

ice and common salt. 8 g of N-p-chlorobenzyl-N'-chloroacetyl-o-phenylene diamine are obtained which can be worked up in the form of the crude product and, in the slightly colored form, has a MP of 130°C.

7.6 g of this compound are boiled with 3.9 g of pyrrolidine in 70 cc of toluene for some hours under reflux. After extraction by shaking with water and treatment with hydrochloric acid the hydrochloride is produced of N-p-chlorobenzyl-N'-pyrrolidylacetyl-o-phenylene diamine together with some 1-p-chlorobenzyl-2-N-pyrrolidylmethyl-benzimidazole. The former, after recrystallization from butanol, melts with foaming at 205°C, the latter, after recrystallization from butanol melts at 239°C to 241°C, and is in the form of white microscopic rods. Boiling in nitrobenzene converts the former compound into the latter.

References

Merck Index 2315

Kleeman & Engel p. 217

OCDS Vol. 1 p. 324 (1977)

I.N. p. 239

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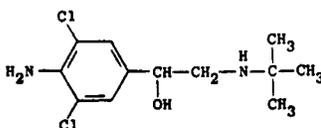
CLENBUTEROL

Therapeutic Function: Antiasthmatic

Chemical Name: 4-Amino-3,5-dichloro-[[{(1,1-dimethylethyl)amino] methyl] benzene-methanol

Common Name: —

Structural Formula:



Chemical Abstracts Registry No.: 37148-27-9

Trade Name	Manufacturer	Country	Year Introduced
Spiropent	Thomae	W. Germany	1977
Monores	Valeas	Italy	1981

Raw Materials

1-(4'-Aminophenyl)-2-t-butylaminoethanol-(1)-HCl
Chlorine
Hydrogen chloride

Manufacturing Process

127 g of 1-(4'-aminophenyl)-2-t-butylaminoethanol-(1)-hydrochloride were dissolved in a mixture of 250 cc of glacial acetic acid and 50 cc of water, and chlorine added while stirring the solution and maintaining the temperature of the reaction mixture below 30°C by cooling with ice water. After all of the chlorine had been added, the reaction mixture was stirred for thirty minutes more, then diluted with 200 cc of water, and made alkaline with concen-

trated ammonia while cooling with ice, taking care that the temperature of the reaction mixture did not rise above 40°C. The alkaline mixture was extracted three times with 200 cc portions of chloroform, and the chloroform extract solutions were combined, dried with sodium sulfate and evaporated. The residue, the free base 1-(4'-amino-3',5'-dichlorophenyl)-2-t-butylaminoethanol-(1), was dissolved in absolute ethanol, gaseous hydrogen chloride was passed through the solution, and the precipitate formed thereby was collected. It was identified to be 1-(4'-amino-3',5'-dichlorophenyl)-2-t-butylaminoethanol-(1)-hydrochloride, melting point 174.0°C to 175.5°C (decomp.).

References

- Merck Index 2316
 DFU 1 (5) 221 (1976)
 Kleeman & Engel p. 218
 DOT 14 (2) 59 (1978) & 17 (8) 339 (1981)
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 Keck, J., Kruger, G., Machleidt, H., Noll, K., Engelhardt, G. and Eckenfels, A.; U.S. Patent 3,536,712; October 27, 1970; assigned to Boehringer Ingelheim G.m.b.H. (Germany)

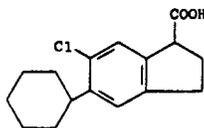
CLIDANAC

Therapeutic Function: Antiinflammatory; antipyretic

Chemical Name: 6-Chloro-5-cyclohexyl-2,3-dihydro-1H-indene-1-carboxylic acid

Common Name: —

Structural Formula:



Chemical Abstracts Registry No.: 34148-01-1

Trade Name	Manufacturer	Country	Year Introduced
Indanal	Takeda	Japan	1981
Britai	Bristol Banyu	Japan	1981

Raw Materials

N-Chlorosuccinimide
 5-Cyclohexyl-1-indancarboxylic acid

Manufacturing Process

N-chlorosuccinimide (8.2 g, 0.0614 mol) was added to a stirred, cooled (ice-water) solution of (±)-5-cyclohexyl-1-indancarboxylic acid (10.0 g, 0.0409 mol) in dimethylformamide (82 ml). The solution was stirred for fifteen minutes at 0°C, thirty minutes at 25°C, nine hours at 50°C, followed by eight hours at 25°C. The solution was diluted with cold water (400 ml) and stirred until the precipitated product turned granular (fifteen minutes). The crude product was collected, washed with cold water, and dried. Crystallization from Skellysolve B with charcoal treatment gave colorless crystals (6.65 g, 58%), MP 149°C to 150°C. The product was recrystallized twice from Skellysolve B to give (±)-6-chloro-5-cyclohexyl-1-indancarboxylic acid as colorless crystals, MP 150.5°C to 152.5°C.