[Contribution from the Chemistry Department of the University of Michigan]

The Schmidt Reaction on o-Substituted Aryl Ketones

By Peter A. S. Smith

Received July 14, 1953

Benzophenones with a methyl, phenyl, chloro, bromo, nitro or carboxyl group as an o-substituent have been submitted to the Schmidt reaction and the ratios of isomeric products then determined. The migration ratios, given in Table I, vary greatly, and do not depend on any single, obvious property of the substituent. Possible origins of these effects are discussed, together with the relation to the relative stability of oxime isomers.

Previous systematic investigations of unsymmetrical ketones in the Schmidt reaction have been concerned principally with the effect of branching in alkyl groups,[1,2] with the effect of p-substituents,[1] or with structural effects in dicarbonyl compounds.[3] In all such studies, the group which preferentially migrates from carbonyl to nitrogen was found to be that which has the greatest bulk in the neighborhood of the carbonyl group. However, some benzophenones bearing o-substituents have also been studied[4-7] and certain of them were found to undergo preferential migration of the *unsubstituted* phenyl group, contrary to expectations based on a simple interpretation of the apparent mechanism.[4,7] Moreover, the corresponding oximes are formed predominantly in the configuration *syn* to the o-substituent, so that Beckman rearrangement also results in preferential migration of the unsubstituted phenyl group.[8] These unexpected effects appear to be confined to benzophenone derivatives. In this paper, the results of the Schmidt reaction on a number of o-substituted acetophenones and benzophenones are reported.
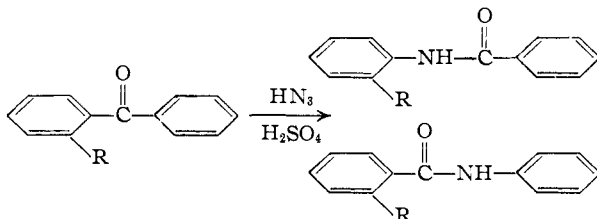
o-Methylacetophenone and acetophenone-*o*-car-

(1) P. S. Smith and J. P. Horwitz, This Journal, **72**, 3718 (1950).

(2) H. Schechter and J. C. Kirk, ibid., **73**, 3087 (1951).

(3) R. Fusco and S. Rossi, Gazz. chim. ital., **81**, 511 (1951).

(4) P. A. S. Smith and B. Ashby, This Journal, **72**, 2508 (1950).

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

(6) G. M. Badger and R. T. Howard, Chemistry and Industry, 601 (1950).

(7) G. M. Badger, R. T. Howard and A. Simons, J. Chem. Soc., 2849 (1952).

(8) Comparison of the migration ratios in the Schmidt reaction with the ratio of the geometrical isomers formed on oximation has heretofore involved tacit assumption that oximes isolated in the solid phase occur in the same ratio of isomers as is present at equilibrium in solution. That this appears to be generally valid is presumably due either to the difference in the heats of crystallization of the two isomers being small, or to negligibly slow achievement of solid state equilibrium during crystallization. If neither of these conditions is fulfilled for a particular pair of oximes, then one might obtain the crystallized oximes in a ratio of isomers very different to that of the corresponding iminodiazonium ions I in solution. For these reasons, migration ratios in

$$R—C—R'$$
$$\underset{N—N_2{}^+}{\overset{\|}{}}\qquad I$$
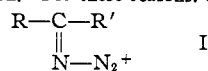
the Schmidt reaction, where no solids are separated until the rearrangement has taken place, are felt to present a picture freer of complications for the study of structural effects on this type of isomerism.

boxylic acid were first investigated in order to compare their behavior to that of the previously studied corresponding benzophenones. With both compounds, formation of acetanilides occurred nearly exclusively; o-substituents apparently are not influential in altering the usual preferred aryl migration in aryl methyl ketones.

The reported conversion of benzophenone-o-carboxylic acid to N-benzoylanthranilic acid by the Schmidt reaction[6,7] has been confirmed. In addition, o-chloro-, o-bromo-, o-nitro-, o-phenyl-, 2,4,6-trimethyl- and o-methoxybenzophenones have been run. The determination of the composition of the mixed benzanilides from the first two was accomplished by halogen analysis of the mixed acids and the mixed acetanilides obtained from them by hydrolysis of the amides followed by acetylation of the amine fraction, since separation of the components of the two pairs could not be efficiently accomplished by differential solubility. Confirmation was achieved by isolation of o-halobenzanilide, the isomer present in larger amount, by fractional crystallization of the unhydrolyzed products of the Schmidt reaction. Because of similar difficulties in separating the pairs of acids and acetanilides from o-methoxybenzophenone, their composition was determined by conversion of the amines to their benzoyl derivatives, and the acids to their anilides. In each case benzanilide is then one of the products and can be separated from the methoxyl analog by means of its very small solubility in benzene–ligroin mixture. The 1:1 ratio so obtained was supported by the result of a methoxyl determination on the benzoic + o-anisic acid mixture. A small amount of N-phenyl-N'-o-anisylurea was also obtained from o-methoxybenzophenone; the manner in which this type of product may arise is discussed in another paper.[9] While urea formation renders the determination of migration ratios uncertain to the extent to which it occurs, the small amount formed would not affect the results greatly.

The separation of the mixtures of o-nitrobenzoic and benzoic acids and of o-nitroaniline and aniline obtained from o-nitrobenzophenone was accomplished by solubility differences. The appearance of an excess of amines over acids in the products was traced to hydrolysis of benzo-o-nitroanilide during the reaction to give benzoic acid, which itself underwent Schmidt reaction to give aniline. These steps were possible in this case because benzo-o-nitroanilide is unusually easily hydrolyzed, and because the conditions necessary to bring about the Schmidt reaction on o-nitrobenzophenone are

(9) P. A. S. Smith, This Journal, **76**, 436 (1954).

unusually vigorous for a ketone, and are sufficient to cause reaction of carboxylic acids in general. This situation was confirmed by the isolation of o-nitroaniline directly from the reaction mixture without hydrolysis, and by the conversion of a sample of benzo-o-nitranilide to aniline and o-nitro-aniline by exposing it to the same Schmidt reaction conditions.

o-Phenylbenzophenone did not present a great problem of separation of mixtures, since the Schmidt reaction on it did not yield mixed amides but gave rise largely to acid-soluble 9-phenylphen-anthridine, in 89% yield in sulfuric acid and 35% in trichloroacetic acid. This cyclization can be formulated readily in terms of the carbonium ion II to be expected from migration of the o-xenyl group. The cyclization did not follow initial formation of o-benzamidobiphenyl, since a sample of that compound was recovered unchanged from exposure to the Schmidt reaction conditions.
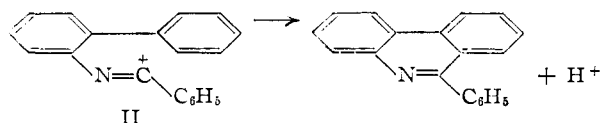
Benzoylmesitylene was similar in presenting no separation problems; only benzoic acid and acet-amidomesitylene were isolated, in understandably very small yield due to the great resistance of this ketone to reaction at the carbonyl group.[7]

The migration ratios obtained are shown in Table I. Due to the nature of the reactions giving rise to them, the precision of these figures varies greatly. Nevertheless, it can be seen from them that the effect of an o-substituent in determining which group migrates preferentially cannot be simply correlated with the bulk of the group, the electrical influence of the group as a substituent, or the migration aptitude of the substituted group in the pinacol rearrangement.

TABLE I

RELATIVE AMOUNTS OF ISOMERIC AMIDES FROM KETONES
o-R-C₆H₄-CO-R'

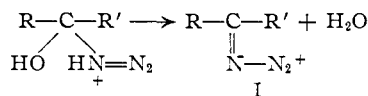| R	R'	Ratio o-R-C₆H₄-NHCOR' to o-R-C₆H₄CO-NH-R' Normalized to a basis of 100
CH₃	CH₃	99:1
COOH	CH₃	>91:9
CH₃	C₆H₅	12:88[4]
COOH	C₆H₅	>98:2[6]
Cl	C₆H₅	30:70.[a] 21:79[b]
Br	C₆H₅	19:81.[a] 17:83[b]
CH₃O	C₆H₅	50:50
NO₂	C₆H₅	70:30.[a] 88:12[b]
C₆H₅	C₆H₅	>95:5.[c,d] 70:30[d,e]
2,4,6-(CH₃)₃	C₆H₅	>95:5

[a] From acidic hydrolysis products. [b] From amine hydrolysis products. [c] In sulfuric acid. [d] Major product. 9-phenylphenanthridine. [e] In trichloroacetic acid.

For the single o-substituents, one can assume: (1) that the configuration of the intermediate iminodiazonium ion I is influenced by direct electrical interaction across space, in addition to the transmitted electrical effect of the substituent, with the former being more marked; (2) that the *syn*

configuration may have a slightly higher internal potential energy (E_p), as might be expected on steric grounds, but that this is overbalanced near room temperature by a difference in the opposite direction between the sums of the zero-point and vibrational–rotational energies $(E_z, RT \ln Q)$ of the stereoisomers of I (that is, that $\Delta E_z - RT \ln (Q_{syn}/Q_{anti}$ may be of opposite sign and greater magnitude than ΔE_p in the equation

$$\Delta F = -RT \ln K = \Delta E_p + \Delta E_z - RT \ln \frac{Q_{syn}}{Q_{anti}}[10]$$

or (3) that the rates of dehydration of the protonated azidohydrin to the respective stereoisomeric imino-diazonium ions I are not in the same ratio as the

$$\begin{array}{c} R-C-R' \longrightarrow R-C-R' + H_2O \\ \diagup \diagdown \qquad\qquad \| \\ HO \;\; HN=N_2 \qquad N-N_2^+ \\ {}^{+} \qquad\qquad\qquad I \end{array}$$

equilibrium concentrations of the stereoisomers. If for any ketone the rate of the dehydration step should be slow compared to the following rearrangement step, the ratio of isomeric amides formed would then depend not on the equilibrium ratios of the geometrically isomeric intermediates as determined by free energies, but on the relative energy barriers in the parallel dehydration steps leading to the respective geometrical isomers. This presupposes the rather improbable circumstance that the dehydration is not reversible. The dehydration presumably occurs by simultaneous acid–base catalysis, by bisulfate ion, for example, involving a hydrogen-bonded bridge (equation 1),[11] which there seems no reason to believe irreversible.
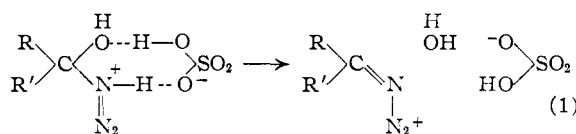
Moreover, in the case of oximes, to which all of the foregoing arguments apply as well, the reversibility of the dehydration would seem a requisite for their hydrolysis. Information available from kinetic measurements of the Schmidt reaction[11] suggests that the dehydration step is not rate-determining and it is generally held that the analogous dehydration step in oximation is also probably not rate-determining.[12] Furthermore, the assumption that the dehydration step is rate-determining in the Schmidt reaction would imply that the ratio of migration in the Schmidt reaction will not be related to the *equilibrium* ratios of the *syn* and *anti* forms of the corresponding ketoximes. Such a parallel with oxime isomerism is quite generally observed, however (with the apparent exception of o-car-boxybenzophenone and o-phenylbenzophenone, *vide*

(10) "Q" is the internal partition function of J. E. and M. G. Mayer, "Statistical Mechanics," John Wiley and Sons, Inc., New York, N. Y., 1940, and is designated "f" by L. P. Hammett, "Physical Organic Chemistry." McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 73, et seq., where the derivation of these relations is described.

(11) P. A. S. Smith and D. M. Howell, Abstracts of Papers, Div. of Org. Chem., National Meeting Am. Chem. Soc., New York, September, 1949.

(12) (a) Cf. L. P. Hammett, "Physical Organic Chemistry." McGraw-Hill Book Co., Inc., New York, 1940, p. 333, et seq.: (b) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 688.

infra); it thus appears probable after all that the migration ratios are determined by the equilibrium ratios of the geometrically isomeric intermediates.

This leaves the choice still to be made between alternatives (1) and (2) to explain the apparent anomaly that several *syn-o*-substituted benzophenoximes and presumably the corresponding iminodiazonium ions I frequently appear to be more stable by about 1 kcal. (*RT* ln *K* = 1.36 kcal. at 0° and *K* = 10) than their *anti* isomers. Furthermore, the absence of any noticeable effect by the *o*-methoxy group on the ratios can hardly be explained without the assumption of two opposing influences. Symmetry alone does not appear to be important, since *m*-methylbenzophenone (as well as the para isomer[13]) gives nearly equal proportions of isomeric oximes, and the results of a rough run indicate analogous behavior in the Schmidt reaction. Direct electric interactions of similar quality and quantity seem improbable between groups of such different electrical character as methyl and halogen on the one hand and diazonium and hydroxyl on the other. It is therefore felt that explanation (2) is the closest to the truth.

Both configurations of benzophenone oximes bearing an *o*-substituent of moderate size appear to be free of internal strain insofar as this can be estimated from Fisher–Hirschfelder models, and this condition holds for a large range of rotational positions of the *o*-substituted phenyl group. Complete revolution, however, is effectively blocked in the *syn*-configuration, which incidentally implies that such compounds may exist in enantiomorphic forms. These circumstances (ΔE_p small, ΔE_z — *RT* ln (Q_{syn}/Q_{anti}) possibly large) might be expected to satisfy the requirements of explanation (2). By contrast, in aliphatic ketoximes with branching at one α-carbon, the configuration with the oxime *syn* to the bulkier alkyl group is strain-free only in a rather sharply restricted rotational position, and while the complete revolution of a group as large as isopropyl is not quite prevented, noticeable interference of the hydrogens with the oxime hydroxyl exists through most of the full circle of rotation. This situation, by giving rise to a larger ΔE_p between the two isomers, is presumably sufficient to account for the generalization[1,3,7] that in an unsymmetrical ketone, that group having the largest bulk in the neighborhood of the carbonyl group will migrate preferentially in either oximation-plus-Beckman rearrangement or the Schmidt reaction. This generalization apparently embraces even benzophenones if they bear two *o*-substituents, as does benzoylmesitylene, where the difference in potential energy of the two configurations is presumably greater than for benzophenones with only one, and would presumably also hold for benzophenones bearing only a single *o*-substituent if it should be bulky enough.[14] The preferred migra-

tion of the methyl group in cyclopropyl methyl ketone[15] may be related to the similar behavior of styryl methyl ketone,[1] in both of which an electron-rich area is in a position to stabilize the *syn*-configuration of the iminodiazonium ion by a kind of chelation. Such an effect, if it exists, might be expected to be more pronounced for the charged iminodiazonium ion than for the uncharged oxime, and thus account for the discrepancy in ratios between the Schmidt reaction[15a] and oximation[15b] for cyclopropyl methyl ketone.

o-Carboxybenzophenone is an apparent exception to the parallelism of migration ratios between oximation-plus-Beckmann rearrangement and the Schmidt reaction. However, the oxime of this ketone may never have been isolated,[16] due to its spontaneous cyclization to a ketobenzoxazine, which undergoes the Beckmann rearrangement to give the monoanilide of phthalic acid. Circumstantial evidence from the behavior of other *o*-carboxy ketones suggests, however, that the configuration of the original oxime is inverted by the process of ketobenzoxazine formation,[17] and the parallel with the Schmidt reaction thereby destroyed.

o-Phenylbenzophenone is the other exception. Beckmann rearrangement of the crude oximes with phosphorus pentachloride in benzene near room temperature gave *o*-phenylbenzanilide and *o*-benzamidobiphenyl in a ratio of 70:30. Rearrangement with polyphosphoric acid at 110–130°[18] gave the corresponding cyclization products, fluorenone anil and 9-phenylphenanthridine, in a similar ratio, 80:20. Possible change of the ratio of stereoisomers in the oxime was indicated by its initial precipitation as a gum, which required six days to change to a crisp solid, notwithstanding various attempts to hasten the process. Repetition of the experiments, using the sirupy oxime immediately after its preparation, showed little difference from those with the crystallized oximes, however. These ratios are in contrast to the result from the Schmidt reaction, where the major product is the isomer formed in smaller amount in the Beckmann rearrangement.

The possibility that fluorenone anil, or the iminocarbonium ion III (isomeric with II) from which it is derived

III
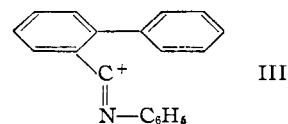
(D. Y. Curtin, Abstracts of Papers, Thirteenth Organic Symposium, 1953) is taken as the criterion of "effective size," the carboxyl and phenyl groups, and presumably the nitro group, are markedly "bulkier" than halogen or methyl.

(15) (a) S. C. Bunce and J. B. Cloke, THIS JOURNAL, **76**, March (1954); (b) A. D. McLaren and R. E. Schachat, *J. Org. Chem.*, **14**, 254 (1949).

(16) The preparation of *o*-carboxybenzophenone oxime, m.p. 118°, has been claimed "by conventional methods" by M. V. Patwardhan, N. L. Phalnikar and B. V. Bhide, *J. Univ. Bombay, Sect. A*, part 5, **18**, 22 (1950). All other reported attempts have resulted in only phenylketobenzoxazine,[17] m.p. 163–164°.

(17) (a) J. Meisenheimer and H. Theilacker, in Freudenberg's "Stereochemie," Edwards Bros., Inc., Ann Arbor, Mich., 1945, p. 1044; (b) J. Meisenheimer and H. Meis, *Ber.*, **57**, 289 (1924).

(18) E. C. Horning and V. L. Stromberg, THIS JOURNAL, **74**, 2680 (1952).

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

(14) It is possible that such an effect may already be operative in *o*-nitro, *o*-phenyl and *o*-carboxybenzophenones. The effective size of groups is usually estimated from their interference with rotation in *o*-substituted biphenyls (R. L. Shriner, R. Adams and C. S. Marvel, in H. Gilman's "Organic Chemistry," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1st ed., 1938, pp. 268f.) with which no correlation of our observations can be made. However, if the "*cis* effect" in olefins

might have been converted under the Schmidt reaction conditions to 9-phenylphenanthridine was considered. It was rejected when it was found that fluorenone anil was recoverable as fluorenone to the extent of 76% after exposure to Schmidt reaction conditions; the only other identifiable product was phenanthridone (9%), which would result from a Schmidt reaction on fluorenone derived from the anil by hydrolysis. Furthermore, treatment of o-phenylbenzanilide with refluxing phosphoryl chloride gave fluorenone anil (isolated as fluorenone) in 79% yield, thus showing that the iminocarbonium ion III, which is presumably the precursor, does not undergo abnormal ring closure to give 9-phenylphenanthridine. Since with this ketone the migration ratio for the Schmidt reaction in trichloroacetic acid was determined from a recovery of identifiable products of only 50%, it is not clear to what extent the ratios obtained reflect a discrepancy of major magnitude. However, some differences between Schmidt reaction and oximation ratios should be expected, in view of their dependence in part on temperature and solvent medium.

Experimental

Melting points are uncorrected, and analyses are by Clark Microanalytical Laboratory.

Materials.—The o-benzoylbenzoic acid used was the commercial product (Eastman Kodak Co.). The o-chloro-[19] and o-bromobenzophenones[20] were prepared by recorded methods. o-Nitrobenzophenone was prepared by von Tatschaloff's method[21] from o-nitrodiphenylmethane, obtained by the Friedel–Crafts reaction with o-nitrobenzyl bromide[22] instead of the previously used chloride. o-Acetylbenzoic acid was kindly provided by Dr. W. R. Vaughan and o-phenylbenzophenone was synthesized by Mr. J. F. Heitsch from o-bromobiphenyl and benzaldehyde.[23] o-Methylacetophenone. b.p. 200° (750 mm.).[24] was prepared in 53% yield from o-tolunitrile and a 50% excess of methylmagnesium iodide in ethyl ether for 21 hours at room temperature. o-Methoxybenzophenone. m.p. 39–40°.[25] was prepared in 66% yield from o-methoxybenzoyl chloride and phenylcadmium in boiling ether for 20 minutes.

Schmidt Reactions.—The procedure used unless otherwise indicated was to add 1.0 g. of solid sodium azide portionwise to a solution of 0.01 mole of ketone and 0.03 mole of concd. sulfuric acid in 25 to 30 g. of fused trichloroacetic acid at 55–60°. The sulfuric acid was omitted with the acetophenones. The addition was customarily made over one to three hours, and the reaction was then allowed to continue until visible gas evolution had ceased (one to five hours). The products precipitated when the resulting mixture was diluted with ca. 100 ml. of water: this was sometimes followed by neutralization with ammonia. The precipitated amides were collected by filtration and washed with water.

From 1.63 g. of o-acetylbenzoic acid there was obtained 1.15 g. (65%) of crude N-acetylanthranilic acid. m.p. 167–170°.[26] Treatment of the acidic filtrate with potassium bromate and bromide precipitated 0.51 g. (15.5%) of tribromoaniline. m.p. 117–119°. The crude acetylanthranilic acid was hydrolyzed with concd. hydrobromic acid, combined with the filtrates from the tribromoaniline. alkalized with sodium hydroxide and distilled. Evaporation of the distillates. which had been caught in hydrochloric acid. left only 50 mg. of a crystalline residue. which would consist of

the hydrochloride of any methylamine formed. The distilland was brominated as before to give 1.84 (87%) of tribromoaniline. m.p. 120–122°. As a check. anthranilic acid was treated with an excess of potassium bromate and hydrobromic acid in dilute solution at room temperature for more than an hour: tribromoaniline. m.p. 119–120°. was precipitated in 99% yield.

The amides from 1.34 g. of o-methylacetophenone were hydrolyzed by refluxing the diluted reaction mixture after the addition of ca. 10 ml. of concd. hydrochloric acid. The amines were extracted with four portions of benzene and one of ether after alkalizing with sodium hydroxide. The combined extracts were washed with hydrochloric acid. and the resulting solution of amine salt was alkalized and treated with acetic anhydride. There resulted 1.08 g. (72.5%) of aceto-o-toluidide. m.p. 107–108°. From the original aqueous solutions there was obtained by acidification with phosphoric acid and repeated extraction with carbon tetrachloride 0.015 g. (ca. 1%) of o-toluic acid. m.p. 103–104°. In another run. the diluted reaction mixture was treated with excess bromide and bromate. which precipitated p-bromo-aceto-o-toluidide, m.p. 155–158°,[27] in 46% yield.

From 1.08 g. of o-chlorobenzophenone there was obtained 1.15 g. (99.5%) of crude. mixed anilides. This was hydrolyzed by refluxing with acetic–hydrochloric acid mixture for 70 hours. after which the mixture was diluted and extracted with five portions of chloroform and one of benzene. The acids were removed from the combined extracts with sodium carbonate solution. set free with hydrochloric acid, and taken up in several portions of ether. Evaporation left 0.60 g. of a crystalline cake. which was finely ground and thoroughly dried: found: Cl. 17.11, 16.90. The analysis corresponds to 74.8% o-chlorobenzoic acid by weight in the mixture (= 70 mole per cent. if the other component is benzoic acid): this would result from a migration ratio of 30:70 o-chlorophenyl–phenyl.

The acid aqueous solution was alkalized with sodium hydroxide after having been concentrated somewhat. and the oil which separated was taken up in four portions of benzene. The dried (NaOH) extracts were heated with acetic anhydride and then evaporated to a crystalline cake. wt. 0.68 g. after having been finely ground and thoroughly dried; *Anal.* found: Cl. 5.19, 5.23. The analysis corresponds to 24.9% of o-chloroacetanilide by weight (= 21 mole per cent. if the other component is acetanilide); migration ratio 21:79 o-chlorophenyl–phenyl.

In another run. the crude benzanilides melted at 116–117.6° after one recrystallization from tetrachloroethane–ligroin mixture. and at 120–121° when mixed with a sample of o-chlorobenzanilide of m.p. 121–122.5°. The acids from the hydrolysis of all of the amides melted at 139–140° after two crystallizations from hot water (benzoic acid m.p. 121°; o-chlorobenzoic acid m.p. 142°[28]).

From 1.31 g. of o-bromobenzophenone there was obtained 1.39 g. of amides. Hydrolysis was accomplished with acetic–hydrobromic acid mixture in a closed system to which some sodium bisulfite had been added to prevent bromine formation. There resulted 0.71 g. of acids after treatment similar to that described for o-chlorobenzophenone. *Anal.* Found: Br. 34.88, 35.16. This corresponds to 87.5% o-bromobenzoic acid: molar migration ratio, 19:81. The corresponding acetylated amines weighed 0.76 g.; *Anal.* found: Br, 9.36, 9.09. This corresponds to 24.6% o-bromoacetanilide; migration ratio 17:83.

In another run. the crude benzanilides melted at 116–118° after one. and at 117–118°[29] after two recrystallizations from tetrachloroethane–ligroin mixture. The acids from hydrolysis of the unrecrystallized benzanilide melted at 145–147°[30] after three recrystallizations from hot water.

The Schmidt reaction on o-nitrobenzophenone (1.14 g.) was very sluggish. and in several runs gas evolution was still evident. although slow. after 24 hours. There was much darkening during the reaction. so the solids that separated were taken up in chloroform. the entire mixture was alkalized with ammonia. and stirred with charcoal. The resulting golden filtrate was extracted with two portions

(19) B. Overton, *Ber.*, **26**. 18 (1893).

(20) P. J. Montagne, *Rec. trav. chim.*, **27**. 327 (1908).

(21) A. von Tatschaloff, *J. prakt. Chem.*, **65**. 308 (1902).

(22) N. Kornblum and D. C. Iffland. THIS JOURNAL. **71**. 2137 (1949).

(23) C. K. Bradsher, *ibid.*, **66**. 45 (1944).

(24) M. Jaspers. *Bull. soc. chim. Belg.*. **34**. 185 (1925).

(25) R. Stoermer and E. Frederici, *Ber.*. **41**. 324 (1908).

(26) B. Pawlewski, *ibid.*, **31**. 661 (1898), reports m.p. 184–186° for the pure material.

(27) E. Wroblevski, *Ann.*, **168**. 162 (1873), reports m.p. 156–157° for the pure material.

(28) G. Fels, *Z. Krist.*. **37**. 485 (1903).

(29) Pure o-bromobenzanilide melts at 123–124°.[17b]

(30) Pure o-bromobenzoic acid melts at 149°; A. F. Holleman and B. R. de Bruyn. *Rec. trav. chim.*. **20**. 206 (1901).

of ether and four of chloroform, acidified with phosphoric acid and again extracted several times. The combined extracts were evaporated, and the residue was refluxed for 48 hours with acetic–hydrochloric acid mixture. In the customary manner there was isolated 0.24 g. of solid acids. Extraction with carbon tetrachloride left 0.06 g. of impure o-nitrobenzoic acid, m.p. 140–142.5°; further digestion with carbon tetrachloride changed this to 0.04 g., m.p. 145–147°. From the extracts there was obtained by evaporation 0.14 g. of impure benzoic acid, m.p. 103–112°. Recrystallization from hot water gave 0.09 g., m.p. 121–122°. The basic products were separated from the neutral materials by extraction with concd. hydrochloric acid of the chloroform solution remaining from the isolation of the acids. Dilution and alkalization with ammonia liberated o-nitroaniline, which was gathered by filtration and extraction of the filtrate with chloroform, wt. 0.24 g., m.p. 71–73°. The neutral materials on evaporation and crystallization from ethanol gave recovered o-nitrobenzophenone, 0.34 g., m.p. 104–106° and 0.09 g., m.p. 85–105°. From the original acidic aqueous solution after removal of the "neutrals," acids and o-nitroaniline, the aniline was precipitated as 2,4,6-tribromoaniline by treatment with potassium bromide and bromate; wt. 0.44 g., m.p. 120–122°. From the 0.005 mole of ketone there was thus obtained roughly 0.00134 mole of aniline, 0.00174 mole of o-nitroaniline, 0.00115 mole of benzoic acid, 0.00024 mole of o-nitrobenzoic acid and 0.00181 mole of recovered ketone. Since the total moles of amines (0.00308) considerably exceeds the moles of acids (0.00139), a meaningful migration ratio cannot be calculated from these figures as they stand.

To determine the cause of the foregoing discrepancy, 1.00 g. of benzo-o-nitroanilide was treated with the usual Schmidt reaction conditions, and the resulting mixture was worked up as before with the omission of the acetic–hydrochloric acid hydrolysis. There was obtained 0.24 g. of 2,4,6-tribromoaniline, m.p. 119–120.5°, and crude o-nitroaniline, m.p. 63–67°. A similar experiment with o-nitrobenzanilide gave no isolable aniline or o-nitroaniline, and the starting material was recovered in 95% yield with undepressed melting point. It is thus clear that in the Schmidt reaction on the ketone, the amount of aniline was augmented at the expense of benzoic acid by secondary reactions—presumably hydrolytic cleavage and further Schmidt reaction. The amounts of the o-nitro products are undisturbed, however, and from them a migration ratio of o-nitrophenyl-phenyl of 88:12 is obtained. Furthermore, one can estimate that 0.00174 − 0.001154 = 0.00059 mole of benzoic acid was converted to aniline. By use of this figure to correct the amount of aniline, 0.00134 − 0.00059 = 0.00075 mole, the value 70:30 can be determined from the ratio of o-nitroaniline to aniline.

2,4,6-Trimethylbenzophenone (1.12 g.) showed hardly noticeable reaction under the usual conditions. After 7.75 hours the mixture was diluted with water, and the resulting oil was refluxed with acetic–hydrochloric acid mixture for nine days. By the customary procedure there was obtained a large amount of recovered ketone as a neutral oil which eventually crystallized, 10 mg. of impure benzoic acid, m.p. 105–110°, which melted at 119–120° after recrystallization from hot water, and 14 mg. of an acetylated amine, m.p. 211–213° (m.p. of acetamidomesitylene, 216°). The conditions used were more than sufficient to hydrolyze mesitoic anilide,[31] which might have given aniline and mesitoic acid had it been present.

From o-methoxybenzophenone (2.14 g.) there was obtained a putty-like amide mixture, which was taken up in several portions of benzene and ether. The sirup left on evaporation of the solvents was hydrolyzed by heating for 47 hours with 5 g. of NaOH in 30 ml. of methanol. The mixture was then diluted with water and separated into neutral, basic and acidic components by customary procedure. Exactly half of the amine fraction in dilute hydrochloric acid solution was treated with acetic anhydride and sodium hydroxide. Extraction with benzene and evaporation of the washed extracts gave 0.72 g. of the mixed acetanilides as a brownish, crystalline cake (88% yield as aceto-o-anisidide, 107% as acetanilide). The other portion of amines was benzoylated under Schotten–Baumann conditions and the product was crystallized from benzene–ligroin mixture. There was obtained 0.48 g. (48.7%) of benzanilide, m.p.

163–166°, undepressed when mixed with an authentic sample. The filtrate on evaporation left an oil, which crystallized on seeding with benzo-o-anisidide, wt. 0.57 g. (50.2%), m.p. 66–69°. The benzene solution of acids from the hydrolysis was also divided into two equal portions, one of which was evaporated to give 0.63 g. of mixed acids (103% as benzoic acid, 83% as o-anisic acid). The other half was treated with 1 ml. of thionyl chloride, the excess reagent was removed through a short column, and the residual acid chlorides were treated with 2 ml. of aniline in benzene. After washing with dilute hydrochloric acid and water, the benzene solution was adjusted to a total volume of 25 ml. of ca. 1:1 benzene–ligroin. There was obtained in two crops 0.33 g. (33.5%) of benzanilide, m.p. 164–166°. Evaporation of the filtrates gave a crystalline cake of o-anisanilide, wt. 0.52 g. (45.8%), m.p. 76–80°. The migration ratio calculated from the amines is 49:51, and that from the acids is 61:39. The first ratio is felt to be more reliable, since there was some loss in converting the acids to their anilides, perhaps due to volatilizing of benzoyl chloride.

In another run with o-methoxybenzophenone, 1.06 g. of ketone gave 0.48 g. of mixed acids, which were finely ground and thoroughly dried: Anal. found: CH₃O, 11.08, 11.40. A separate run gave 1.29 g. of acids from 2.12 g. of ketone: Anal. found: CH₃O, 11.51, 11.22. These figures correspond to 55% by weight of o-anisic acid in the mixtures, from which a migration ratio of 49.5:50.5 can be calculated. Analyses of the acetylated mixtures of amines from these runs did not give reproducible results.

In several runs with o-methoxybenzophenone, a small neutral fraction remained after hydrolysis. When the reflux time during hydrolysis was appreciably less than 30 hours, this was mostly unhydrolyzed amides, and in the runs of longer duration there was almost no neutral material. From hydrolyses of intermediate duration the neutral material could be crystallized from ligroin as colorless crystals, m.p. 144–145°, maximum yield 6%. At an early stage a rather impure sample was analyzed. Anal. Calcd. for $C_{14}H_{14}O_2N_2$: C, 69.40; H, 5.83; N, 11.56. Found: C, 68.70; H, 5.63; N, 12.63. This was subsequently identified by mixed melting point with N-phenyl-N'-o-anisylurea, reported to have m.p. 144°.[32] However, the reference sample prepared from o-anisidine and phenyl isocyanate melted at 159–160° after several crystallizations from benzene and aqueous ethanol, and a sample of the material from the Schmidt reaction melted at 153–156° after crystallization from benzene–ligroin mixture. The sharpness of the lower melting points suggests that different crystalline modifications were involved, but the subject was not further investigated.

From 1.96 g. of m-methylbenzophenone there was obtained an oily mixture of amides which was hydrolyzed by refluxing for 24 hours with acetic–hydrochloric acid mixture. The acidic products, separated by customary procedure, were oxidized in hot, dilute potassium hydroxide solution with 6 g. of potassium permanganate, the excess of which was destroyed with methanol after 40 min. of boiling. After filtration from manganese dioxide, acidification precipitated 0.57 g. (34%) of isophthalic acid, which sublimed above 250°. Repeated extraction of the filtrate with carbon tetrachloride recovered 0.25 g. (20%) of benzoic acid, m.p. 120–122° (some benzoic acid was unfortunately volatilized during removal of the solvent). The basic products from the hydrolysis were benzoylated under Schotten–Baumann conditions; crystallization of the resulting amides from benzene gave 0.59 g. (30%) of crude benzanilide, m.p. 161–164° and 0.16 g. (8%) of less pure material, m.p. 158–160°. Evaporation of the benzene mother liquors left 1.25 g. (59% as benzo-m-toluidide) of benzo-m-toluidide containing some benzanilide, m.p. 90–108°.

The Schmidt reaction with 1.29 g. (0.005 mole) of o-phenylbenzophenone gave a crude product containing much insoluble, uncrystallizable, non-hydrolyzable material, from which the other components could be separated by repeated extractions with benzene and centrifugation. Extraction of the resulting clear benzene solution with several portions of 10% hydrochloric acid followed by alkalization of the extracts gave 0.45 g. (35%) of 9-phenylphenanthridine, m.p. 104–106°, not depressed when mixed with authentic material of m.p. 105.5–107.5°.[33] Evaporation of the remaining

(31) R. Leuckart, J. prakt. Chem., 41, 308 (1890).

(32) J. H. Ransom, Am. Chem. J., 23, 40 (1900).

(33) G. T. Morgan and L. P. Walls, J. Chem. Soc., 2447 (1931).

benzene solution left an oil which was crystallized slowly from ligroin to give 0.21 g. (15%) of o-phenylbenzanilide, m.p. 110–111° alone and when mixed with authentic material, depressed when mixed with 9-phenylphenanthridine. A repetition of this experiment gave substantially the same results. In another experiment where sulfuric acid (15 ml.) was used in place of trichloroacetic acid, none of the insoluble material was formed, and there was obtained 1.13 g. (89.5%) of pale yellow 9-phenylphenanthridine which melted at 104–108°, and 107–108.5° after recrystallization from methanol and ligroin. It was isolated by extraction into 10% hydrochloric acid from a benzene solution of the reaction products. Evaporation of the benzene solution left only a small amount of yellow oil which resisted all attempts to induce crystallization. Unless the reaction mixture was alkalized with ammonia, most of the product precipitated as its sulfate.

Beckmann Rearrangement of o-Phenylbenzophenone Oxime.—o-Phenylbenzophenone (5.16 g.) was converted to its oxime by refluxing with 1.6 g. of hydroxylamine hydrochloride in 7 ml. of pyridine and 9 ml. of absolute ethanol for 24 hours. A viscous oil separated on dilution with water, and solidified slowly during six days while covered with dilute acetic acid; wt. 5.3 g., m.p. 94–113°. It was dissolved in 40 ml. of benzene; exactly half of this solution was taken and 3.0 g. of phosphorus pentachloride was added; the temperature rose slightly but remained below 35°. After 7.5 hours the mixture was decomposed with ice-water, the benzene was evaporated, and the residue was alkalized with ammonia. The cream colored, gummy product was completely insoluble in concd. hydrochloric acid, as shown by alkalizing the decanted acid. It crystallized from ethanol as white needles, m.p. 107–110°, wt. 1.11 g. (41%), undepressed when mixed with o-phenylbenzanilide, markedly depressed when mixed with o-benzamidobiphenyl or 9-phenylphenanthridine.

The mother liquors were evaporated and refluxed with acetic–hydrochloric acid mixture for six days. The acidic products were isolated in customary fashion (wt. 0.85 g.) and were separated by digestion with 100 ml. of warm water. The residue of o-phenylbenzoic acid, m.p. 111–113°, weighed 0.35 g. (17.5%); the extracts on neutralization with sodium bicarbonate, concentration to a small volume, and reacidification gave 0.29 g. of crude benzoic acid, m.p. 110–117°, which could not readily be separated from accompanying traces of o-phenylbenzoic acid. The corre-

sponding amines were not separated quantitatively, but o-aminobiphenyl was isolated as water-insoluble o-acetamidobiphenyl, wt. 0.12 g., m.p. 121–122° and aniline was isolated by precipitation as p-bromoacetanilide, wt. 0.31 g., m.p. 164–166°, after recrystallization from benzene.

The benzene solution of the other half of the oxime was evaporated, and 70 g. of preheated polyphosphoric acid was poured on the residue. After 15 minutes at 110–130°, the mixture was diluted with 350 ml. of water and alkalized with ammonia. The bright yellow oil which separated was taken up in two portions of benzene, and the extracts were washed first with dilute, then concd. hydrochloric acid, and finally with water. Neutralization of the acid washings precipitated 0.42 g. (16.5%) of 9-phenylphenanthridine, m.p. 105–107°. The benzene was then evaporated and the residue was extracted with warm ligroin. The residue of fluorenone after evaporation of the ligroin was crystallized from methanol in several crops; wt. 0.95 g. (53%), m.p. 82.5–84.5°.

Schmidt Reaction on Fluorenone Anil.—Fluorenone anil[34] (1.27 g.) in 25 g. of trichloroacetic acid and 0.75 ml. of concd. sulfuric acid at 55–60° was treated with 0.5 g. of sodium azide added over one hour. After 5 hours the mixture was poured on ice, and the red oil which separated changed to yellow crystals overnight; wt. 1.07 g., m.p. 67–190°. Extraction of the solid with hot ligroin left 0.09 g. (9%) of phenanthridone, m.p. 286–288° with sublimation. The extracts were evaporated, and the residue of fluorenone was crystallized from methanol in several crops; wt. 0.68 g. (76%), m.p. 82–84°. The original acidic solution gave only a faint opalescence when excess sodium hydroxide was added, and presumably contained only aniline from hydrolysis of unreacted fluorenone anil.

Cyclization of o-Phenylbenzanilide.—o-Phenylbenzanilide (0.25 g.) was allowed to stand with 1 ml. of phosphorus oxychloride for 1 hour, and then refluxed for 1 hour. Hydrolysis with cold water gave an orange oil which slowly turned to a bright yellow solid, wt. 0.15 g., m.p. 65–75°. Extraction of the solid with hot petroleum ether (b.p. 60–75°) and evaporation of the solvent gave 0.12 g. (79%) of fluorenone, m.p. 79–82°. The original acid filtrate did not precipitate any 9-phenylphenanthridine when excess potassium hydroxide was added, but only became cloudy.

(34) G. Reddelien, Ber., 43, 2476 (1910).

ANN ARBOR, MICHIGAN

Observations on the Formation and Breakdown of Tetrazoles[1]

BY PETER A. S. SMITH

The formation of ureas in the Schmidt reaction on certain diaryl ketones has been related to the non-cyclic imidyl azide I precursor of tetrazoles, which is capable of undergoing a Curtius-like rearrangement. Carbodiimides are suggested to be the intermediate products capable of hydration to ureas, and in one case a carbodiimide has been isolated from a tetrazole preparation. The cyclization of imidyl azides to tetrazoles has been shown to be probably reversible, and in strong acid at temperatures above 160° the complete disruption of 1,5-diaryltetrazoles to two moles of amines can be accomplished. This has been applied to the conversion of 1-benzoylphenanthrene through the oxime, Beckmann rearrangement, and formation and disruption of the tetrazole, to 1-phenanthrylamine in 82% over-all yield. The von Braun and Rudolf method for preparing tetrazoles from imidyl chlorides and anhydrous hydrogen azide solutions has been shown to proceed with some success in aqueous sodium azide solutions.
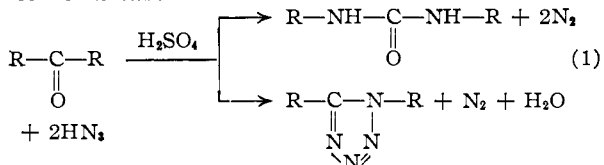
The recent discovery of two cases of the formation of a urea from a monoketone during the course of a Schmidt reaction[2,3] calls for explanation. The usual side-products in Schmidt reactions on ketones are 1,5-disubstituted tetrazoles (equation 1); it therefore seemed that further investigation of the factors governing the formation and breakdown

of tetrazoles might elucidate the occasional formation of ureas.

$$
R-\underset{\underset{O}{\|}}{C}-R \xrightarrow{H_2SO_4}
\begin{cases}
\longrightarrow R-NH-\underset{\underset{O}{\|}}{C}-NH-R + 2N_2 \\
\\
\longrightarrow R-\underset{\substack{\| \\ N \;\; N \\ \diagdown N \diagup}}{C}-N-R + N_2 + H_2O
\end{cases}
\tag{1}
$$

+ 2HN₃

From o-methoxybenzophenone, one of the ketones observed to give a urea, two isomeric tetra-

(1) Presented at the National Meeting of the Am. Chem. Soc., Los Angeles, 1953.
(2) P. A. S. Smith and T.-Y. Yu, J. Org. Chem., 17, 1281 (1952).
(3) P. A. S. Smith, THIS JOURNAL, 76, 431 (1954).