[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF MICHIGAN]

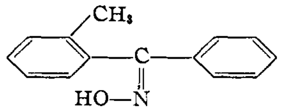
# The Influence of Substituents on the Schmidt Reaction on Some Benzophenones

BY PETER A. S. SMITH AND BRUCE ASHBY

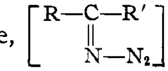
In an earlier communication,[1] it was shown that para-substituted benzophenones give very nearly equal quantities of isomeric anilides when subjected to the Schmidt reaction by treatment with hydrogen azide and sulfuric acid. *p*-Methoxybenzophenone, however, was shown to give a ratio of benzanisidide to anisanilide of 68:32, which is a greater departure from a ratio of 50:50 than was thought to be due entirely to experimental error. Furthermore, the discrepancy is in the direction to be expected if it should be a result of the great ease of migration of the anisyl group as observed in the Beckmann and pinacol rearrangements.[2,3]

To determine whether this apparent nonconformity is due to a real influence of "migration aptitudes," the behavior of two ketones containing the anisyl group in competition with a group which is known to migrate only with difficulty in other nucleophilic rearrangements has been investigated. Any effect which "migration aptitudes" might have in the rearrangement of *p*-methoxybenzophenone should in these cases be greatly magnified. The products of the Schmidt reactions on both *p*-nitro-*p'*-methoxybenzophenone and *p*-chloro-*p'*-methoxybenzophenone consisted of essentially equal quantities of the two possible isomeric amides, as determined from the amounts of the respective hydrolysis products. It thus seems proper to conclude that the influence of "migration aptitudes" does not appear in the Schmidt reaction on benzophenones.

The ratio of *cis* and *trans* oximes resulting from oximation of *o*-methylbenzophenone has been investigated with the aid of the Beckmann rearrangement by Bachmann and Barton,[4] who reported that the *syn*-*o*-tolyl isomer is formed preferentially, in the proportion 0.75:0.25. This result seemed improbable from steric considerations, and since, in addition, the experimental procedure used to determine this value[5] was not free from question, we have repeated the determination. The preponderance of the *syn* isomer is definitely confirmed in a revised ratio 0.96:0.04, which we believe to be accurate to 0.05. *syn*-*o*-Methylbenzophenoxime would, of course, be strain-free when the toluene ring is turned with its methyl group away from the oximino group, thus



The behavior of 2,6-dimethylbenzophenone, in whose oxime interference with the *syn* configuration would be more likely to be encountered, has not been determined, because of its great resistance to oximation.[4]

With one exception (1-benzoylphenanthrene),[6] all ketones previously subjected to the Schmidt reaction have shown preferential migration of the bulkier group, if there existed a difference in bulk in the neighborhood of the carbonyl group.[1] This has been attributed to the orientation of a hypothetical intermediate,  $\left[\begin{matrix}\mathrm{R-C-R'}\\ \| \\ \mathrm{N-N_2}\end{matrix}\right]^+$, capable of displaying geometrical isomerism similar to that of oximes. In view of the unusual result on oximation of *o*-methylbenzophenone, it became a matter of considerable interest to subject this ketone to the Schmidt reaction. The results revealed that the phenyl group migrates preferentially, in spite of its lesser bulk, in the proportion 0.88:0.12. (Since the over-all yield of hydrolysis products was appreciably less than from the Beckmann rearrangement, we do not believe this ratio to be as accurate as the 0.96:0.04 ratio determined for the latter case.) If *trans*-migration is assumed to occur in the Schmidt reaction, as it is known to occur in the Beckmann rearrangement, this result means that the intermediate is produced predominantly in the configuration *cis* to the *o*-tolyl group, as is the corresponding oxime. This is an unexpected result if the influence of the methyl group is presumed to be only repulsion due to its bulk. In view of these considerations, a systematic investigation of the effect of ortho-substituents on the Schmidt reaction is being undertaken.

An unanticipated incidental observation was made as a result of the hydrolysis of the mixture of *o*-toluanilide and benzo-*o*-toluidide obtained from *o*-methylbenzophenone. Although *o*-toluanilide was the major component of the mixture, the small amount remaining unhydrolyzed after four days of heating at 100° with 30% hydrogen bromide in acetic acid was benzo-*o*-toluidide. The unexpectedly large difference in the rates of hydrolysis of the two isomers, to which this result must be due, is in accord with the parallel observation on the isomeric amides derived from 1-benzoylphenanthrene.[4,6]

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[1] P. A. S. Smith and J. P. Horwitz, THIS JOURNAL, **71**, 3418 (1949).

[2] Summarized by H. Adkins in H. Gilman's "Organic Chemistry," 2nd ed., Vol. I, Chap. 13; John Wiley and Sons, Inc., New York, N. Y., 1943.

[3] *Cf.* also G. W. Wheland, "Advanced Organic Chemistry," John Wiley & Sons, Inc., New York, N. Y., p. 494, *et seq.*, 1949.

[4] W. E. Bachmann and M. X. Barton, *J. Org. Chem.*, **3**, 300 (1938).

[5] M. X. Barton, Ph.D. Thesis, Univ. of Michigan, 1938.

[6] J. R. Dice and P. A. S. Smith, *J. Org. Chem.*, **14**, 179 (1949).

## Experimental[7]

**Ketones.**—*p*-Chloro-*p*′-methoxybenzophenone and *p*-nitro-*p*′-methoxybenzophenone were prepared by the reaction of anisole with the corresponding acid chlorides in the presence of aluminum chloride, using excess anisole as solvent. *o*-Methylbenzophenone was prepared by the reaction of phenylmagnesium bromide with *o*-tolunitrile.

**Schmidt Reactions.**—The Schmidt reactions were carried out on a scale of 0.01 mole by treating the ketones with sodium azide and sulfuric acid in molten trichloroacetic acid.[6] The resulting mixtures of anilides were hydrolyzed by heating with acetic–hydrobromic acid mixture under reflux for five days, or with 30% hydrogen bromide in glacial acetic acid in a sealed tube at 100° for about twelve hours. This procedure has previously been shown to bring about simultaneous demethylation of those products containing a methoxy group.[1]

*p*-Chloro-*p*′-methoxybenzophenone (2.47 g.) gave 2.51 and 2.54 g. (96 and 97%) of mixed anilides in different runs. The hydrolysis mixtures obtained from these were diluted with water and extracted four times with ether. Evaporation of the ether left a mixture of *p*-hydroxybenzoic and *p*-chlorobenzoic acids weighing 1.11 g. and 1.14 g. The *p*-hydroxybenzoic acid was extracted by digestion with two 50-ml. portions of water; the residues of *p*-chlorobenzoic acid weighed 0.74 g. and 0.79 g., and melted[7] at 237–240°. The purified acid was obtained as white crystals, m. p. 239–240° with sublimation (lit.,[8] 240°), by solution in sodium bicarbonate solution, decolorizing with charcoal, and precipitating with hydrochloric acid, with only small mechanical losses. The solution from which the acids were extracted was alkalized with excess sodium carbonate and again extracted with ether. The extracts were treated with excess acetic anhydride, and the mixtures of acetylated amines were obtained by evaporation; wt. 1.43 g. and 1.28 g. Digestion of these mixtures with 50-ml. portions of water removed the acetylated *p*-aminophenol and left 0.68 g. and 0.79 g. of *p*-chloroacetanilide, m. p. 176–178° and 173–176° (lit.,[9] 178°). The mole-ratios of anisyl migration *vs.* *p*-chlorophenyl migration calculated from these figures are 0.54:0.46 and 0.52:0.48.

*p*-Nitro-*p*′-methoxybenzophenone (2.57 g.) gave 2.52 g. (93%) of mixed amides by the Schmidt reaction; the yellow filtrates yielded a small additional amount of material on extraction with ether. The entire product was hydrolyzed and demethylated with 30% hydrogen bromide in acetic acid. Dilution with water precipitated a mixture of *p*-nitrobenzoic acid and *p*-nitroaniline, which was augmented by additional material obtained by extracting the filtrate five times with ether. The *p*-nitrobenzoic acid was separated by solution in sodium bicarbonate solution and precipitation with hydrochloric acid; wt. 0.68 g. (40%), m. p. 231–236°. Recrystallization from boiling water raised the melting point to 236–238° with sublimation (lit.,[10] 240° with sublimation) without appreciable loss. The material not extracted by sodium bicarbonate was a tacky mass of olive-yellow crystals, consisting apparently of *p*-nitroaniline, quinone (from oxidation of *p*-aminophenol), unreacted ketone, and unhydrolyzed amides; wt. 1.02 g. Extraction with 75 cc. of boiling water gave 0.52 g. (41%) of *p*-nitroaniline on cooling, m. p. 144–146° (softened 136–144°) (lit.,[11] 147°); treatment with acetic anhydride in warm benzene gave *p*-nitroacetanilide, m. p. 213–214° (lit.,[9] 216°). The aqueous filtrates from the *p*-nitroaniline yielded on extraction with ether 0.34 g. of a tarry mixture of quinone and a little *p*-nitroaniline. The mole-ratio of anisyl migration to *p*-nitrophenyl migration was calculated from the respective weight of *p*-nitrobenzoic acid and *p*-nitroaniline to be 0.49:0.51.

*o*-Methylbenzophenone[12] (1.96 g.) gave 2.03 g. (96%) and 2.07 g. (98%) of amides in different runs. Hydrolysis was nearly complete after heating for four days at 100° in a sealed tube with 25 cc. of 30% hydrogen bromide in acetic acid. From the diluted solution there was obtained by filtration and ether extraction a mixture of acids with a little neutral material. By solution in potassium carbonate solution and reprecipitation with hydrochloric acid there was obtained 0.72 g. of nearly pure *o*-toluic acid, m. p. 101–103°, and by ether-extraction of the filtrate, 0.19 g. of mixed benzoic and *o*-toluic acids. The combined acids were oxidized with potassium permanganate according to Bachmann and Barton.[4] The resulting mixture of acids was separated into 0.98 g. (55%) of phthalic acid, m. p. 197–198°, and 0.07 g. (5.8%) of benzoic acid, m. p. 114–117°. The neutral products from the hydrolysis gave 0.05 g. (2.4%) of benz-*o*-toluidide, m. p. 142–144° (lit.,[13] 145–146°), on recrystallization from boiling petroleum ether. The calculated ratio of *o*-tolyl migration *vs.* phenyl is 0.88:0.12. No satisfactory separation of *o*-toluidine from aniline could be devised. Another run in which methanolic potassium hydroxide was used instead of hydrogen bromide in acetic acid for hydrolysis gave rise to an appreciable amount of *o*-methylbenzhydrol in addition to the other products,[14] showing that the Schmidt reaction had not been complete. As a further verification of the preponderance of *o*-toluanilide, the mixed amides were recrystallized from ligroin–benzene and ligroin–tetrachloroethane mixtures. Pure *o*-toluanilide, m. p. 126–127°,[15] was obtained in good yield.

**Beckmann Rearrangement of *o*-Methylbenzophenoxime.**—*o*-Methylbenzophenone (3.94 g.) yielded 3.80 g. of oxime when treated with hydroxylamine hydrochloride in refluxing pyridine. This was rearranged in benzene solution with 3.0 g. of phosphorus pentachloride; yield 3.75 g. of mixed amides. The amides were hydrolyzed with 30% hydrogen bromide in glacial acetic acid as described for the amides from the Schmidt reaction. There was obtained 1.98 g. (82%) of nearly pure *o*-toluic acid, m. p. 103–106°, and 0.18 g. of mixed acids. Oxidation of the combined acids gave 2.25 g. of phthalic acid, m. p. 202–205°, and 0.07 g. of benzoic acid, m. p. 120–122°, separated by virtue of the latter's solubility in carbon tetrachloride. The ratio of migration of the *o*-tolyl group *vs.* the phenyl group computed from these weights is 0.04:0.96.

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## Summary

Three ketones, *p*-chloro-*p*′-methoxybenzophenone, *p*-nitro-*p*′-methoxybenzophenone and *o*-methylbenzophenone, have been subjected to the Schmidt reaction with hydrogen azide and sulfuric acid. The ratios of isomeric amides produced from the first two ketones were close to 1:1,

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[7] All melting points are corrected.

[8] H. Lettré, H. Barnbeck, W. Fuhst and F. Hardt, *Ber.*, **70**, 1410 (1937).

[9] "Organic Reagents for Organic Analysis," Hopkins and Williams Research Laboratory, Chemical Publishing Co., Inc., Brooklyn, N. Y., 1946, pp. 131-133.

[10] G. Fieser, *Ann.*, **127**, 137 (1863).

[11] H. Hübner, *Ber.*, **10**, 1716 (1877).

[12] We wish to acknowledge the assistance of Mr. Herbert Title in the preparation of this ketone and its oxime.

[13] P. Jacobson and L. Huber, *Ber.*, **41**, 663 (1908).

[14] Bachmann and Barton (ref. 3) report the formation of *o*-methylbenzhydrol from the alkaline hydrolysis of the mixed amides from the Beckmann rearrangement of the crude oximes of *o*-methylbenzophenone.

[15] The recorded m. p. of *o*-toluanilide appearing in most melting point tables is the value of 125° reported by A. W. Smith (*Ber.*, **24**, 4047 (1891)) for a sample prepared by the Beckmann rearrangement. A sample of *o*-toluanilide prepared from *o*-toluyl chloride and aniline was kindly lent to us by Dr. W. R. Vaughan; when recrystallized from ligroin-benzene it melted at 129-129.5°, and when mixed with our product from the Schmidt reaction melted at 127-128.5°.

showing that even large differences in the electronic properties of the migrating groups do not significantly influence the relative extents of migration. *o*-Toluanilide was the major product obtained from *o*-methylbenzophenone, as is also the case when this ketone is oximated and subjected to the Beckmann rearrangement.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF TEXAS]

# Allylic Chlorides. X. Configuration of the 3-Chloro-2-buten-1-ols and the 1,3-Dichloro-2-butenes

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The recent preparation and study of the 1,3-dichloro-2-butenes has resulted in considerable information pertaining to these compounds and the corresponding chloroalcohols (3-chloro-2-buten-1-ol).[2] These data, however, furnish only indirect evidence as to the arrangement of atoms and groups around the carbon–carbon double bond, and the conclusion drawn as to the structure of the two isomers was based upon an assumption of structure for the two isomers of 1,3-dichloropropene which was subsequently shown to be incorrect.[3] The purpose of the present investigation was to obtain further evidence pertaining to the geometrical configuration of the 3-chloro-2-buten-1-ols (and indirectly, of the 1,3-dichloro-2-butenes).

Previous work with the 3-chloro-2-propen-1-ols has shown that the isomer with the chlorine and hydrogen atoms *trans* to one another will dehydrochlorinate more readily than when they are in the *cis* position.[4] This behavior is in keeping with the generally accepted theory of the relative ease of *trans* elimination.[5] This same reaction, therefore, should be useful in elucidating the structure of the 3-chloro-2-buten-1-ols.

The results of the dehydrochlorination of both isomers of 3-chloro-2-buten-1-ol are given in Table I. It was not possible to determine accurately the purity of the *beta* isomer, but it is thought to be substantially *beta*-3-chloro-2-buten-1-ol.

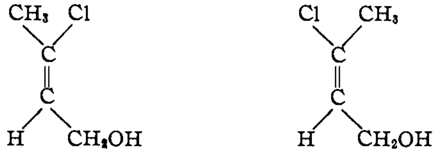
TABLE I

DEHYDROCHLORINATION OF 3-CHLORO-2-BUTEN-1-OL

| Run | Isomer | Time, hr. | NaOH, % | Reflux temp., °C. | Reacted (from $Cl^-$), % |
|---|---|---|---|---|---|
| 1 | α | 2 | 0.0 | 98.2 | 0.4 |
| 2 | α | 2 | 1.0 | 98.4 | 14.6 |
| 3 | α | 2 | 2.5 | 98.9 | 25.5 |
| 4 | α | 2 | 5.0 | 99.6 | 28.8 |
| 5 | α | 2 | 10.0 | 100.7 | 32.0 |
| 6 | α | 2 | 20.0 | 105.7 | 39.0 |
| 7 | α | 2 | 30.0 | 111.8 | 51.5 |
| 8 | α | 2 | 40.0 | 115.0 | 56.6 |
| 9 | α | 2 | 50.0 | 134.5 | 66.5 |
| 10 | α | 0.5 | 30.0 | 111.8 | 29.2 |
| 11 | α | 1 | 30.0 | 111.8 | 40.3 |
| 12 | α | 2 | 30.0 | 111.8 | 51.1 |
| 13 | α | 3 | 30.0 | 111.8 | 55.6 |
| 14 | α | 4 | 30.0 | 111.8 | 59.3 |
| 15 | α | 6 | 30.0 | 111.8 | 60.4 |
| 1 | β | 2 | 5 | 100.3 | 23.2 |
| 2 | β | 2 | 10 | 101.3 | 27.2 |
| 3 | β | 2 | 20 | 106.4 | 36.7 |
| 4 | β | 2 | 30 | 112.5 | 45.6 |
| 5 | β | 2 | 40 | 115.7 | 54.6 |
| 6 | β | 1 | 30 | 112.5 | 34.7 |
| 7 | β | 3 | 30 | 112.5 | 47.8 |
| 8 | β | 4 | 30 | 112.5 | 49.5 |
| 9 | β | 6 | 30 | 112.5 | 50.5 |

These data show that under varying conditions of time and concentration of sodium hydroxide solution the α-3-chloro-2-buten-1-ol dehydrochlorinates more readily. While the difference in the degree of reactivity is not so great as with previously reported geometrical isomers, the difference is a real one. The magnitude of difference in reactivity is not so significant as the fact that there is a difference. It is probable that because the β-3-chloro-2-buten-1-ol is thermally less stable than the α-isomer, partial rearrangement to the more reactive α-isomer occurs during the dehydrochlorination reaction. It is also possible, but not too probable, that the rate at which the chloroalcohols dissolve in the basic aqueous medium is the controlling factor in respect to the rate of reaction.

Because the α-isomer is more reactive than the β-isomer it follows that the α-isomer has the chlorine atom *trans* to the hydrogen atom.



α- β-

3-Chloro-2-buten-1-ol

α-3-Chloro-2-buten-1-ol is produced from α-1,3-dichloro-2-butene and the α-dichloride can be regenerated from the α-chloroalcohol.[2] The β-

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(1) Department of Chemistry, Cornell College, Mount Vernon, Iowa.

(2) Hatch and Ballin, THIS JOURNAL, **71**, 1039, 1041 (1949).

(3) Hatch and Perry, *ibid.*, **71**, 3262 (1949).

(4) Hatch and Moore, *ibid.*, **66**, 285 (1944).

(5) (a) Michael, *J. prakt. Chem.*, [2] **52**, 289 (1895); (b) Michael, THIS JOURNAL, **40**, 704, 1674 (1918); (c) Wislicenus and Schmidt, *Ann.*, **313**, 216 (1900); (d) Chavanne, *Compt. rend.*, **154**, 776 (1912).