stirred mixture of 12 cc. of 1 *M* methylmagnesium iodide in 25 cc. of dry benzene. The mixture was stirred and refluxed for 3.5 hours and poured into 75 cc. of saturated ammonium chloride. The benzene layer was extracted with two 50-cc. portions of *N* hydrochloric acid. To the combined extracts was added 10 cc. of concentrated hydrochloric acid and the solution refluxed for fifty hours. The resulting dark oil was dried in ether and evaporatively distilled at 150–170° (0.5 mm.). Recrystallization of the distillate from methanol gave 0.15 g. of prisms, m. p. 71–73°. The m. p. was not depressed by mixture with X previously prepared.

Summary

In the bromination of tetrahydroanthracene, 9-bromo-1,2,3,4-tetrahydroanthracene is formed in a yield of *ca.* 30%.

Its structure has been established by linking it with 9-anthroic acid.

A simple and efficient preparative method for 9-anthroic acid is described.

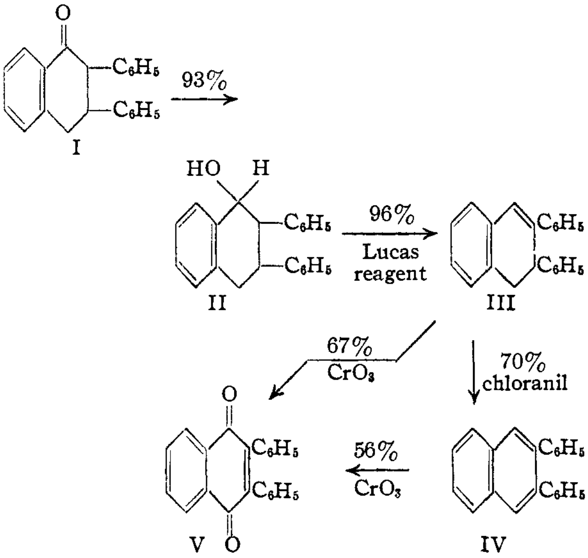
BETHESDA 14, MD. RECEIVED OCTOBER 23, 1947

[CONTRIBUTION FROM THE SANDERS LABORATORY OF CHEMISTRY, VASSAR COLLEGE]

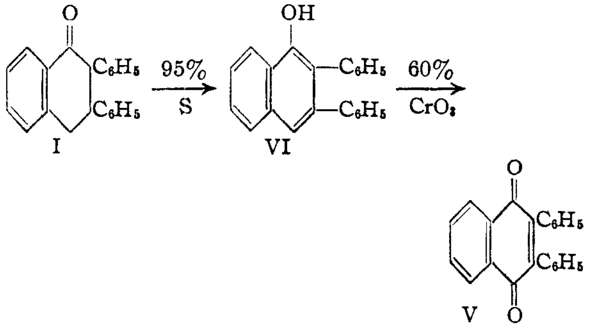
The Preparation of 2,3-Diphenyl-1,4-naphthoquinone and its Reaction with Phenylmagnesium Bromide and Phenyllithium

BY H. MARJORIE CRAWFORD

2,3-Diphenyl-1,4-naphthoquinone has been prepared by Crawford and Nelson[1] by the series of reactions



and by Bergmann and Szmuszkovic[2] as follows:



In preparing this quinone in larger quantities for the study reported here, variations in these procedures were carried out in attempts to improve the yield. Direct oxidation of 2,3-diphenyl-1,2-dihydronaphthalene (III) with chromium trioxide in glacial acetic acid gave 67% of the quinone (V). This makes the over-all yield of the quinone from the tetralone about 60% as compared to 35% when the dehydrogenation step is included. This is a more satisfactory method of preparing the quinone than that described by Bergmann[2] for, although three steps are involved instead of two, the yield is about the same and the products are much more easily purified.

Dehydrogenation of the tetralone (I) by sulfur gave the naphthol (VI) in 85–90% yields but there were red products formed which made the purification of the naphthol by recrystallization very difficult. In variations of the dehydrogenation reaction, selenium and chloranil gave poorer yields than sulfur. In the oxidation of the naphthol (VI) with chromium trioxide, the quinone (V) was obtained in 30–60% yields, accompanied by a high molecular weight white compound melting at 265–267°, and considerable quantities of yellowish oils.

As it has already been shown,[3,4,5] the reactions of phenylmagnesium bromide with methyl substituted naphthoquinones give complex mixtures of products. The solid compounds isolated from these mixtures resulted from both 1,2-additions to the carbonyl group and 1,4-additions to the conjugated systems, as well as reduction of the quinones to the hydroquinones and the accompanying formation of biphenyl. When phenyllithium reacted with these methyl substituted naphthoquinones the only products isolated were those resulting from the 1,2-addition of two molecules of the reagent to the carbonyl groups.

The behavior of 2,3-diphenyl-1,4-naphthoquinone has now been studied, hoping that the phenyl groups would be large enough to prevent the 1,4-

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[1] Crawford and Nelson, THIS JOURNAL, **68**, 134 (1946).

[2] Bergmann and Szmuszkovic, *ibid.*, **68**, 1662 (1946).

[3] Crawford, *ibid.*, **57**, 2000 (1935).

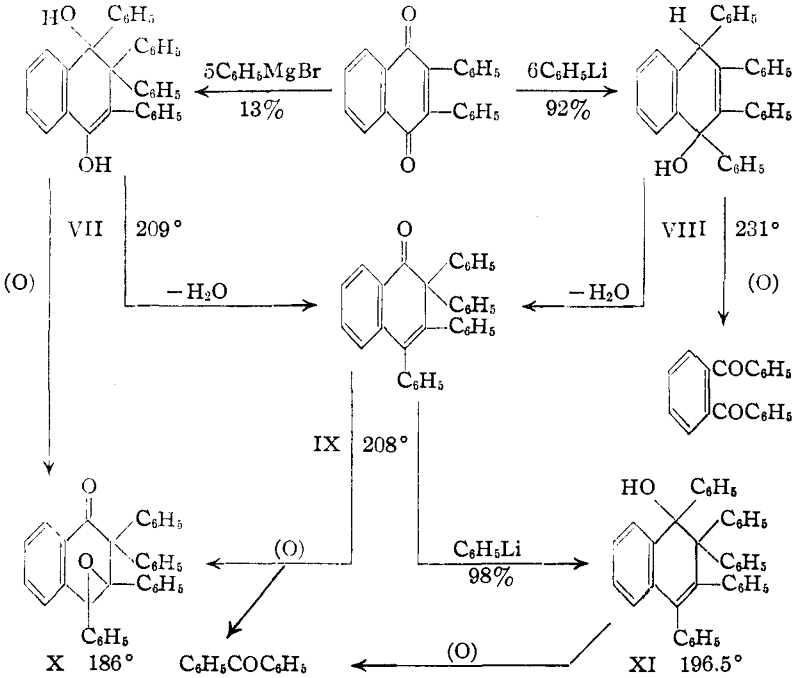
[4] Crawford, *ibid.*, **61**, 3310 (1939).

[5] Crawford, *ibid.*, **63**, 1070 (1941).

addition of the phenylmagnesium bromide to the conjugated system. This hope has not been realized, for the only addition product isolated was that resulting from the 1,2- and 1,4-addition of two molecules of phenylmagnesium bromide to one molecule of the quinone. Biphenyl and the hydroquinone were formed as in the other cases. Phenyllithium, on the other hand, gave excellent yields (92%) of the 1,2-1,2-diaddition product.

The two diols resulting from these reactions were dehydrated with great ease to give practically quantitative yields of a single rearrangement product.

The relationships of these compounds are summarized below.



The structure of VIII was established by oxidation to benzoic acid and *o*-dibenzoylbenzene (38%). It was impossible to obtain direct evidence for the structure of VII since attempts to oxidize it with potassium permanganate gave only unchanged starting material, and oxidation with chromium trioxide in glacial acetic acid gave the same product (X) which was formed by the oxidation of IX. Later it was shown that simply boiling VII in glacial acetic acid for one hour caused dehydration and rearrangement to give IX. In other cases of the addition of phenylmagnesium bromide to naphthoquinones[3,5,6] the principal product has always been the compound resulting from 1,2- and 1,4-additions of two molecules of phenylmagnesium bromide to one molecule of the quinone. Analytical data show that VII is a diaddition product, and it is different from VIII which is the 1,2-1,2-diaddition compound. The structure proposed for VII would represent the first product of the reaction but it may well exist in the keto form.

Compound IX is quite inert, having been recovered unchanged from boiling for one hour with potassium permanganate or potassium dichromate, from attempts to make a 2,4-dinitrophenylhydrazone, from treatment with perbenzoic acid, and from treatment with alkaline hydrogen peroxide. Oxidation of IX with chromium trioxide in glacial acetic acid gave benzoic acid, benzophenone (identified as the 2,4-dinitrophenylhydrazone) and compound X. This type of rearrangement accompanying dehydration has been encountered before[4] in compounds similar in structure to VII and VIII and the formation of benzophenone locates two of the phenyl groups on the same carbon atom. Compound IX reacted readily with phenyllithium to give a 98% yield of a product for which structure XI is proposed. Phenylmagnesium bromide also reacted readily and gave a mixture of products which have not been identified. Compound X corresponds to the addition of one atom of oxygen to IX, and the epoxide structure is suggested as the most probable one although it is inert toward every reagent tried with the exception of phenyllithium. It was recovered unchanged from attempts to make the 2,4-dinitrophenylhydrazone, from heating for forty hours with acetic acid and potassium iodide or for eight hours with dilute sulfuric acid. Its inertness to oxidation is indicated by its mode of formation.

Experimental

Preparation of 2,3-Diphenyl-1,4-naphthoquinone, V.—This quinone was prepared by the oxidation of various compounds by chromium trioxide in glacial acetic acid. The oxidation of 2,3-diphenylnaphthalene[1] (IV) gave 56% of the quinone. The oxidation of 2,3-diphenyl-1-naphthol[2] (VI) gave 30–60% of the quinone. The oxidation of 2,3-diphenyl-1,2-dihydronaphthalene (III) is described here for the first time.

Oxidation of 2,3-Diphenyl-1,2-dihydronaphthalene, III.—2,3-Diphenyl-1,2-dihydronaphthalene (16 g.) was refluxed for fifteen minutes with 32 g. of chromium trioxide, 25 ml. of water and 200 ml. of glacial acetic acid. After pouring onto ice and diluting with water, the solid was filtered off and crystallized from ethyl alcohol. The resulting 2,3-diphenyl-1,4-naphthoquinone (11.9 g., 67%) melted at 133–140°. Another crystallization from ethyl alcohol or glacial acetic acid raised the melting point to 138–140°.

Dehydrogenation of 2,3-Diphenyl-1-keto-1,2,3,4-tetrahydronaphthalene (I) by Selenium and by Chloranil.—Heating 4.5 g. of the tetralone (I) and 1.3 g. of selenium at 290° for twelve hours, dissolving the cooled mass in ether,

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(6) Smith and Hoehn, This Journal, 61, 2619 (1939).

boiling with Norite and filtering from Norite and selenium gave 0.9 g. (20%) of the naphthol (VI) and much black tar.

The tetralone (4.5 g., 0.015 mole) was refluxed for five hours with 4.5 g. (0.018 mole) of chloranil and 20 ml. of xylene. The mixture was cooled, diluted with petroleum ether and allowed to stand overnight, after which most of the tetrachlorohydroquinone could be removed by filtration. The last traces could be removed by extraction with 4% potassium hydroxide solution, as the 2,3-diphenyl-1-naphthol was not dissolved under these conditions. Evaporation of the solvent gave 1.03 g. of unchanged tetralone and black tar. This result is in marked contrast to the good yield (70%) of 2,3-diphenylnaphthalene (IV) obtained from 2,3-diphenyl-1,2-dihydronaphthalene (III) by means of chloranil.[1]

The Reaction between 2,3-Diphenyl-1,4-naphthoquinone and Phenylmagnesium Bromide.—As in other studies of this type[3,5,7] the quantities of reactants and the method of procedure were varied. In some cases the phenylmagnesium bromide (0.1 mole) was added to a solution of 6.2 g. (0.02 mole) of the quinone in ether. In other cases the quinone (0.02 mole) in ether was added to the phenylmagnesium bromide (0.1 mole) in ether. In still other cases the quinone (0.025 mole) was extracted from a soxhlet by a boiling solution of phenylmagnesium bromide (0.15 mole) in ether. After standing overnight, the reaction mixtures, usually containing a brown solid, were decomposed with ice and either dilute hydrochloric acid or ammonium chloride solution. The dried ether extracts of these mixtures were allowed to stand and various crops of solids were filtered off and recrystallized.

These variations made little difference in the amounts of the products obtained from this quinone. The only solid addition product which could be isolated was the white compound VII which was obtained in about 13% yield. The quinone or the hydroquinone could always be isolated and steam distillation of the residue gave biphenyl. The final residue was a dark oil. Even when the hydroquinone was detected among the products, recrystallization in the presence of air caused its oxidation to the quinone and there was always the problem of separating the quinone from VII. This could be best accomplished by using a mixture of benzene and petroleum ether as the solvent for recrystallization.

1,2,2,3-Tetraphenyl-1,4-dihydroxy-1,2-dihydronaphthalene, VII, m. p. 208–210°.—This white solid was the only addition product isolated (13%) from the reaction between 2,3-diphenyl-1,4-naphthoquinone and phenylmagnesium bromide. It is soluble in the usual solvents such as ether, ethyl alcohol, ethyl acetate and benzene, but is only slightly soluble in petroleum ether. The best solvent for separating it from quinone (after first filtering the mixture of solids from the oily reaction mixture) was a mixture of benzene and petroleum ether. VII was recovered unchanged after three hours of refluxing with alkaline potassium permanganate. When 1 g. of VII was refluxed for six hours with 3 g. of potassium dichromate, 25 ml. of glacial acetic acid, 1 ml. of water and 10 drops of concd. sulfuric acid, the only product isolated was benzoic acid. When 1 g. of VII was boiled for five minutes with 1 g. of chromium trioxide and 10 ml. of glacial acetic acid the only product obtained was X, which was the same compound obtained by the oxidation of IX. When 0.75 g. of VII was refluxed for one hour with 0.4 g. of iodine in 10 ml. of glacial acetic acid it lost a molecule of water and was converted quantitatively into IX. After the oxidation of VII was found to give the same product as the oxidation of IX, experiments were carried out to show that the iodine was not necessary in the dehydration. Boiling VII with acetic anhydride or with glacial acetic acid for one hour converted it into IX. Since this was the case, no conclusion could be drawn as to the structure of VII from the oxidation experiments.

Anal. Calcd. for $C_{34}H_{26}O_2$ (466.6): C, 87.5; H, 5.6. Found: C, 87.6, 87.1; H, 5.8, 5.8; mol. wt., 456.

1,2,3,4-Tetraphenyl-1,4-dihydroxy-1,4-dihydronaphthalene, VIII, m. p. 231–233°.—This white solid was the only product of the reaction between 2,3-diphenyl-1,4-naphthoquinone and phenyllithium. The phenyllithium (0.15 mole) in ether was refluxed and the quinone (0.025 mole) was extracted from a soxhlet. The extraction required about one hour. The mixture was then decomposed with ice and dilute hydrochloric acid. The clear ether and water layers were separated from the white solid and the water layer was discarded. Evaporation of the ether layer gave more solid identical with that separated earlier. Crystallization from ethyl alcohol and ethyl acetate gave a pure compound melting 231–233° (yield 92%). Refluxing VIII (3 g.) for one hour in 50 ml. of glacial acetic acid with 0.5 g. of iodine gave IX (yield, 90%). Refluxing VIII (0.5 g.) with 10 ml. of acetic anhydride gave a quantitative yield of IX. Oxidation of VIII (2 g.) by refluxing for five minutes with 2 g. of chromium trioxide and 10 ml. of glacial acetic acid gave *o*-dibenzoylbenzene (38%) and benzoic acid, identified by comparison with known samples. Oxidation of VIII (2 g.) by boiling for four hours with 6 g. of potassium dichromate in 50 ml. of glacial acetic acid gave 1.75 g. of solid, which was a mixture of IX and a small amount of an unidentified white solid, m. p. 168–170°, which may have been impure X.

Anal. Calcd. for $C_{34}H_{26}O_2$ (466.6): C, 87.5; H, 5.6. Found: C, 85.9, 86.3; H, 6.2, 6.0; mol. wt., 468.

2,2,3,4-Tetraphenyl-1-keto-1,2-dihydronaphthalene, IX, m. p. 208–210°.—This pale yellow compound was formed very readily and in excellent yields (90–100%) from either VII or VIII by the loss of a molecule of water, accompanied by the migration of a phenyl group. The dehydration could be brought about by boiling either of the diaddition products with acetic anhydride, with glacial acetic acid and a trace of iodine, or with glacial acetic acid alone if a longer time were allowed. The solution was diluted with water, the solid filtered off and recrystallized from ethyl alcohol and ethyl acetate. IX was quite soluble in the latter and only slightly soluble in the former. The only reagents which had any effect on IX were phenylmagnesium bromide, phenyllithium and chromium trioxide. Treatment of IX (2.24 g.) with a large excess of phenyllithium caused the ether to boil vigorously. After refluxing for five minutes, the mixture was poured onto ice and made acid with dilute hydrochloric acid. The ether layer gave 2.58 g. (98%) of XI. IX does not react in such a clean cut fashion with phenylmagnesium bromide but gave a mixture of yellow products. IX does not react with cold chromium trioxide but is oxidized on heating. Two grams of IX, 2 g. of chromium trioxide and 10 ml. of glacial acetic acid were refluxed for five minutes, then poured onto ice. After the ether extract was treated with potassium hydroxide solution, benzoic acid was isolated from the alkaline layer and benzophenone and X (46%) were recovered from the ether layer. The benzophenone was identified as the 2,4-dinitrophenylhydrazone. IX was recovered unchanged after boiling for two hours with potassium dichromate in glacial acetic acid, after boiling with neutral or acid potassium permanganate, after treatment with perbenzoic acid or alkaline hydrogen peroxide, and after attempts to make a 2,4-dinitrophenylhydrazone.

Anal. Calcd. for $C_{34}H_{24}O$ (448.5): C, 91.0; H, 5.4. Found: C, 91.1, 91.0; H, 5.7, 5.7; mol. wt., 453.

2,2,3,4-Tetraphenyl-1-keto-3,4-epoxy-1,2,3,4-tetrahydronaphthalene, X, m. p. 186–187°.—This white compound was formed by the chromium trioxide oxidation of IX or VII (probably following its rearrangement to IX). It is very inert, having been recovered unchanged after attempts to make a 2,4-dinitrophenylhydrazone, after eighteen hours heating on the steam-bath with 10 ml. of glacial acetic acid, 8 ml. of water and 2 ml. of concd. sulfuric acid, and after refluxing for six days with sodium hydroxide in alcohol, or forty hours with potassium iodide and acetic acid. It turns yellow when exposed to light. With phenyllithium it reacts to give a white compound, melting about 260°, which was not identified.

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(7) Smith and Crawford, THIS JOURNAL, 50, 869 (1928).

Anal. Calcd. for $C_{34}H_{24}O_2$ (464.5): C, 87.9; H, 5.2. Found: C, 87.4, 87.4; H, 5.4, 5.2; mol. wt., 467.

1,2,2,3,4-Pentaphenyl-1-hydroxy-1,2-dihydronaphthalene, XI, m. p. 196.5–197.5°.—This white compound was formed in 98% yield from the reaction of phenyllithium on IX. Oxidation of 1.5 g. of XI by boiling for five minutes with 1.5 g. of chromium trioxide in 10 ml. of glacial acetic acid gave only a pinkish oil from which a small amount of benzophenone could be isolated as the 2,4-dinitrophenylhydrazone.

Anal. Calcd. for $C_{40}H_{30}O$ (526.6): C, 91.2; H, 5.7. Found: C, 90.4, 89.9; H, 5.9, 6.2; mol. wt., 520.

Summary

The reactions of 2,3-diphenyl-1,4-naphthoquinone with phenylmagnesium bromide and phenyllithium have been studied.

Structures have been proposed for the main products of these reactions and for the compound which results from the dehydration of both of them.

Five new compounds are described.

An improved method is described for the preparation of 2,3-diphenyl-1,4-naphthoquinone in three steps from 2,3-diphenyl-1-keto-1,2,3,4-tetrahydronaphthalene in 60% over-all yield.

POUGHKEEPSIE, NEW YORK RECEIVED AUGUST 4, 1947

[CONTRIBUTION FROM THE WELLCOME RESEARCH LABORATORIES]

Amines Related to 2,5-Dimethoxyphenethylamine. IV. 2,5-Diethoxy, 2-Hydroxy-5-methoxy and 2-Hydroxy-5-ethoxyphenylalkanolamines[1]

BY WALTER S. IDE AND RICHARD BALTZLY

In continuation of our studies on this interesting family of pressors, we report the preparation of the primary and secondary β-hydroxy-β-(2,5-diethoxyphenyl)-ethylamines and isopropylamines, and their analogs having hydroxyl groups in the 2-position with methoxyl or ethoxyl groups in the 5-position.

The 2,5-diethoxy family (I–IV) was prepared by a line of synthesis shown in the upper part of Chart I. In the main, this approach resembles that used in Paper II[2] of this series to prepare the corresponding dimethoxy compounds. The 2,5-diethoxyphenylalkanolamines and their precursors tend to be more soluble and less readily crystallized than their methoxy analogs and were usually isolated in lower yield.

The preparations of the 2-hydroxy-5-alkoxyphenylalkanolamines (V–XII) largely followed the scheme used in Paper III of this series[3] for the 2-hydroxy-5-methylphenylalkanolamines. These syntheses are outlined in the lower part of Chart I. A few comments are in order.

In the first preparation of the aminoalcohol VII, the isonitrosoketone VIIb was reduced directly with platinum in ethanolic hydrogen chloride solution. Compound VII was obtained without difficulty although it later became apparent that other substances were present in the mother liquors. In a later preparation, palladized charcoal was used for the first stage of the reduction and the 2-benzyloxyaminoketone hydrochloride, VIIa, was isolated as the major product. It is rather surprising that the 2-benzyl group was retained in the presence of this catalyst; the only rational explanation is that the sample of palladized charcoal had been partially inactivated. Successive hydrogenations of VIIa with fresh palladized charcoal and with platinum yielded VII.

In the preparation of Compound IX, the usually reliable hexamethylenetetramine method broke down, only traces of chloroform-insoluble material being obtained from the reaction of hexamethylene tetramine and IXc.[4] The bromoketone was then treated with benzhydrylamine[5] but apparently considerable tertiary as well as secondary amine was formed and the desired product was not readily separated. The synthesis of IX was finally accomplished by treating IXc with dibenzylamine. The reaction was slow and far from quantitative (in contrast to similar reactions with benzylmethylamine) but the tertiary amine IXb was isolated easily. On hydrogenation with palladized charcoal, IXb absorbed two mols of hydrogen rapidly at room temperature and a third more slowly at 65°.[6]

At the time this work was started, attempts were made to prepare amino alcohols having the

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[1] This work is part of a joint research being carried out in collaboration with a pharmacological group in the same laboratories.

[2] Baltzly and Buck, THIS JOURNAL, **62**, 164 (1940).

[3] Ardis, Baltzly and Schoen, *ibid.*, **68**, 591 (1946).

[4] Although this bromoketone is not especially active the failure of the preparation cannot be attributed to sluggishness since IXc reacts with reasonable speed with benzylmethylamine, benzhydrylamine and dibenzylamine. We are inclined to suspect that the initial reaction product was relatively soluble in chloroform and was accordingly exposed to the further reactions with bromoketone that should be possible from the conventional formula for hexamethylenetetramine but which are usually avoided by the precipitation of the first reaction-product. In the work reported in Paper III of this series it was found that if the temperature in a hexamethylenetetramine reaction was above 30–40°, the usual reaction product sometimes failed to precipitate. The original paper on this method as applied to phenacyl halides (Mannich and Hahn, *Ber.*, **44**, 1542 (1911) states that the reactions were carried out at room temperature but gives no indication that this condition is essential.

[5] *Cf.* Suter and Ruddy, THIS JOURNAL, **66**, 747 (1944).

[6] *Cf.* Simonoff and Hartung, *J. Amer. Pharmaceutical Assoc.*, **35**, 306 (1946). Obviously, this method involves a cleavage of benzylphenacylamine. It has gradually become apparent that although the benzyl group is usually removed preferentially from benzylphenacyl, benzyl β-hydroxyphenethyl and benzyl phenethylamines, these other groups have considerable labilizing effect, cleavage being achieved under conditions comparable with those required for cleavage of dibenzylamines.