

The derivatives tabulated below were obtained merely by shaking the corresponding amine with slightly more than a molar equivalent of benzylchlorocarbonate in the presence of excess 10% sodium hydroxide solution. The product solidified in a few minutes, was filtered and then recrystallized from ethyl alcohol. The yields of recrystallized material were between 60 and 90% of the theoretical amount.

Product, carbonate	M. p., °C.	Nitrogen, %	
		Calculated	Found
N-Phenyl-benzyl	77	6.16	6.11
N- <i>p</i> -Tolyl-benzyl	83	5.81	5.64
N- <i>o</i> -Tolyl-benzyl	83.5	5.81	5.62
N- <i>p</i> -Methoxy-phenyl-benzyl	98.0	5.83	5.65
N- <i>m</i> -Bromophenyl-benzyl	58.0	4.58	4.45

Orthoanisidine produced a liquid derivative which was not further investigated. Three of the above compounds have been prepared previously by the isocyanate method: N-phenyl-benzyl carbamate,<sup>3</sup> N-*o*-tolyl-benzyl carbamate,<sup>4</sup> and N-*p*-methoxyphenyl-benzyl carbamate.<sup>5</sup> The remaining two benzyl carbamates have not previously been reported. Nitrogen analyses were made by the Dumas method. Carbobenzoxy chloride was prepared by the method of Bergmann and Zervas.<sup>2</sup>

The low melting points and low melting point spread of these derivatives indicate that they would be of little value in the identification of the amines investigated. On the other hand they are prepared in excellent yield and seem to offer a convenient method for "masking" amino groups.

(3) Soden and Rojahn, *Ber.*, **34**, 2809 (1901).

(4) Gattermann and Cantzler, *ibid.*, **25**, 1807 (1892).

(5) Brunner and Wohol, *Monatsh.*, **63**, 374 (1930).

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### Percain Analogs. The Preparation of $\beta$ -Diethylaminoethoxyethyl 2-Alkoxy-cinchonates

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Most 2-alkoxy-cinchonic acid derivatives exhibit a local anesthetic effect. In a series of  $\beta$ -diethylaminoethylamides of this acid prepared by Aeschlimann,<sup>1</sup> percain, the butoxy derivative, is the strongest, being ten times as active as cocaine, and is used in medicine.

Luré<sup>2</sup> showed that in a series of amino esters of these acids the anesthetic effect was to some extent dependent on the nature of the alkoxy group in the 2-position, but more on the side chain in the 4-position, the effect increasing with the increase of the number of the carbon atoms.

In a series of a different type of amides of these acids Magidson<sup>3</sup> proved that an increase in the

(1) Aeschlimann, *J. Chem. Soc.*, 2906 (1926).

(2) Luré, *J. Gen. Chem.* (U. S. S. R.), **9**, 287 (1938).

(3) Magidson, *ibid.*, **9**, 2097-2103 (1939).

number of the hydroxyl groups in the side chain in the 4-position decreases the anesthetic effect.

With these views in mind, we prepared a series of  $\beta$ -diethylaminoethoxyethanol esters of 2-alkoxy-cinchonic acids containing an O-atom in the side chain in the 4-position, and studied the change in the local anesthetic effect when the alkoxy group in the 2-position was varied.

$\beta$ -Diethylaminoethoxyethanol was prepared by the method of Horne and Shriner.<sup>4</sup> 2-Chlorocinchonic acid was prepared by the method of Aeschlimann<sup>1</sup> or Thielepape,<sup>5</sup> and it was converted into a series of 2-alkoxycinchonic acids by the action of sodium alcoholate in the corresponding alcohols. From these, the acid chlorides, the esters, and finally the ester hydrochlorides were prepared.

**2-Alkoxy-cinchonic Acid Chloride.**—This was prepared by the action of thionyl chloride on a solution of the corresponding alkoxy-cinchonic acid<sup>1,5</sup> in benzene following the procedure of Gardner and Hammel.<sup>6</sup> In several repetitions of this procedure we found the yield to be dependent on the time of heating, as follows

Time of heating, min.	Amount of 2-alkoxy-cinchonic acid used, g.	Amount of acid recovered, g.
10	0.38	0.30
35	1.20	.25
60	1.40	.19

**$\beta$ -Diethylaminoethoxyethyl 2-Alkoxy-cinchonate Hydrochloride.**—To a solution of the alkoxy-cinchonate chloride in about ten times its weight of benzene was added a slight excess of  $\beta$ -diethylaminoethoxyethanol. The mixture was heated at 60° for fifteen minutes. After cooling, the benzene solution was extracted with dilute hydrochloric acid. The ester was precipitated by neutralizing the acid solution with sodium carbonate, and was extracted with benzene. The benzene solution was dried with anhydrous sodium sulfate and treated with the calculated amount of hydrogen chloride gas. The mixture was allowed to stand for several hours and the precipitate was filtered off, washed with benzene, and dried in a desiccator. Yields and melting points are given in the table.

### $\beta$ -DIETHYLAMINOETHOXYETHYL 2-ALKOXY-CINCHONATE HYDROCHLORIDES

Alkoxy	Yield, %	M. p., °C.	Formula	Percentage composition			
				Nitrogen		Chlorine	
				Calcd.	Found	Calcd.	Found
-ethoxy-	64	80	C <sub>20</sub> H <sub>22</sub> O <sub>4</sub> N <sub>2</sub> Cl	7.02	7.10	8.94	9.03
-isopropoxy-	68	75	C <sub>21</sub> H <sub>24</sub> O <sub>4</sub> N <sub>2</sub> Cl	6.95	6.94	8.64	8.72
-butoxy-	66	108	C <sub>22</sub> H <sub>26</sub> O <sub>4</sub> N <sub>2</sub> Cl	6.72	6.77	8.35	8.50
-pentoxy-	66	78	C <sub>23</sub> H <sub>28</sub> O <sub>4</sub> N <sub>2</sub> Cl	6.50	6.53	8.08	8.12

These compounds, in 1% aqueous solution, produce a local anesthetic effect when tested by the tongue, but the pharmacological properties will be further investigated.

(4) Horne and Shriner, *THIS JOURNAL*, **54**, 2925-2930 (1932).

(5) Thielepape, *Ber.*, **55**, 133-134 (1922).

(6) Gardner and Hammel, *THIS JOURNAL*, **56**, 1360-1361 (1936).

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### Derivatives of Phenothiazine

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In connection with other investigations<sup>1</sup> at this institution, several new derivatives of pheno-

(1) Nicholson and McCulloch, *J. Am. Vet. Med. Assoc.*, **101** (No. 786), 205 (1942).