racemization, even though the initial addition product is trans.[14]

Preliminary microbiological studies using 5 species of bacteria have been attempted; however, no significant inhibition of bacterial growth has been observed.

Experimental Section[15]

Intermediate Derivatives.—Cyclopentanone cyanohydrin was prepared from cyclopentanone in 86% yield,[16] converted into 1-cyanocyclopentene in 86% yield,[17] and finally, the latter compd was hydrolyzed to yield 1-cyclopentenecarboxylic acid in 50% yield.[18]

2-Amino-1-hydroxycyclopentanecarboxylic Acid.—Numerous attempts to prep the desired analog *via* a chlorohydrin reaction followed by ammonolysis failed, and the only amino acid isolated from these reactions was the isomeric product. For example, a soln of monochlorourea (40 ml), prepd from 5.5 g (0.77 mole) of Cl_2, 8 g (0.13 mole) of urea, and 6.7 g (0.067 mole) of $CaCO_3$,[7] was added to a mixt of 11.2 g (0.1 mole) of 1-cyclopentene-1-carboxylic acid in the presence of 5 ml of HOAc and 25 g of crushed ice, and the resulting mixt was stirred overnight with cooling in an ice bath. Attempts to isolate the chlorohydrin were unsuccessful, and the impure material was mixed with concd NH_4OH (350 ml) and allowed to stand at room temp for a 7-day period. The resulting soln was concd *in vacuo* and desalted by a modification of the procedure reported by Piez, *et al.*[19] The amino acid was crystd from H_2O–EtOH; mp 295–298° dec;[20] ir (KBr) 3.08, 3.37, 6.15, 9.0, and 12.6 μ; nmr δ 3.80 (t, 1 H, methine hydrogen), 1.60–2.64 (m, 6 H, $CH_2CH_2CH_2$). *Anal.* ($C_6H_{11}NO_3$): N.[21]

1-Amino-2-methoxycyclopentanecarbocylic Acid.—The synthesis of 1-bromo-2-methoxycyclopentanecarboxylic acid was patterned after a previously reported route for threonine[13] whereby a mixt of 56.2 g (0.5 mole) of 1-cyclopentene-1-carboxylic acid, 159.3 g (0.5 mole) of $Hg(OAc)_2$, and 750 ml of MeOH was stirred at room temp for 7 days to yield 149.2 g of adduct, mp 195–200° (presumably 1-acetoxymercuri-2-methoxycyclopentanecarboxylic acid). This material was added in small portions to a soln of 90 g (0.75 mole) of KBr in 500 ml of H_2O, cooled to 10°, and exposed to direct sunlight, and a soln of 80 g (0.5 mole) of Br_2 and 90 g (0.75 mole) of KBr in 150 ml of H_2O was added slowly with stirring. After extn with Et_2O and acidification with 47% HBr, there was recovered an amber oil (73.6 g, presumably 1-bromo-2-methoxycyclopentanecarboxylic acid) which failed to give a satisfactory elemental anal. *Anal.* (Calcd for $C_7H_{11}BrO_3$): C, 37.69; H, 4.97. Found: C, 38.51, 38.63; H, 5.25, 5.27.

A sample of this material (44.6 g) was added to 1350 ml of concd NH_4OH (cooled to 10–15°) and allowed to stand at room temp for 13 days. The resulting dark reaction mixt was filtered and reduced to near dryness *in vacuo*, and the residue was covered with Me_2CO to induce solidification. Ascending paper chromatograms indicated the presence of 2 ninhydrin-active components including a weak spot corresponding to 1-amino-2-hydroxycyclopentanecarboxylic acid (R_f 0.45, *n*-BuOH–HOAc–H_2O, 3:1:1); however, the major product was a ninhydrin-active compd with a different R_f value (R_f 0.68, *n*-BuOH–HOAc–H_2O, 3:1:1). This material was dissolved in H_2O, treated with decolorizing charcoal, and recrystd twice from H_2O–EtOH to yield white cryst free of the lower ninhydrin-active component which sublimes above 285°. *Anal.* ($C_7H_{13}NO_3 \cdot H_2O$): C, H, N.

An anhyd sample of 1-amino-2-methoxycyclopentanecarboxylic acid was obtained by vacuum sublimation at 124–140° (0.15 mm); ir (KBr) 3.38, 6.12, 7.20, 7.50, and 8.85 μ; nmr δ 4.20 (*t*, 1 H, CH), 3.52 (s, 3 H, OCH_3), 1.68–2.80 (m, 6 H, $CH_2CH_2CH_2$). *Anal.* ($C_7H_{13}NO_3$): C, H, N.

1-Amino-2-hydroxycyclopentanecarboxylic Acid.—A mixt 10.3 g of 49% HI and 0.7 g (0.0023 mole) of 1-amino-2-methoxycyclopentanecarboxylic monohydrate (0.70 g) was heated under reflux for 2 hr. The reaction mixt was concd to dryness *in vacuo*, and the resulting residue was dissolved in EtOH and reduced to dryness twice to remove excess HI. The clear, viscous residue was finally dissolved in a small vol of EtOH, adjusted to pH 8–9 with concd NH_4OH, and placed in the refrigerator. The pptd amino acid was filtered, and recrystd from H_2O–EtOH to yield 0.26 g (46% of theory) of 1-amino-2-hydroxycyclopentanecarboxylic acid: mp 288–290° dec; mmp with 2-amino-1-hydroxycyclopentanecarboxylic acid, 275–282°; ir (KBr) 3.35, 6.05–6.40, 7.20, 7.55, 9.15, 11.7, and 12.7 μ; nmr δ 4.54 (t, 1 H, CH), 1.60–2.80 (m, 6 H, $CH_2CH_2CH_2$). *Anal.* ($C_6H_{11}NO_3$): C, H, N.

Microbiological Assays.—Assays with *Escherichia coli* 9723 were carried out in a previously described inorganic salts medium[22] and incubated at 37° for 18 hr; assays using *Leuconostoc dextranicum* 8086, *Streptococcus lactis* 8039, *S. faecalis* 8043, and *Pediococcus cerevisiae* 8042 were determined in an acid-hydrolyzed casein medium.[23] For *P. cerevisiae*, the purine and pyrimidine supplement was increased to 1.2 ml/100 ml of basal media and the phosphate concn was increased fourfold. The phosphate concn was also increased fourfold with *L. dextranicum*, and 0.1 μg/tube of pantethine was added. The latter 4 microorganisms were incubated at 30° for about 16 hr. A previously reported amino acid medium[24] was utilized in the assay with *Lactobacillus arabinosus* 17-5 except that 1 μg/tube of calcium pantothenate was added, and the assays were incubated at 30° for 20 hr.

Acknowledgment.—We wish to thank the Robert A. Welch Foundation and the Samuel Roberts Noble Foundation for their support of this research.

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(15) All melting points were determined with a Thomas-Hoover capillary melting point apparatus. Nmr spectra were obtained on D_2O solns containing a trace amount of HCl. The spectra were detd using a Jeolco JNM-PS-100 instrument. Ir spectra were obtained on KBr pellets with a Perkin-Elmer 237 grating spectrophotometer. The gas chromatographic data were obtained on a Loenco Model 2300 Series Graphimatic gas chromatograph.

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(17) W. S. Rapson and R. Robinson, *ibid.*, 1533 (1935).

(18) A. H. Cook and R. P. Linstead, *ibid.*, 956 (1934).

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Antiviral Agents. 1. Benzothiazole and Benzoxazole Analogs of 2-(α-Hydroxybenzyl)benzimidazole

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Since the discovery[2] of the antiviral activity of 2-(α-hydroxybenzyl)benzimidazole (HBB), many analogs have been synthesized in attempts to broaden and improve upon the antiviral effects.[3-6] The importance of the α-hydroxybenzyl group as well as a fused bicyclic ring[7] has been emphasized. Some evidence was found

(1) Postdoctoral NATO Fellow, SRI.

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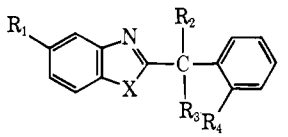
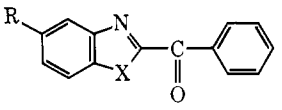
TABLE I[a]



Compd	X	R_1	R_2	R_3	R_4	Mp, °C	% yield	Crystln solvent[b]	Formula[c]
1	O	H	H	OH	H	125–126	43	A	$C_{14}H_{11}NO_2$
2	S	H	H	OH	H	120–121[d]	78	B	
3	O	H	H	H	OH	141–142	65	A	$C_{14}H_{11}NO_2$
4	S	H	H	H	OH	154–159	80	C	$C_{14}H_{11}NOS$
5	O	Cl	H	OH	H	140–142	40	A	$C_{14}H_{10}ClNO_2$
6	S	Cl	H	OH	H	145–146	19	A	$C_{14}H_{10}ClNOS$
7	O	Cl	H	H	OH	180–182	52	A	$C_{14}H_{10}ClNO_2$
8	S	Cl	H	H	OH	192–194	48	A	$C_{14}H_{10}ClNOS$
9	O	H	CH_3	OH	H	74–75	56	D	$C_{15}H_{13}NO_2$
10	O	Cl	CH_3	OH	H	*e*	73		$C_{15}H_{12}ClNO_2$

[a] Ir and nmr spectra of the compounds of this table are consistent with the proposed structure. [b] A = EtOH–H_2O; B = PhMe; C = EtOH; D = hexane. [c] Anal. for C H, N (**4** was also analyzed for S). Anal. results obtained were within ±0.1% of the theoretical values. [d] V. M. Znbarovskii, *Zh. Obshch. Khim.*, **21**, 2199 (1951). [e] Gummy compound; purified through column chromatography (silica gel, EtOAc–cyclohexane (20:80) as eluent).

TABLE II[a]



Compd	X	R	Mp, °C	% yield	Crystln solvent	Formula[c]
11	O	H	76–77[b]	93	EtOH	$C_{14}H_9NO_2$
12	S	H	104–112[c]	80	EtOH	
13	O	Cl	118–120	73[d]	EtOH	$C_{14}H_8ClNO_2$
14	S	Cl	128–129	49[d]	EtOH	$C_{14}H_8ClNOS$

[a] See footnote *a*, Table I. [b] Although this compd has been reported, no mp or other data are reported. S. Skraup and M. Moser, *Chem. Ber.*, **55B**, 1080 (1922). [c] See footnote *d*, Table I. [d] These yields are referred to the method of synthesis by oxidn with CrO_3. [e] See footnote *c*, Table I.

TABLE III

CYTOTOXICITY OF COMPOUNDS TESTED

Compd	Cytotoxicity, μg/ml
1	125
2	>500
3	62
4	62
5	62
6	500
7	62
8	62
9	31
10	250
11	125
12	62
13	4
14	31

that an intramolecular H bond plays an important role in the antiviral activity of this series.

However, two active analogs without the α-hydroxybenzyl group were found; 1,2-bis(2-benzimidazolyl)-1,2-ethanediol[8] and 2-(α-methoxybenzyl)benzimidazole.[9,10] Further structural modifications were undertaken in our laboratories in order to define the structure–activity functions for antiviral activity in more detail. Although the influence of a heterocyclic system in place of both aromatic rings appearing in HBB has been studied,[11–13] no attempts had knowingly been made to replace the imidazole ring with another isosteric ring.[14] A group of benzothiazoles and benzoxazoles (Tables I and II) were synthesized and evaluated in tissue culture for their antiviral activity. Cytotoxicity of these compounds is summarized in Table III. None had antiviral activity. Reference standards for the antiviral screen are included in Table IV.

2-(α-Hydroxybenzyl)benzoxazoles and -benzothiazoles as well as 2-(*o*-hydroxybenzyl)benzoxazoles and -benzothiazoles (**1–8**) were synthesized by direct condensation of the suitable aminophenol or aminothiophenol with the substituted phenylacetic acid. The 2-benzoylbenzoxazoles and -benzothiazoles (**11–14**) were obtained from the corresponding 2-(α-hydroxybenzyl) compounds by oxidation with CrO_3 in AcOH, and the 2-(α-hydroxy-α-methyl)benzoxazoles (**9**, **10**) were prepared by reaction of MeMgBr on **11** and **13**, respectively. The direct condensation of phenols and carboxylic acids proceeds normally with good yields and without by-products. However, in the case of the reaction between 4-chloro-2-aminophenol or 4-chloro-2-aminothiophenol and mandelic acid, by-products were formed that were identified as 5-chloro-2-benzoylbenzoxazole (**13**) and 5-chloro-2-benzoylbenzothiazole (**14**).

Such an easy oxidation of an analogous carbinol has been reported by Wagner, *et al.*,[13] in the case of 2-(2-pyridyl-α-hydroxymethyl)benzimidazole. However, 2-(α-hydroxybenzyl)-5-chlorobenzoxazole (**5**) and 2-(α-hydroxybenzyl)-5-chlorobenzothiazole (**6**) appear to be stable when isolated and do not undergo oxidation during purification.

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(14) After this work was under way, the publication of Tamm, *et al.* (ref 10), appeared. Since our antiviral data differ, we include those compds common to both studies.

TABLE IV
RESPONSE OF REFERENCE ANTIVIRAL AGENTS IN TISSUE CULTURE ASSAY SYSTEM

Virus system	Compd	Conen, μg/ml: Cytotoxic	Conen, μg/ml: Lowest level causing 100% reduction in cytopathic effect of the virus	EC_{50}[a]
Polio-1	Guanidine·HCl	250	62	36
Echo-12	2-(α-Hydroxybenzyl)benzimidazole	250	62	28
Echo-12	Rhodanine[b]	250	62	23
Influenza-(A-2)	Amantadine·HCl	32	8	0.3
Vesicular stomatitis	No active compounds known			
Adeno-7	2′-Desoxy-5-iodouridine (IUDR)	>500	500	115
Vaccinia	9-β-D-Arabinofuranosyladenine (ARA-A)	16	~8	3
Vaccinia	1-β-D-Arabinofuranosylcytosine (ARA-C)	62	1	0.3
Vaccinia	2′-Desoxy-5-iodouridine	>500	125	22

[a] Conen, in μg/ml, resulting in 50% reduction in cytopathic effect of the virus; estimated using the logarithmic-probit method (L. C. Miller and M. L. Tainter, *Proc. Soc. Exp. Biol. Med.*, **57**, 261, 1944). [b] H. J. Eggers, M. A. Koch, A. Furst, G. D. Daves, Jr., J. J. Wilczynski, and K. Folkers, *Science*, **167**, 294 (1970).

Biological Methods.—All tests were carried out in roller tube cultures of Rhesus monkey kidney that were obtained commercially as primary cultures. Each of the compounds with the exception of **10** was tested for activity against 6 viruses; polio virus (type 1), Echo-12, influenza-A-2, vesicular stomatitis, adeno virus-7, and vaccinia. Compound **10** because of insufficient quantity was tested only against Echo-12. Compound **6** was tested only for cytotoxicity due to insufficient sample. Large pools of each virus were prepared in Rhesus monkey kidney cultures, distributed in small amounts in ampules, and frozen and stored at −70°. The tissue culture ID_{50} ($TCID_{50}$) of each pool was then determined.

Each compound was tested to determine the highest concentration that could be tolerated by the cell culture without inducing obvious cellular damage (MTD). To make this determination, approximately 20 mg of compound was dissolved in an amount of tissue culture medium to give a concentration of 500 μg/ml. If the compound did not go into solution, it was subjected to sonic vibration to produce a homogeneous suspension and serially diluted twofold, and 2 ml of each dilution, serving as sole source of medium, was then added to 4 monkey kidney tubes. The tubes were then placed in a roller drum at 35° and incubated for 7 days. The cultures were examined microscopically at intervals to determine the highest concentration of the compound that was nontoxic.

In the test for antiviral activity, the highest nontoxic concentration of compound in culture medium (*i.e.*, one-half of the cytotoxic concentration), was added to 8 tissue culture tubes. To 4 of the tubes, 0.2 ml of virus containing approximately 100 $TCID_{50}$ was added. The remaining tubes received no virus and were observed as toxicity controls. Additional controls consisted of a simultaneous titration of the virus suspension used in the test to determine the exact amount of virus present.

An estimate of the activity of the test compound in reducing the cytopathic effect (CPE) was ascertained for each compound against each of the 6 test viruses. This was based on frequent microscopic observations of the tubes and any differences between treated and untreated tubes were recorded on a numerical scale. In this manner it was possible to detect compounds with all grades of antiviral activity, ranging from 0 to 100%. Any compound found to have greater than 75% antiviral activity at MTD was retested quantitatively to determine the smallest concentration that would inhibit cytopathic effects of the virus.

Discussion of Antiviral Activity.—None of the benzothiazole or benzoxazole analogs of HBB exhibited any antiviral activity in our test system although HBB was quite active against Echo-12 virus. Tamm, *et al.*,[10] found 2-(α-hydroxybenzyl)benzothiazole (**2**) to be somewhat active against Echo-6 virus suggesting a selectivity within the Echo series. Against Echo-12 virus, the benzimidazole moiety appears necessary for activity when the group in the 2 position is α-hydroxybenzyl.

Experimental Section

2-(α-Hydroxybenzyl)benzoxazole (1).—A mixt of *o*-aminophenol (4.36 g, 0.04 mole), and *dl*-mandelic acid (9.14 g, 0.06 mole) was refluxed in xylene (50 ml), until the theoretical amount of H_2O was collected. The soln was cooled, and the white solid was filtered; recrystn from dil EtOH gave plates, mp 118–120°; yield, 3.6 g. Physical constants are reported in Table I together with those of **2–8** obtained in the same manner.

5-Chloro-2-(α-hydroxybenzyl)benzoxazole (5).—A mixt of *dl*-mandelic acid (9.13 g, 0.06 mole) and 4-chloro-2-aminophenol (8.65 g, 0.06 mmole) was refluxed for 24 hr in 300 ml of xylene until the theoretical amount of H_2O was obtained. After cooling, a solid (2.4 g, 14%) that was recrystd from EtOH was collected. It had the correct anal. ($C_{14}H_{12}ClNO_2$: C, H, N) and the correct ir and nmr spectra for 2-hydroxy-5-chloromandelanilide (**15**).

The xylene mother liquors, treated with petr ether gave 6.2 g (40%) of 5-chloro-2-(α-hydroxybenzyl)benzoxazole (**5**) (Table I). From the evapn of the xylene–petr ether soln, 2.1 g (14%) of 5-chloro-2-benzoxylbenzoxazole (**13**) was obtained (Table II).

5-Chloro-2-(α-hydroxybenzoyl)benzothiazole (6).—A mixt of *dl*-mandelic acid (4.56 g, 0.03 mole) and 4-chloro-2-aminothiophenol (4.8 g, 0.03 mole) was refluxed for 15 hr in xylene (100 ml) until the right amount of H_2O was collected. After cooling, 4.05 g (50%) of 2-benzoylchlorobenzothiazole (**14**) was obtained (Table II). The xylene mother liquors were evapd to dryness, and the resulting oil was washed with EtOAc–cyclohexane (20:80) to give 1.6 g (19%) of **6** (Table I).

Reduction of 14 with LAH.—A better yield of **6** can be obtained by reducing **14** with LAH. A soln of **14** (0.8 g) in anhyd Et_2O was dropped into a suspension of LAH (0.106 g) with stirring and cooling. After 1 hr at room temp the soln was added to H_2O, and the org layer was sepd and dried ($MgSO_4$). After removal of the solvent, an oil was obtained that was washed with EtOAc–cyclohexane (20:80) to give 0.4 g (4%) of **6**.

2-Benzoylbenzoxazole (11).—A soln of **1** (4.5 g) in 30 ml of AcOH was slowly added to a soln of CrO_3 (1.8 g) in 100 ml of AcOH with stirring and cooling. The temp was slowly increased to 115° and maintained in this range for 30 min. After cooling,

H_2O was added to ppt 4.4 g of **11**. Other compds in Table II were obtained by this method.

2-(α-Methyl-α-hydroxybenzyl)benzoxazole (9).—A soln of **10** (2.65 g) in anhyd Et_2O (50 ml) was dropped slowly into a soln of MeMgBr (1.36 g) in 50 ml of anhyd Et_2O with stirring and cooling. After 6 hr at room temp 30 ml of H_2O and 1 ml of concd HCl were added, and the org layer sepd, was washed with H_2O, and dried ($MgSO_4$). After evapn of the solvent, 1.6 g of white solid (**9**) was collected. 2-(α-Methyl-α-hydroxybenzyl)-5-chlorobenzoxazole (**10**) was obtained in the same way (Table I).

Acknowledgments.—The authors wish to thank J. Sorge and K. Young for carrying out the antiviral experiments. The financial assistance of the SRI-Institute Research and Development Program is acknowledged for the antiviral studies.

3- and 4-Carbazole Dialkylaminocarbinols as Potential Antimalarial Agents

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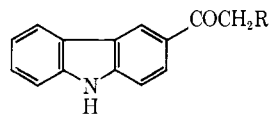
The important role of quinolinemethanol compounds in malaria chemotherapy has prompted the investigation of other heteroaryl carbinols for antimalarial activity. Accordingly we have synthesized 3- and 4-(α-hydroxy-β-dibutylaminoethyl)carbazole and tested the compounds for their antimalarial action against *Plasmodium berghi* in mice. Unfortunately neither compound showed significant activity in this test system, as shown in Table I.

TABLE I

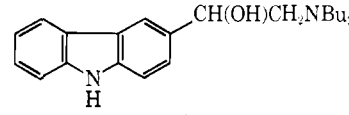
	Antimalarial bioassay result[a]			
	Dose, mg/kg			
Compd	40	160	320	640
4	0.3	0.3		0.5
8	0.2	0.4	0.8	

[a] Increase in survival time (days) of treated mice beyond that of untreated controls after single sc dosages (3 days postinfection). Average survival time of untreated controls was 7.0 ± 0.5 days. The infecting organism was *P. berghei*.

The synthesis of the 3 isomer began with 3-acetylcarbazole **1** followed by bromination and reaction of the bromo ketone **2** with Bu_2NH. Reduction of the amino ketone **3** with $NaBH_4$ readily afforded the amino alcohol **4**. The acid chloride of carbazole-4-carboxylic acid **5** was treated with CH_2N_2 to give the chloromethyl ketone **6**. A similar displacement with Bu_2NH and reduction yielded **8**.



1, R = H
2, R = Br
3, R = NBu_2



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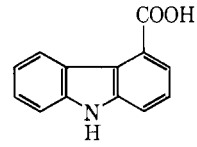

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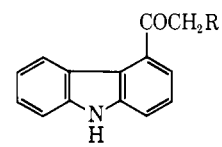
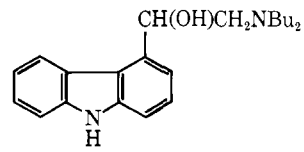


6, R = Cl
7, R = NBu_2



8

Experimental Section

Compounds followed by empirical formulas only were analyzed for C, H, N with values within ±0.4% of theoretical.

3-Bromoacetylcarbazole (2).—A mixt of 10.7 g (0.029 mole) of $PhMe_3N^+ \cdot 3Br^-$, 6.0 g (0.029 mole) of 3-acetylcarbazole[1] (**1**), and 100 ml of THF was stirred at room temp for 5 hr, then evapd *in vacuo*. The residue was thoroughly washed with H_2O and Et_2O to yield 7.1 g (86%); mp 158–159°; anal. sample, mp 160–162° (C_6H_6). *Anal.* ($C_{14}H_{10}BrNO$): Br.

3-Dibutylaminoacetylcarbazole (3).—A mixt of 7.4 g of **2**, 40 ml of *n*-Bu_2NH, and 150 ml of MeOH was refluxed 3 hr and evapd *in vacuo*, finally at 1 mm. The residue was treated with 200 ml of H_2O, acidified to pH 1–2 with concd HCl, and washed with 200 ml of EtOAc. The acid phase containing much insol, oily HCl salt of the product was alkalized with 10% NaOH to pH 10–11. The oily ppt was extd into 200 ml of Et_2O which was washed with H_2O, dried ($MgSO_4$), and evapd to leave 4.4 g of syrup. After two pentane washes the syrup was dried at 1 mm to leave 4.0 g which solidified. A portion was recrystd for anal., mp 106–112° (pentane–C_6H_6). *Anal.* ($C_{22}H_{28}N_2O$): C, calcd 78.5; found 78.0.

3-(α-Hydroxy-β-di-*n*-butylamino)ethylcarbazole (4).—A mixt of 4.0 g of **3**, 1.5 g of $NaBH_4$, and 150 ml of EtOH was warmed into soln and stirred for 20 hr at room temp. The solvent was evapd *in vacuo* and the residue was partitioned between Et_2O and H_2O. The Et_2O was dried ($MgSO_4$) and evapd to leave 2.7 g of gum, which was extd with three 90-ml portions of boiling pentane. The ext was gassed with HCl. The hygroscopic salt was collected and triturated with 10 ml of Me_2CO and the white cryst were collected (1.10 g, 25%), mp 165–168°. *Anal.* ($C_{22}H_{30}N_2O \cdot HCl$).

4-Chloroacetylcarbazole (6).—The mixt of tetrahydrocarbazole-5- and -7-carboxylic acids[2] was readily sepd as the Me esters by silica gel chromatography. Dehydrogenation of the 5 isomer followed by saponification afforded 4-carboxycarbazole (**4**).[3] A soln of the acid chloride (from 3.16 g of acid and 1.1 ml of $SOCl_2$ in 50 ml of C_6H_6) in 40 ml of CH_2Cl_2 was added dropwise to 45 mmoles of CH_2N_2 in 150 ml of Et_2O at 0–5°. After 1 hr at 0–5° the soln was gassed with HCl for 20 min and evapd *in vacuo* (2.52 g). Chromatography on silica gel gave 2.07 g (57%), mp 158–160.5°. *Anal.* ($C_{14}H_{10}ClNO$).

4-Dibutylaminoacetylcarbazole (7).—A mixt of 1.47 g of **6** and 20 ml of Bu_2NH was stirred at 35–40° for 15 hr. A work-up similar to that for the 3 isomer gave an orange syrup (1.0 g, 49%), which slowly crystd; recrystd, mp 196–204° (EtOH). Elemental anal. and bands at 3.9–4.2 μ in the ir indicated a carbonate salt. *Anal.* $(C_{22}H_{28}N_2O)_2 \cdot H_2CO_3$.

4-(α-Hydroxy-β-di-*n*-butylamino)ethylcarbazole Picrate (8).—The ketone **7** was reduced with $NaBH_4$ in EtOH as above to yield a yellow syrup (36%). The picrate, mp 174–179°, was obtained from EtOH–H_2O. *Anal.* ($C_{28}H_{33}N_5O_8$).

(1) E. Meizner, *J. Amer. Chem. Soc.*, **57**, 2327 (1935).

(2) W. M. Collar and S. G. Plant, *J. Chem. Soc.*, 808 (1926).

(3) P. H. Carter, S. G. Plant, and M. Tomlinson, *ibid.*, 2210 (1957).