Anal. Calcd. for $C_6H_4N_3O_8Na$: C, 26.78; H, 1.50; N, 15.61; Na, 8.55. Found: C, 26.91; H, 1.52; N, 15.20, 16.22; Na, 8.38.

An unidentified, water-soluble sulfonate (3.9 g., m.p. > 300°) was also isolated. The salt was fractionally precipitated by dissolving in 75% ethanol and adding increments of absolute ethanol. The initial fractions, which were dark and amorphous, were discarded. Ultimately, a well crystallized, tan-colored solid was obtained; a sample was dried at 105° for 40 hr. before analysis.

Anal. Found: C, 21.87, 21.46; H, 1.60, 1.75; N, 15.75, 15.65; S, 9.17, 9.13; Na, 10.25, 10.81.

The *p*-toluidine salt of the above sulfonate was prepared in 5 *N* hydrochloric acid; after recrystallization from water it was obtained as rosettes of orange-red needles, m.p. 196–197° (vigorous decomposition).

Anal. Calcd. for $C_{14}H_{16}N_5O_{11}S$: C, 36.36; H, 3.49; H, 15.15; S, 6.93. Found: C, 36.44; H, 3.34; N, 15.19; S, 7.10.

Regeneration of the sodium salt from the recrystallized *p*-toluidine salt gave a compound which was analytically the same as the starting sodium salt.

Much dark orange, amorphous, water- and ethanol-soluble material was also formed.

1,3,5-Trinitrobenzene with Sodium Sulfite–Sodium Nitrite in Aqueous Methanol.—The reaction was performed as in the previous experiment except that 20 g. of TNB, 10 g. of sodium sulfite, 10 g. of sodium nitrite, 300 ml. of methanol, and 120 ml. of water were used. Much dark purple solid was present in the mixture throughout the 2.5-hr. heating period. After the solution had been cooled to room temperature, this precipitate was removed by filtration, washed once with 40 ml. of 75% aqueous methanol, then three times with 50-ml. portions of absolute methanol. There was left 9.4 g. of the TNB-sodium sulfite complex admixed with some sodium sulfate (based on X-ray powder pattern).

When the combined mother liquors and washings were cooled overnight at 0°, there was recovered 7.3 g. of material, m.p. 85–100°. Recrystallization from ethanol gave 3.2 g. of TNB, m.p. 121–123°. Probably some 3,5-dinitroanisole was present but no effort was made to isolate and characterize it in this experiment.

The mother liquor was next evaporated to 75 ml. under reduced pressure and cooled at 5° for 24 hr. The mixture of yellow plates and orange powder was removed by filtration. Extraction with warm water dissolved the orange powder and left 1.35 g. of insoluble material, m.p. 90–110° (probably TNB). Evaporation of the water extracts gave 1.8 g. (7.5% conversion; at least 20% yield) of sodium picrate monohydrate which was identified by comparison of its X-ray powder pattern with that of an authentic sample and by conversion to picric acid, m.p. 121–122°, mixed melting point undepressed.

3,5-Dinitroanisole.—A solution consisting of 10 g. of 1,3,5-trinitrobenzene, 12.5% of potassium cyanate, 190 ml. of methanol, and 40 ml. of water was refluxed and stirred for 2.5 hr. Ammonia was evolved from the orange-red solution. After the reaction mixture had been cooled to 5°, the long, orange-brown needles were removed by filtration and washed with 25 ml. of cold 50% ethanol. The yield of dried product, m.p. 107–108°, was 8 g. (86%).

By evaporating the mother liquors to dryness, dissolving the residue in water, and acidifying the resulting solution, there was recovered 0.6 g. of a mixture of TNB and dinitroanisole, melting at 75–80°.

When the above procedure was repeated using ethanol instead of methanol and keeping the temperature 60–61°, 7.0 g. of TNB, m.p. 120–121°, was recovered. By diluting the mother liquors with a large volume of water and cooling, there was precipitated 1.0 g. of solid melting 75–80°. Three recrystallizations, one from methanol and two from absolute ethanol, gave a small quantity of material melting sharply at 97–98°. Blanksma[13] reported a m.p. of 96° for 3,5-dinitrophenetole.

Acknowledgment.—The author wishes to thank Prof. Hans Jonassen, Tulane University, for numerous helpful discussions, Dr. Allen Olsen for the infrared spectra, and Fred Bien for the e.p.r. measurement.

(13) J. J. Blanksma, *Rec. trav. chim.*, **24**, 40 (1905).

The Reductive Acylation of Schiff Bases Using Trimethylamine Borane. IV

JOHN H. BILLMAN AND JOHN W. MCDOWELL

Contribution No. 1043 from the Chemistry Laboratory of Indiana University, Bloomington, Indiana

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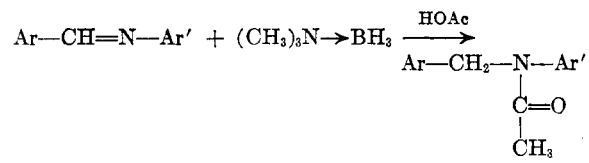
During the course of the investigation dealing with the use of dimethylamine borane for the reduction of Schiff bases[1] an attempt was made to utilize trimethylamine borane for the same purpose. It was found that this reagent would likewise reduce a Schiff base to the corresponding secondary amine. However, it was also discovered that, upon prolonged refluxing with an excess of the amine borane in glacial acetic acid, the acetamide corresponding to the acetyl derivative of the secondary amine was obtained.



This reaction is unique in that the acid itself is the acylating agent, whereas usually more reactive acid derivatives, such as the acyl halides or anhydrides, must be used for this purpose. This reagent thus is capable of reducing and acetylating the Schiff base in a single reaction process. There have been several examples of reductive acylation in the literature, all of which involve an integrated use of two reagents, one for reduction and one for acylation. For example, azo compounds or hydrazones containing an active methylene group were reduced with a metal reducing agent and an aliphatic acid anhydride to form the corresponding acylated amine.[2] Another case was the reductive acetylation of the actinomycins using hydrogenation over platinum in acetic anhydride followed by addition of pyridine to promote acetylation.[3] In light of these facts, it was decided to investigate this reaction

(1) J. H. Billman and J. W. McDowell, *J. Org. Chem.*, **26**, 1437 (1961).

(2) K. Pfister and M. Tishler, U.S. Patent 2,489,927; *Chem. Abstr.*, **44**, 2552 (1950).

(3) H. Brockmann and B. Franch, *Angew. Chem.*, **68**, 68 (1956).

TABLE I
REDUCTIVE ACYLATIONS OF SCHIFF BASES

Schiff bases Ar—CH=N—Ar' Ar	Ar'	Acid	Reflux time, hr.	Acetylated product	M.P., °C. (corr.)	Yield, %
Phenyl	Phenyl	Acetic	11	N-Phenyl-N-benzylacetamide	57–58[a]	60.9
Phenyl	Phenyl	Propionic	11	N-Phenyl-N-benzylpropionamide	...[b]	64.7
Phenyl	Phenyl	Benzoic	12	N-Phenyl-N-benzylbenzamide	106.0–106.5[c]	26.2
Phenyl	*p*-Chlorophenyl	Acetic	11	N-*p*-Chlorophenyl-N-benzylacetamide	91–92[a]	67.2
p-Chlorophenyl	*p*-Chlorophenyl	Acetic	12	N-*p*-Chlorophenyl-N-*p*-chlorobenzylacetamide	104–105[a]	66.4
p-Nitrophenyl	*p*-Nitrophenyl	Acetic	18	N-*p*-Nitrophenyl-N-*p*-nitrobenzylacetamide	148–149[a]	22.9
Phenyl	*p*-Hydroxyphenyl	Acetic	11	N-*p*-Hydroxyphenyl-N-benzylacetamide	169.5–170.0[a]	88.0
p-Methoxyphenyl	Phenyl	Acetic	12	N-Phenyl-N-*p*-methoxybenzylacetamide	53.5–54.0[a]	25.5
Phenyl	*p*-Methoxyphenyl	Acetic	9	N-*p*-Methoxyphenyl-N-benzylacetamide	...[a,d]	68.6
Phenyl	*p*-Carbethoxyphenyl	Acetic	12	N-*p*-Carbethoxyphenyl-N-benzylacetamide	57–58[a]	35.1
Phenyl	*p*-Sulfonamidophenyl	Acetic	12	...[e]	...	10.9

[a] J. H. Billman and J. W. McDowell, *J. Org. Chem.*, **26**, 1437 (1961). [b] High-boiling liquid, b.p. 156–157° (1.0 mm.); *Anal.* Calcd. for C: 80.30; found: 79.99. Calcd. for H: 7.12; found: 7.15. [c] J. H. Billman and A. C. Diesing, *J. Org. Chem.*, **22**, 1069 (1957). [d] High-boiling liquid, b.p. 174–176° (0.7 mm.). [e] Mono- and diacetylated products obtained.

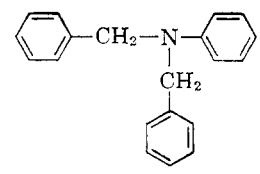
further to determine its generality, both from a standpoint of using variously substituted Schiff bases and of using different acids. The results of this investigation are shown in Table I.

As can be seen from this table, the yields varied considerably. However, it is apparent that electron-donating substituents, particularly on the benzene ring attached directly to the nitrogen atom, tend to increase the amount of acylation. The Schiff bases which contain a nitro, carbethoxy, or sulfonamido group on this ring gave low yields of the acetamides. This result was not surprising since the same trend has been noted in acylations using other reagents.[4]

In order to obtain the optimum yields of the acetamides it was necessary that the temperature of the initially occurring reduction reaction be carefully controlled to prevent hydrolysis of the Schiff base in the acid solution. This was accomplished by cooling and by the slow addition of the amine borane to the Schiff base until reduction was complete. The acylation was then effected by heating the reaction mixture under reflux in the presence of an excess of the amine borane.

The amount of trimethylamine borane used in all cases was one and one-third of an equimolar amount of the Schiff base. This was enough to permit reduction of the Schiff base and still have present an equimolar amount to effect acylation. It was found in several experiments in which the secondary amine, N-*p*-chlorophenylbenzylamine, was treated with trimethylamine borane in glacial acetic acid, that the role of the amine borane is apparently not one of a true catalyst. When equimolar amounts of the amine and the amine borane were used, acetylation occurred in 87.5% yield. However, when only 10% of the equimolar amount of amine borane was employed, the yield of the acetamide was 21.3%. Therefore, equimolar amounts were used in all cases during this work. A "blank" reaction was also run on the above secondary amine in order to dispel any doubt that it was actually the trimethylamine borane which allowed acylation to occur and not some reactive impurity in the acid used, such as the anhydride. Absolutely no acetylation could be detected when the amine was subjected to refluxing with only acetic acid.

Since benzoic acid was not suitable to also serve as a solvent in the case of the reductive benzoylation of N-benzylidenaniline, a slightly modified procedure was used, wherein, xylene was employed as a solvent and twice the equimolar amount of benzoic acid used to provide an acidic media and effect the benzoylation. A second product, in addition to the benzamide, was isolated from this reaction and was shown to be the tertiary amine, N,N-dibenzylaniline (I). The probable explanation for the



I

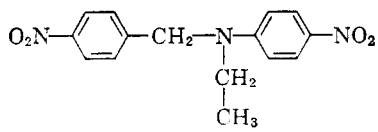
formation of this amine is the reduction by trimethylamine borane of the benzamide initially formed. It may well be that borane is the reagent responsible for this reduction during the prolonged heating in an inert solvent like xylene, since Brown[5]

(4) N. D. Cheronis and J. B. Entrikin, "Semimicro Qualitative Organic Analysis," Interscience Publishers, Inc., New York, N. Y., 1958, p. 409.

(5) H. C. Brown and H. C. Subba Rao, *J. Am. Chem. Soc.*, **82**, 681 (1960).

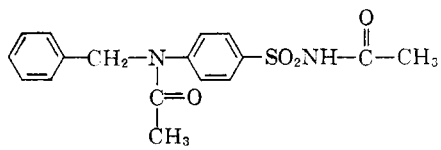
has shown that amides are reduced with diborane.

A similar product was obtained in the case of the reductive acetylation of N-*p*-nitrobenzylidene-*p*-nitroaniline. This particular reaction was allowed to reflux considerably longer than the others, since in a previous attempt, very little acetylation had occurred after only twelve hours. The yield obtained after eighteen hours was still much lower than the majority of these reactions. In addition to the acetamide, 25.9% of the secondary amine and 2.7% of the tertiary amine, N-ethyl-N-*p*-nitrobenzyl-*p*-nitroaniline (II) were isolated. This latter product may likewise be formed by the reduction of the acetamide.



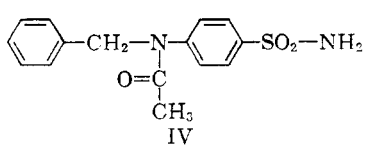
II

The reductive acetylation of N^4-benzylidenesulfanilamide also resulted in the isolation of several different compounds. A small amount of the diacetyl derivative was obtained and was shown to be identical to the product obtained from the acetylation of the secondary amine by conventional methods.[1] This compound was assigned the structure of N^1-acetyl-N^4-acetyl-N^4-benzylsulfanilamide (III) on the basis of the positions of the two carbonyl bands in the infrared spectrum. The band observed at 6.16 μ was in the range expected for an ordinary amide carbonyl function, whereas, the band at 5.85 μ was in the range expected for an acetyl carbonyl attached to the sulfonamide nitrogen, due to the electron-withdrawing power of the sulfonyl group also attached to this nitrogen atom.



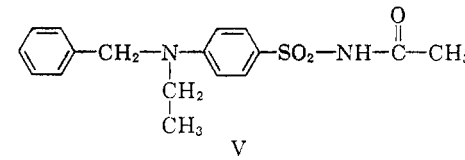
III

A monoacetylated derivative was also isolated in relatively high yield from this reaction and appears to be N^4-acetyl-N^4-benzylsulfanilamide (IV). The same considerations of the infrared spectrum for this compound as those just mentioned above led to the assignment of this structure in preference to the alternative possibility which could arise from the acetylation of the sulfonamide nitrogen.



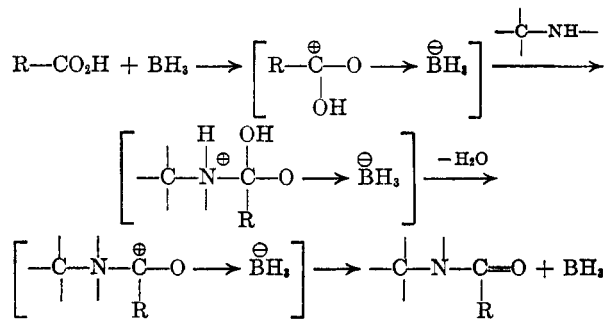
IV

A third compound was also obtained from this reaction and was thought to be the tertiary amine derivative, N^1-acetyl-N^4-benzyl-N^4-ethylsulfanilamide (V), formed from the reduction of the acetyl group attached to the secondary amino nitrogen atom of the diacetylsulfanilamide (III). The infrared spectrum of this material strongly supported the assignment of this structure to the compound rather than several others for which the elemental analyses would agree.



V

The mechanism of the acylation reaction is probably very similar to that for Friedel-Crafts acylation. The borane could coördinate with the carbonyl oxygen of the acid to create an electrophilic species which can then attack the electron pair of the amine nitrogen.



This mechanism is supported by the observed tendency for electron-withdrawing groups in the ring attached to the nitrogen atom to reduce the amount of acetylation obtained since this would tend to make the amino group a weaker nucleophile.

Experimental

N-*p*-Chlorophenyl-N-*p*-chlorobenzylacetamide (Typical Procedure).—A suspension of 25 g. (0.1 mole) of N-*p*-chlorobenzylidene-*p*-chloroaniline in 50 ml. of glacial acetic acid was placed in a 300-ml. three-necked flask equipped with a magnetic stirrer, reflux condenser, dropping funnel, and thermometer and which was placed in an ice bath. A solution of 9.8 g. (0.113 mole) of trimethylamine borane in 30 ml. of glacial acetic acid was added slowly to the Schiff base suspension through the dropping funnel until reduction was complete, *i.e.*, until no further increase in reaction temperature was observed. The remainder of the trimethylamine borane solution was added rapidly and the reaction mixture heated under reflux for 12 hr. The reaction mixture was allowed to cool and then treated with approximately 200 ml. of a 6 *N* sodium hydroxide solution. The semi-solid which formed was removed by extraction with three 50-ml. portions of ether and the combined ether extracts dried over Drierite for 12 hr. The Drierite was removed by filtration and the ether taken off under vacuum. The white solid which remained was dissolved in the smallest possible amount of 95% ethanol with heating and this solution treated with Norit, filtered, and refrigerated. The solid which formed was collected by suction filtration and dried at room temperature. The yield of acetamide was 19.52 g. of 66.4 % of the theoretical amount of white crystals melting at 104–105°. A melting point of 104.5–105.0° is recorded in the literature for this compound.[1]

N-Phenyl-N-benzylbenzamide.—A solution of 5.83 g. (0.032 mole) of N-benzylidenaniline and 7.85 g. (0.064 mole) of benzoic acid in 40 ml. of xylene was placed in a 100-ml. three-necked flask equipped with a magnetic stirrer, reflux condenser, dropping funnel, and thermometer. To this mixture was added a solution of 3.20 g. (0.043 mole) of trimethylamine borane in 20 ml. of xylene. The reaction mixture was heated under reflux (140°) for 12 hr. The color of the solution was a dark yellow-brown. The reaction mixture was allowed to cool and then poured into a separatory funnel. This solution was washed twice with 50-ml. portions of a 10% sodium carbonate solution and once with 50 ml. of a 10% sodium hydroxide solution. The xylene solution was then washed with two 50-ml. portions of 15% hydrochloric acid and dried for several hours over anhydrous magnesium sulfate. The drying agent was removed by filtration and the xylene taken off under diminished pressure. The oil which remained solidified upon standing. This crude product melted at 90–97°. Upon recrystallization twice from ethanol the product melted at 106.0–106.5°. The infrared spectrum and melting point of this product were identical with those for an authentic specimen of N-phenyl-N-benzylbenzamide. The yield was 2.40 g. or 26.2% of the theoretical amount.

A second crop of crystals was obtained from the filtrates of the recrystallizations. This product melted at 60–64° and after recrystallization twice from ethanol melted at 66.5–67.0°.

Anal. Calcd.: C, 87.91; H, 6.96. Found: C, 87.98; H, 7.05.

The melting point, (lit., m.p. 67°[6]) infrared spectrum, and elemental analysis all indicated that this material was the tertiary amine, N,N-dibenzylaniline. The preparation of the picrate derivative, which melted at 133.5–134.0° dec. as compared to 131–132° dec. reported in literature,[6] confirmed this fact.

N-*p*-Nitrophenyl-N-*p*-nitrobenzylacetamide.—The typical procedure was employed for the preparation of this compound except that the reaction was allowed to reflux for 18 hr. A yield of 4.16 g. of a yellow solid formed upon cooling the reaction mixture. This product was recrystallized from absolute ethanol and three different fractions obtained.

The first fraction was shown to be the secondary amine, N-*p*-nitrobenzyl-*p*-nitroaniline, by means of the infrared spectrum and mixed melting point (188–189°).

The second fraction was a mixture of the secondary amine and the acetamide, which was separated by means of extracting out the acetamide with a benzene–cyclohexane solvent mixture.

The third fraction was also a mixture and was separated by means of chromatography over Merck acid-washed alumina. Using petroleum ether (b.p. 30–60°), a mixture of equal parts of petroleum ether and benzene, and benzene successively as eluents, two principal compounds were obtained. The first compound was shown to be the tertiary amine, N-*p*-nitrobenzyl-N-ethyl-*p*-nitroaniline, by means of its infrared spectrum and the elemental analyses.

Anal. Calcd.: C, 59.70; H, 4.99; N, 13.95. Found: C, 59.60; H, 5.04; N, 14.25.

The yield of this amine was 2.76 % of the theoretical amount of yellow crystals melting at 133.5–134.0°. The second product isolated from this fraction was more of the secondary amine.

N^1-Acetyl-N^4-acetyl-N^4-benzylsulfanilamide.—The typical procedure was used in the preparation of this compound. However, the product obtained from the reaction mixture yielded two fractions upon recrystallization from ethanol.

The first fraction consisted of two compounds which were separated by means of a fractional crystallization. The first compound, melting at 191–192°, was shown to be the monoacetylated derivative, N^1-acetyl-N^4-benzylsulfanilamide, from its infrared spectrum (single carbonyl peak at 6.16 μ) and elemental analyses (Calcd.: N, 9.21. Found: N, 9.17). The other compound was thought to be the tertiary amino derivative. This material melted at 187–188° and its infrared spectrum (single carbonyl peak at 5.85 μ) and elemental analyses (Calcd.: N, 8.44; S, 9.65. Found: N, 8.49; S, 9.63) were consistent with the structure for N^1-acetyl-N^4-benzyl-N^4-ethylsulfanilamide.

The second fraction also appeared to be a mixture and was chromatographed over Merck acid-washed alumina using ethyl ether and ethyl acetate for elution. The first compound isolated was identical to the one from the first fraction which was assigned the structure for N^1-acetyl-N^4-benzyl-N^4-ethylsulfanilamide. The second and third compounds obtained were the monoacetylated derivative identical with the one from the first fraction and some of the diacetyl derivative as shown by a mixed melting point and infrared spectrum.[1]

(6) C. Matzudaira, *Ber.*, **20**, 1611 (1887).

Conversion of 2-Duroylresorcinol into a Fluorenone Derivative[1]

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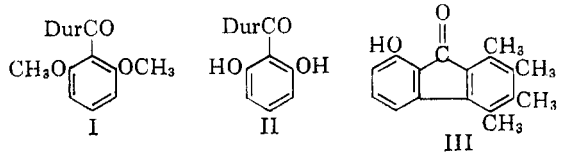
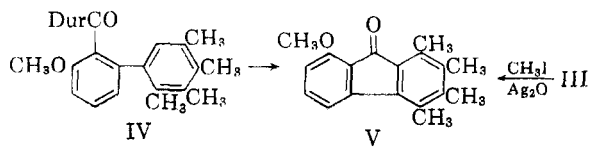
Received November 10, 1961

When the dimethyl ether of 2-duroylresorcinol (I) is demethylated with hydrobromic acid or aluminum chloride the phenol II may undergo further reaction. With hydrobromic acid in fact it suffers cleavage to resorcinol and duroic acid. Production of phenol II has been accomplished with aluminum chloride, but long heating with this reagent brings about change to 1,2,3,4-tetramethyl-8-hydroxyfluorenone (III).



Isomerization of the duryl radical to the corresponding prehnityl group had been observed earlier[3]; the ring closure thus made possible is remarkable in that it is an arylation of an aromatic ring by a phenol.

The structure of the new fluorenone was established by an independent synthesis of its methyl ether; ether I reacted with prehnitylmagnesium bromide to give 2-duroyl-3-prehnitylanisole (IV).



(1) This research was supported in part by a grant from the Office of Ordnance Research, U. S. Army (Contract No. DA-11-022-ORD-874).

(2) Chas. Pfizer Co. Fellow, 1961–1962.

(3) G. Baddely, G. Holt, and S. M. Makar, *J. Chem. Soc.*, 2415 (1952).