under reflux for 20 hours. The cooled solution, after acidification, was extracted with ether (four times). The ether was removed and the acidic residue was esterified with diazomethane to yield 5.2 g. (52% on the basis of the unsaturated nitrile used) of XII as a colorless oil, b.p. 108° (2 mm.), n^{36}D 1.4637.

Anal. Calcd. for $C_{11}H_{16}O_4$: C, 62.26; H, 7.54. Found: C, 62.94; H, 7.52.

Methyl 1-Methyl-2-carbomethoxycyclopentaneacetate (XIII).—A solution of 4.6 g. of the unsaturated diester (XII) in 15 ml. of glacial acetic acid and 0.5 g. of prereduced Adams platinum catalyst were stirred until a little more than the theoretical amount of hydrogen was absorbed in less than 12 hours. The residue obtained by evaporation of the solvent from the filtered solution was distilled; b.p. 105° (2 mm.); $n^{36.5}$D 1.4522; yield 3.82 g.

Anal. Calcd. for $C_{11}H_{18}O_4$: C, 61.68; H, 8.41. Found: C, 62.02; H, 8.40.

1-Methyl-2-carboxycyclopentaneacetic Acid Anhydride (XIV).—A mixture of 3.3 g. of XIII, 15 ml. of acetic acid, 10 ml. of concentrated hydrochloric acid and 7 ml. of water was refluxed for 12 hours. After removal of the acetic acid and hydrochloric acid under reduced pressure the residue was treated with 30 ml. of acetic anhydride as described before to yield the anhydride as a gum, b.p. 130° (2 mm.), which later solidified, crude m.p. 90°; yield 2.1 g. (84%).

Anal. Calcd. for $C_9H_{12}O_3$: C, 64.29; H, 7.14. Found: C, 63.70; H, 7.34.

***cis*-1-Methyl-2-carboxycyclopentaneacetic Acid (VI, R = H).**—The above anhydride was converted into the *cis*-acid as described before. One crystallization from water yielded the pure *cis*-acid, m.p. 164° alone and when mixed with the *cis*-acid obtained from I.

Conversion of *cis*-1-Methyl-2-carboxycyclopentaneacetic Acid to the *trans*-Acid.—The dimethyl ester prepared from 0.9 g. of the *cis*-acid by means of diazomethane was refluxed for 12 hours with a solution of potassium *t*-butoxide prepared from 0.8 g. of potassium and 25 ml. of *t*-butyl alcohol. To the brown solution was added 30 ml. of water and the mixture refluxed for four hours longer. The white residue, obtained by evaporation of the reaction mixture to dryness on a steam-bath, was dissolved in a small quantity of water, acidified and again evaporated to dryness. The residue was extracted seven times with dry acetone–ether mixture. The oily residue, obtained after removal of the solvent, was dissolved by dilute hydrochloric acid and allowed to stand in the cold. The first crop of crystals was found to be a mixture of stereoisomers. The second crop, obtained by concentrating the mother liquor, melted at 90–95° and weighed 0.2 g. After three crystallizations the product melted at 105.5° alone and when mixed with the *trans* acid obtained from I.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF SOUTHERN CALIFORNIA]

Methylation of Some Amides in Acetone[1]

BY IRWIN J. PACHTER AND MILTON C. KLOETZEL

Amides were methylated in acetone solution by treatment with potassium hydroxide and a methylating agent. The method was applied to the methylation of an amide in the presence of an amine and also to the methylation of one amino group in the presence of another.

The usual method for the alkylation of amides, involving metallic sodium and an inert solvent,[2] is at best a rather inconvenient and somewhat dangerous procedure. Fones[3] has recently suggested the more convenient use of sodium hydride in place of sodium metal, but this improved method is still subject to certain limitations. For example, *p*-nitroacetanilide was unaffected by six hours of refluxing with sodium hydride in xylene and could not be alkylated.[3] In contrast, it was found in the present study that the methylation of *p*-nitroacetanilide can be accomplished conveniently and in good yield merely by refluxing the anilide in acetone solution with potassium hydroxide and methyl iodide for one minute. In similar fashion *p'*-nitrobenzanilide and acetanilide were methylated in good yield.

The method was also applied to the selective methylation of an amide in the presence of an amine. *p*-Benzamidodiphenylamine yielded *p*-(N-methylbenzamido)-diphenylamine in 90% yield when refluxed in acetone solution with methyl iodide and potassium hydroxide. That the product was not the isomeric *p*-benzamidodiphenylmethylamine was proved when the latter was prepared from *p*-nitrodiphenylamine by methylation, reduction and subsequent benzoylation, and found to be different from *p*-(N-methylbenzamido)-diphenylamine.

When large differences in proton availability exist, the method may also be applied to the selective methylation of one amino group in the presence of another. For example, an acetone solution of *p*-amino-*p'*-nitrodiphenylamine, upon treatment with potassium hydroxide and methyl iodide, yielded *p*-amino-*p'*-nitrodiphenylmethylamine in 83% yield. The structure of the product was proved when it was converted into an alkali-soluble benzenesulfonamide and when, upon reduction, it yielded bis-(*p*-aminophenyl)-methylamine, identical with the compound obtained upon methylation and reduction of bis-(*p*-nitrophenyl)-amine.

Experimental[4]

Methylations of amides were run as described here for the methylation of *p*-nitroacetanilide, with the exceptions that the reflux periods were varied as listed in Table I.

To 5.00 g. (0.028 mole) of *p*-nitroacetanilide dissolved in 100 cc. of warm acetone[5] was added 6 g. (0.1 mole) of powdered potassium hydroxide.[6] The hot mixture was refluxed gently while 6 g. (0.042 mole) of methyl iodide in 15 cc. of acetone was added. After one minute, the solution was

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[1] Abstracted from a portion of the dissertation submitted by Irwin J. Pachter to the Graduate School of the University of Southern California in partial fulfillment of the requirement for the degree of Doctor of Philosophy.

[2] P. Hepp, *Ber.*, **10**, 327 (1877).

[3] W. S. Fones, *J. Org. Chem.*, **14**, 1099 (1949).

[4] Microanalyses are by Mr. Joseph Pirie. Melting points are uncorrected.

[5] In this experiment and in the methylation of *p'*-nitrobenzanilide, analytical grade acetone was used. In all other methylations mentioned in this paper, commercial acetone was employed. It is advantageous to use pure acetone when the amide is easily hydrolyzed.

[6] When half this amount of potassium hydroxide was used in the methylation of *p'*-nitrobenzanilide, a yield of 78% of N-methyl-*p'*-nitrobenzanilide was obtained together with 9% of unchanged starting material.

TABLE I

AMIDES PREPARED BY METHYLATION IN ACETONE

Product	Reaction time, min.	Yield, %	M.p., °C.
N-Methyl *p*-nitroacetanilide	1	81	153–154[a]
N-Methyl-*p*′-nitrobenzanilide	5	86	110.5–111.5[a]
N-Methylacetanilide	15	80	99–100[a]
p-(N-Methylbenzamido)-diphenylamine	20	90	125
p-(N-Methylbenzamido)-diphenylmethylamine[b]	30	90	106

[a] No depression of m.p. obtained upon admixture with an authentic sample. [b] Prepared through the reaction of *p*-benzamidodiphenylmethylamine with methyl sulfate. In all other methylations mentioned in this paper, methyl iodide was used as the methylating agent.

filtered, concentrated, diluted with water and cooled. There was obtained 4.36 g. (81%) of pure N-methyl-*p*-nitroacetanilide, m.p. 153–154°. An additional 0.67 g. of crude product, m.p. 143–147°, was obtained on concentration of the mother liquor.

p*-(N-Methylbenzamido)-diphenylamine.**—p*-Benzamidodiphenylamine**, m.p. 162–163°, was prepared by treating *p*-aminodiphenylamine with benzoyl chloride according to the method used by Claisen[7] for the preparation of benzanilide.

Anal. Calcd. for $C_{19}H_{16}N_2O$: C, 79.15; H, 5.60. Found: C, 79.16; H, 5.68.

Methylation yielded *p*-(N-methylbenzamido)-diphenylamine (see Table I).

Anal. Calcd. for $C_{20}H_{18}N_2O$: N, 9.28. Found: N, 9.14.

By the procedure used by Storrie and Tucker[8] for the methylation of *o*-nitrodiphenylamine, with the exception that methyl iodide was used instead of methyl sulfate, *p*-nitrodiphenylamine[9] was methylated to give yellow prisms of ***p*-nitrodiphenylmethylamine**, m.p. 68–68.5°, in 90.5% yield.

Anal. Calcd. for $C_{13}H_{12}N_2O_2$: N, 12.27. Found: N, 12.01.

Reduction of *p*-nitrodiphenylmethylamine in ethanol solution with Raney nickel and hydrogen at 3 atm. pressure gave *p*-aminodiphenylmethylamine, m.p. 68–69°, in 85% yield.

Anal. Calcd. for $C_{13}H_{14}N_2$: N, 14.13. Found: N, 14.25.

The amine was benzoylated in 95% yield by Claisen's method[7] to give ***p*-benzamidodiphenylmethylamine**, m.p. 154°.

Anal. Calcd. for $C_{20}H_{18}N_2O$: N, 9.28. Found: N, 9.50.

Methylation yielded *p*-(N-methylbenzamido)-diphenylmethylamine (see Table I).

Anal. Calcd. for $C_{21}H_{20}N_2O$: N, 8.85. Found: N, 8.77.

***p*-Amino-*p*′-nitrodiphenylamine** was prepared by the method of Ullmann and Dahmen[9] with the exception that the hydrolysis of the sulfonic acid was carried out as follows: To a solution of 375 cc. of concd. sulfuric acid in 175 cc. of water at 100° was added 90 g. of *p*-amino-*p*′-nitrodiphenylamine-*o*′-sulfonic acid. The mixture was swirled and maintained at 100–105° for ten minutes. The clear brown solution was poured into 2 l. of water and the amine sulfate separated. Filtration of this salt followed by its treatment with ammonium hydroxide yielded 44.5 g. (66%) of *p*-amino-*p*′-nitrodiphenylamine. Ullmann and Dahmen reported the color of this compound to be red-brown. In the present study, however, when a benzene–acetone solution of the product was passed through a column of alumina and the eluate was concentrated, yellow crystals, m.p. 207–208°, were obtained. The yellow compound gradually became orange on standing.

***p*-Amino-*p*′-nitrodiphenylmethylamine.**—To 4.58 g. of *p*-amino-*p*′-nitrodiphenylamine dissolved in a refluxing mixture of 150 cc. of acetone and 25 cc. of benzene[10] was cautiously added 5 g. of powdered potassium hydroxide. A solution of 3.2 g. of methyl iodide in 25 cc. of acetone was added dropwise over a period of 15 minutes to the refluxing mixture. The intense purple-red color disappeared as the last of the methyl iodide was added. The mixture was poured into 500 cc. of water and the benzene layer was separated. The aqueous layer was extracted with an additional portion of benzene and the combined benzene solutions were concentrated to yield 4.01 g. (83%) of *p*-amino-*p*′-nitrodiphenylmethylamine, m.p. 157–158°.

Anal. Calcd. for $C_{13}H_{13}N_3O_2$: N, 17.28. Found: N, 17.22.

The product formed an alkali-soluble **benzenesulfonamide**, m.p. 213–214°.

Anal. Calcd. for $C_{19}H_{17}N_3O_4S$: N, 10.95. Found: N, 10.85.

Reduction of 2.00 g. of *p*-amino-*p*′-nitrodiphenylmethylamine in methanol with Raney nickel and hydrogen at 3 atm. pressure yielded 1.55 g. (89%) of bis-(*p*-aminophenyl)-methylamine, which crystallized in prisms, m.p. 174–175°.

Anal. Calcd. for $C_{13}H_{15}N_3$: N, 19.70. Found: N, 19.80.

Bis-(*p*-nitrophenyl)-amine[11] was methylated in the same manner as was *p*-nitrodiphenylamine. The reaction mixture, on dilution with water, yielded **bis-(*p*-nitrophenyl)-methylamine**, m.p. 175–179°, in 98% yield. Recrystallization from acetone gave yellow plates, m.p. 180.5°.

Anal. Calcd. for $C_{13}H_{11}N_3O_4$: N, 15.38. Found: N, 15.32.

The compound was reduced in the manner described for the reduction of *p*-amino-*p*′-nitrodiphenylamine. The m.p. of bis-(*p*-aminophenyl)-methylamine thus obtained was not depressed upon admixture with a sample derived from *p*-amino-*p*′-nitrodiphenylmethylamine.

LOS ANGELES, CALIFORNIA RECEIVED AUGUST 6, 1951

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[7] L. Claisen, *Ber.*, **27**, 3182 (1894).

[8] F. R. Storrie and S. H. Tucker, *J. Chem. Soc.*, 2255 (1931).

[9] F. Ullmann and R. Dahmen, *Ber.*, **41**, 3744 (1908).

[10] Benzene was added to aid in dissolving the *p*-amino-*p*′-nitrodiphenylamine. It is not essential for the success of the reaction.

[11] R. Nietzki and O. N. Witt, *Ber.*, **12**, 1399 (1879).