replaced by a globule of bright metallic mercury. When gas evolution became very slow an additional 2 g. of mercuric oxide was added and the mixture allowed to stand at room temperature for 2 hours with occasional shaking, dried (magnesium sulfate), filtered and evaporated at 35–40° (140 mm.). The clear oil (20 g.) deposited a crystalline solid on standing. Trituration with petroleum ether gave 9 g. (46.5%) of crude dibenzylmercury, m.p. 83–98°. Several crystallizations from nitromethane gave white needles, m.p. 110–113° (lit.[28] m.p. 111°).

Anal. Calcd. for $C_{14}H_{14}Hg$: C, 43.92; H, 3.68. Found: C, 43.91, H, 3.73.

The petroleum ether filtrate from the above trituration was evaporated at 70° (140 mm.) and the residue distilled. There was obtained 3.5 g. (23.6%) of 1-phenyl-2,2-dimethylpropane, b.p. 86–88° (20 mm.), shown by infrared analysis to be identical with an authentic sample [b.p. 75–76° (15 mm.)] prepared from benzylmagnesium chloride and *t*-butyl chloride [lit.[29] b.p. 185.6–186° (757.6 mm.)].

(28) P. Wolff, *Ber.*, **46**, 65 (1913).

(29) A. Bygden, *ibid.*, **45**, 3479 (1912).

Mercuric Oxide Oxidation of 1-*n*-Butyl-1-benzylhydrazine. (A) **In Methylene Dichloride.**—The reaction was carried out as indicated for the *t*-butyl derivative. Fractionation yielded 20% of a liquid, b.p. 90–94° (15 mm.), $n^{27}D$ 1.4870, shown by infrared analysis to be identical with an authentic sample of *n*-amylbenzene prepared from benzylmagnesium chloride and *n*-butyl *p*-toluenesulfonate by the method of Gilman and Beaber.[30]

(B) **In Ethanol.**—A stirred mixture of 25 g. of mercuric oxide[27] and 100 ml. of 95% ethyl alcohol was refluxed while 17.8 g. of the hydrazine was added in one portion. Within a short period a vigorous reaction set in and continued for 10–15 minutes after which the mixture was refluxed for 45 min. longer. The hot mixture was filtered and on standing overnight deposited 7 g. of white needles, m.p. 53–55°. Recrystallization of a portion from methanol gave the tetrazene XIII as small white crystals, m.p. 53.5–54.5°.

Anal. Calcd. for $C_{22}H_{32}N_4$: C, 74.95; H, 9.15. Found: C, 75.19; H, 9.23.

(30) H. Gilman and N. J. Beaber, THIS JOURNAL, **47**, 518 (1925).

AMHERST, MASS.

[CONTRIBUTION FROM THE ORGANIC CHEMICAL RESEARCH SECTION, LEDERLE LABORATORIES DIVISION, AMERICAN CYANAMID CO., PEARL RIVER, N. Y.]

Quinazolinone Sulfonamides. A New Class of Diuretic Agents[1]

BY ELLIOTT COHEN, BETTY KLARBERG AND JAMES R. VAUGHAN, JR.

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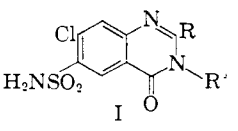
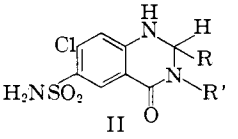
Investigation of diuretic activity in other heterocyclic systems has demonstrated that the benzothiadiazine 1,1-dioxide system is not unique in its effect on diuresis, natriuresis and chloruresis. A series of corresponding 7-chloro-6-sulfamyl-4(3H)-quinazolinones and 7-chloro-6-sulfamyl-1,2,3,4-tetrahydro-4-quinazolinones are described which have activity equal to or better than the benzothiadiazine 1,1-dioxides in experimental animals.

The current interest in orally active, heterocyclic diuretic agents, which are neither organic mercurial compounds nor primarily carbonic anhydrase inhibitors, has prompted intensive research in this field in many laboratories, both in this country and abroad.[2] In view of the well demonstrated clinical effectiveness of 6-chloro-7-sulfamyl-1,2,4-benzothiadiazine 1,1-dioxide and its 3,4-dihydro derivative, much of this research has been directed toward compounds of this type or, to other, similar systems.[2b,3] In our laboratories, the approach has been somewhat different in that, as a first step, we sought to determine the necessity for and the importance of the ring sulfur–1,1-dioxide system on the diuretic, chloruretic and natriuretic activities reported for this class of compounds. Consequently we prepared a series of 7-chloro-6-sulfamyl-4(3H)-quinazolinones (I) and 7-chloro-6-sulfamyl-1,2,3,4-tetrahydro-4-quinazolinones (II) for evaluation.



I



II

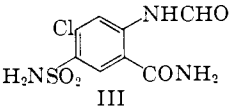
(1) A preliminary report on this work appears in THIS JOURNAL, **81**, 5508 (1959).

(2) (a) F. C. Novello and J. M. Sprague, *ibid.*, **79**, 2028 (1957); (b) Symposium on Chlorothiazide and its Derivatives, *Int. Rec. Med.*, **172**, Nos. 8, 9 (1959); see original articles for a very complete list of references.

(3) G. de Stevens, L. H. Werner, A. Halamandaris and S. Ricca, *Experientia*, **14**, 463 (1958).

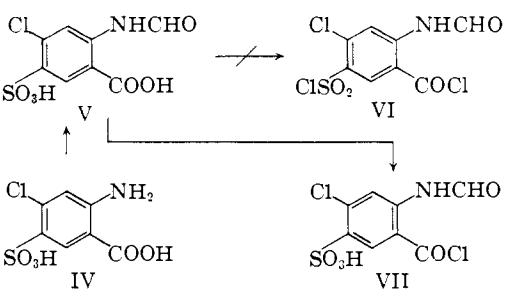
These examples, which may be considered as analogs of the benzothiadiazine-1,1-dioxides in which the cyclic $>SO_2$ group is replaced by $>C{=}O$, showed an activity equal to or better than that of the corresponding compounds in the benzothiadiazine series.[1]

Initial synthetic efforts in this program were directed toward the preparation of the diamide III. However, after sulfonation of 4-chloro-



III

anthranilic acid to give the sulfonic acid derivative IV, and subsequent formylation to V, all further attempts to make the diacid chloride VI, as an intermediate to the preparation of III, failed. The only product isolated was the mono-acid chloride VII.



V VI IV VII