flask, at this stage, had to be immersed in a freezing bath to prevent the temperature from getting too high. After the temperature was under control, the solution was heated to 58° C. whereupon the rearrangement occurred. The heating was continued until 70° C. was reached. The solution was cooled, the oil layer separated and the solution extracted with benzene, using 60 cc. each time. The benzol solution was washed twice with 50 cc. portions of water and 148 grams of concentrated hydrochloric acid slowly added to it. The amine-hydrochloric acid solution was extracted twice with 30 cc. portion of benzol. The amine was then precipitated with sodium hydroxide solution (30%). The water from the precipitated amine was extracted three times with 60 cc. portions of benzol. The benzol solution was washed twice with 100 cc. washes and then vacuum distilled. Yield: 131 grams of purified amine, B. P. 105° C./30 mm., 69.0% of theory.

Results of the ethylation experiments using dimethyl sulfate and methyl iodide indicated that it was possible to get a much greater degree of ethylation using methyl iodide. It was found impossible to get the 108° C. amide by starting from mono benzyl ethyl aceto acetate; however, the 108° C. amide results from introducing the methyl group in ethyl aceto acetate first and then the benzyl group.

Methyl methyl aceto acetate was prepared from methyl acetate in good yields. A large run was made starting with methyl acetate and carrying the synthesis through to the amine. Time tests indicated that methyl benzyl methyl aceto acetate will go over to methyl benzyl acetamide in aqueous ammonia to the extent of approximately 50% in two weeks, standing at room temperature.

Methyl benzyl acetamide

100 grams of methyl benzyl methyl aceto acetate is added to 400 cc. of 28–29% aqueous NH_4OH and allowed to stand for 7 days. A yield of 50 grams of methyl benzyl acetamide was obtained.

As exemplifying the isomer formation of alpha-amino, beta-phenyl propane, instead of the desired alpha-phenyl, beta-amino propane, the following run was made:

1. First step — preparation of benzyl aceto acetic acid methyl ester: To 1630 grams aceto acetic acid methyl ester there is added 164 grams sodium dissolved in 1200 grams absolute methyl alcohol during 1¼ hours. 15 minutes after the last of the sodium methylate solution has been added, the mixture is added to 932 grams benzyl chloride. The resulting mixture is agitated for 1 hour at 30° C.–47° C., and then heated to refluxing temperature for 1 hour. The excess methanol is distilled off on steam bath. 1800 cc. water are added and the oil which separates washed with water. The oil is distilled when 560 grams aceto acetic acid methyl ester and 1300 grams benzyl aceto acetic acid methyl ester are obtained.

2. Second step—preparation of methyl benzyl aceto acetic acid methyl ester: 184 grams sodium are dissolved in 1340 grams methanol. To this solution of sodium methylate is added 1650 grams benzyl aceto acetic acid methyl ester (from first step). Then there is added immediately 1008 grams dimethyl sulfate in the course of 1½ hours. The reaction mixture is refluxed for 15 minutes after all the dimethyl sulfate is added. Then the excess methanol is distilled off on the water bath. The precipitate formed is dissolved by adding one liter of water. The oil which separates is washed with 500 cc. 10% caustic solution and then with 500 cc. water washes until free of caustic. The oil is then distilled. Yield: 1570 grams methyl benzyl aceto acetic ester.

3. The steps from here on to the preparation of the final amine compound are the same as the corresponding steps in the preparation of the alpha-phenyl-beta-amino propane. That is the steps are in order, cleaving of the methyl benzyl aceto acetic ester, hydrolysis of methyl benzyl acetic acid methyl ester to the corresponding acid; preparation of methyl benzyl acetyl chloride, by reaction of methyl benzyl acetic acid with thionyl chloride, then preparation of the corresponding amide by reaction with ammonia, and finally preparation of the final amine compound from the amide by means of the Hofmann reaction. Now the same shortcut may be taken in this series of reactions as may be taken in the preparation of the alpha-phenyl-beta-amino-propane, that is the amide compound may be prepared directly from the methyl benzyl aceto acetic acid methyl ester by reaction with ammonia, and the amino compound then prepared from the amide by the Hofmann reaction.

Data by which the two isomeric amines can be distinguished:

1. Melting points of the corresponding amines—
   - (*a*) The amide which gives alpha-phenyl-beta-amino-propane, that is, the correct product, has a melting point of 108° C.
   - (*b*) The amide which gives beta-phenyl-alpha-amino-propane, that is the isomer, has a melting point of 70° C.
2. The melting points of the hydrochlorides of the two amines are as follows—
   - (*a*) Melting point of hydrochloride of alpha-phenyl-beta-amino-propane 146°–150° C.
   - (*b*) Melting point of hydrochloride of beta-phenyl - alpha-amino-propane 119°–121° C.
3. The boiling points of the free amines are—
   - (*a*) The alpha-phenyl-beta-amino-propane 205°–206° C.
   - (*b*) The beta-phenyl-alpha-amino-propane 204.2°–204.8° C.

It will now be appreciated that there has been disclosed a novel process for the preparation of alpha-phenyl - beta - amino-propane, substantially free from undesired side reaction products, which desirable result is essentially obtained by ensuring the initial methylation of the active carbon of aceto acetic ester used as a starting material, which may then be followed by benzylation of the methylated compound. As set out in the description of the isomer formation of alpha-amino-beta-phenyl propane, an initial benzylating step precludes the formation of the desired pure isomer-free-intermediate product benzyl methyl acetoacetic methyl ester which is especially suited for use in the preparation of pure alpha-phenyl-beta-amino propane free from its isomer alpha-amino-beta-phenyl propane.

What is claimed is:

1. In the preparation of isomer-free benzyl methyl acetoacetic methyl ester from monosodium acetoacetic methyl ester, the improve-