The Acid-Catalyzed Solvolysis of Benzoin Tosylate in Aromatic Solvents

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Abstract: Benzoin tosylate (**1**) has been found to be readily available through the reaction of desyl bromide with silver tosylate. The reaction of **1** in aromatic solvents under acidic conditions rapidly produces 2,2-diarylacetophenones. The mechanistic aspects of this unusual conversion have been studied using benzoin-d_1 tosylate (**5**). The results of this experiment indicate that solvolysis proceeds through the enolic form of **1** by pathway C.

During a study of the photolysis of desyl compounds[1] we had occasion to examine the thermal decomposition of benzoin tosylate (**1**). This paper describes the unusual solvolysis that **1** undergoes in aromatic solvents, and a convenient synthesis of this rather sensitive material.

Földi initially reported that the benzenesulfonate of benzoin decomposes when heated above 150°, the only discrete product being benzenesulfonic acid.[2] In order to study this thermal reaction under more informative conditions, **1** was refluxed in toluene for about 12 hr. After a considerable induction period the starting ketone was rapidly consumed to yield a product mixture from which 2-phenyl-2-*p*-tolylacetophenone (**2**) could be isolated in 50% yield. The remaining material was examined by nmr and seemed to be a mixture of tolyl isomers as judged from the observation of two aromatic methyl groups and two methinyl hydrogens.

This peculiar induction period was explained when it was observed that no reaction occurred when the tosylate **1** was refluxed for 18 hr in toluene containing 2,4,6-collidine. Conversely, if the tosylate **1** was added to a refluxing solution of toluene containing 1 equiv of toluenesulfonic acid, solvolysis occurred immediately to produce the same mixture of isomers of **2** observed in the initial experiment. The tosylate **1** is recovered unchanged after prolonged refluxing in benzene, but the addition of toluenesulfonic acid produces immediate solvolysis to yield 2,2-diphenylacetophenone (**3**) in 85% yield. The Lewis acid, BF_3–Et_2O, is also capable of initiating this reaction.

Indeed, when benzoin is refluxed in a benzene solution of *p*-toluenesulfonic acid, **3** is formed in 65% yield. When this reaction is followed by tlc, the presence of significant amounts of an intermediate material is observed. This intermediate has been isolated from partially completed reaction mixtures and shown to be benzoin tosylate by comparison with an authentic sample. Benzoin acetate also produces **3** when treated under similar conditions, but in this instance the reaction proceeds much more slowly, and no intermediate benzoin tosylate has been detected.

One can conceive of at least three possible mechanisms that would account for these novel reactions. In mechanism A the tosylate would be activated by protonation, and then undergo reaction by the usual Friedel–Crafts mechanism to yield **3**. This type of acid-catalyzed arylation of tosylates has adequate analogy in systems where the tosylate is not adjacent to a carbonyl function.[3] Mechanism B is simply a variation of the pinacol rearrangement. Finally, mechanism C gains more support from the recently observed solvolysis of vinyl tosylates.[4]

If mechanism B were active, one might expect that the reaction of benzoin tosylate in toluene would yield a mixture of 2-phenyl-2-tolylacetophenones as a result of tolyl migration and 2,2-diphenylmethylacetophenones as a result of phenyl migration. That this does not seem to be the case is indicated by the fact that a careful examination of the reaction mixture by mass spectrometry shows that the crystalline ketone and the residual oil both fragment to give an extremely intense peak at *m/e* 105 with no significant peak at *m/e* 119. This not only confirms the structure of **2**, since **2** and **4** have very similar properties (for example, their melting points are 96–97 and 99–100°, respectively),[5] but it also would seem to eliminate mechanism B from further consideration.

In an effort to distinguish between mechanism A and C benzoin-d_1 tosylate (**5**) was synthesized from 2-phenyl-2,2-d_2-acetophenone,[6] using the same method that had been applied in synthesizing **1**. The deuterated deoxybenzoin was brominated in anhydrous ether, and the crude monodeuteriodesyl bromide allowed to react with silver tosylate in anhydrous acetonitrile to yield **5** (90–95% d_1 by nmr). This material was solvolyzed in benzene with added toluenesulfonic acid, and the reaction quenched with 2,4,6-collidine after it was about 42% complete. The product **3** isolated from this reaction contained about 40% deuterium in the two position, whereas the recovered starting material **5** had suffered no appreciable reduction in deuterium content.

It is felt that caution should be exercised in attaching too much significance to the quantity of deuterium re-

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[1] J. C. Sheehan and R. M. Wilson, *J. Amer. Chem. Soc.*, **86**, 5227 (1964).

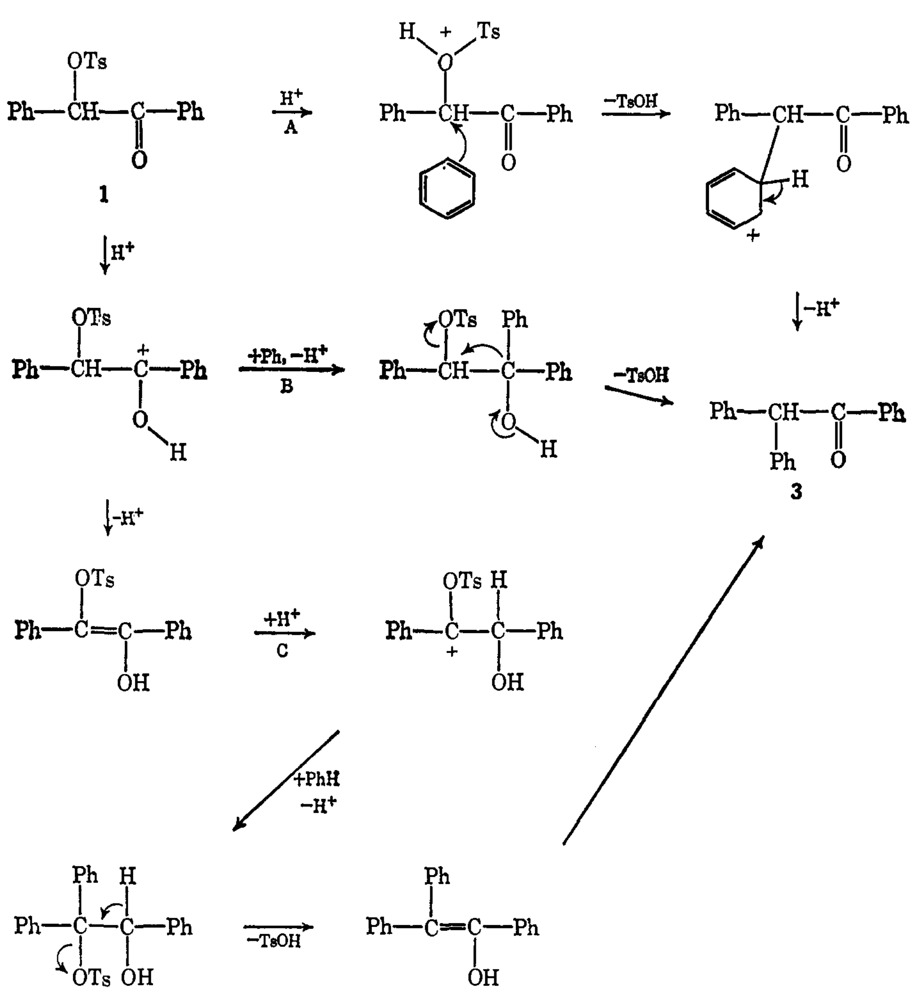
[2] Z. Földi, *Chem. Ber.*, **60**, 656 (1927).

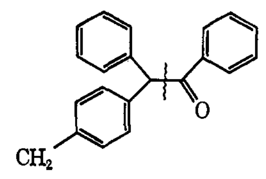
[3] M. Z. A. Badr and W. J. Hickinbottom, *J. Chem. Soc.*, 4101 (1965), No. 14 in a series of papers dealing with this topic; Z. Földi, *Ber.*, **61**, 1609 (1928); Y. Ogata, R. Kometani, and R. Oda, *Bull. Inst. Phys. Chem. Research* (Tokyo), 22, 583 (1943); *Chem. Abstr.*, **43**, 7797*g* (1949); C. D. Nenitzescu, S. Tzitzeica, and V. Ioan, *Bull. Soc. Chim. Fr.*, 1272 (1955); C. D. Nenitzescu, V. Ioan, and L. Teodorescu, *Chem. Ber.*, **90**, 585 (1957).

[4] P. E. Peterson and J. M. Indelicato, *J. Amer. Chem. Soc.*, **90**, 6515 (1968).

[5] P. I. Pollak and D. Y. Curtin, *ibid.*, 72, 961 (1950).

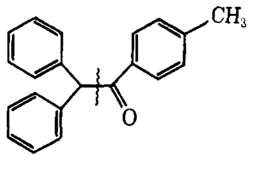
[6] E. J. Corey and J. P. Schaefer, *ibid.*, **82**, 918 (1960).





m/e 105

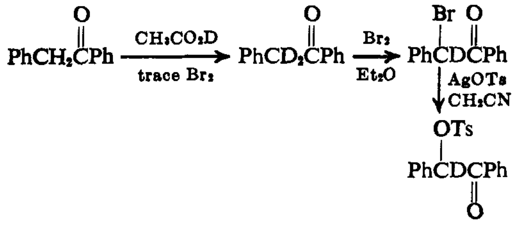
2



m/e 119

4

maining in the 2,2-diphenylacetophenone. If mechanism A is active, the product, once formed, could undergo significant deuterium exchange. On the other hand, if mechanism C is active, one has no guarantee that the deuterium atom originally associated with a given molecule of **5** is freely exchanged with the hydrogen pool during the course of the reaction, since these processes are taking place in an aprotic, nonpolar medium where association of these polar species might be favored.[3]



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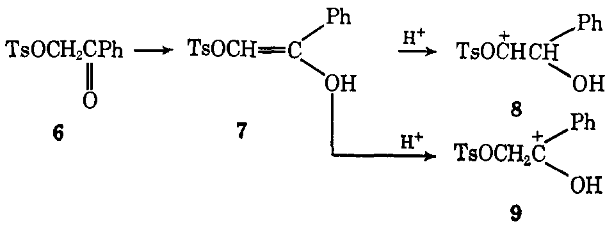
Far more significance is placed on the fact that the starting tosylate **5** does not exchange to an appreciable extent, or, perhaps more appropriately, does not survive enolization. This, coupled with the appreciable hydrogen content of the product, tends to support mechanism C.

In further support of mechanism C is the observation that α-tosyloxyacetophenone (**6**) does not form deoxybenzoin when subjected to the aforementioned solvolysis conditions. This can be rationalized as being due to the sense of protonation of the double bond of the enol (**7**). The carbonium ion **9** will most certainly be more favored than **8**, and it is possible that this preference is so pronounced as to exclude effectively the formation of **8**, which is a necessary intermediate if the reaction is to proceed further.



In limited experiments to determine the scope of this reaction, **1** has been heated in ethyl benzoate to yield benzoin benzoate and benzil, but no nuclear substitution products were observed. On the basis of these observations it is felt that the scope of this novel alkylation is restricted to carbonyl functions with activated α-tosyloxy groups and to aromatic systems that are not deactivated by electron-withdrawing substituents.

Experimental Section[7]

Preparation of Benzoin Tosylate (1). A solution of 8.0 g (0.0287 mol) of silver tosylate and 7.5 g (0.0273 mol) of desyl bromide in 45 ml of acetonitrile was heated on a steam bath for 15 min.[8] After the silver bromide had been removed by filtration and the acetonitrile by evaporation, the residue was dissolved in benzene and filtered to remove the last traces of silver salts. Crude **1** was obtained by the addition of *n*-hexane to the filtrate (7.3 g, 73%), mp 101–107.5°. Further recrystallizations from *n*-hexane–dichloromethane and then from acetone–water raised the melting point to 107–108.5° (lit.[9] 106–108°).

Preparation of Benzoin-d_1 Tosylate (5). The starting material, 2-phenyl-2,2-d_2-acetophenone (*5*), was prepared by the method of Corey and Schaefer[6] (% H = 11; % D = 89 by mass spectrometry). This was converted to 2-phenyl-2-bromo-2-d_1-acetophenone by treatment with bromine in anhydrous ether, and the crude bromide transformed to the tosylate by the above procedure with two recrystallizations from anhydrous *n*-hexane–dichloromethane. The deuterium content of the resulting benzoin-d_1 tosylate was about 95% by nmr.

Solvolysis of Benzoin Tosylate (1) in Toluene. A solution of 1.012 g (0.0024 mol) of **1** in 5 ml of toluene was refluxed (110–114°) for 14 hr. The reaction mixture was then diluted with benzene, extracted with sodium carbonate solution, and filtered through 1 g of activity III Woelm alumina. The filtrate was concentrated and the oily, crystalline residue recrystallized twice from hot methanol and once from *n*-hexene–dichloromethane to yield 0.357 g (46%) of **2**, mp 94–96° (lit.[5] 96–97°). The mother liquors showed only one spot on tlc which had the same R_f value as **2**.

Solvolysis of Benzoin Tosylate (1) in Toluene with Added 2,4,6-Collidine and with Added Toluenesulfonic Acid. A solution of 1.000 g (0.00274 mol) of **1** and 0.334 g (0.00276 mol) of 2,4,6-collidine in 5 ml of toluene was refluxed for 12 hr without affecting the decompositon of **1**, as judged by tlc analysis.

A solution of 0.526 g (0.00277 mol) of toluenesulfonic acid monohydrate in 7 ml of toluene was evaporated with heating until the water had been removed; additional toluene was added to maintain the 7-ml level. A concentrated toluene solution of 1.00 g (0.00274 mol) of **1** was added dropwise at a rate such that boiling continued and the 7 ml level was maintained. Immediately after the addition was completed the reaction mixture was allowed to cool and treated in the same manner as above to yield 0.362 g (50%) of **2**, mp 94–96.5°. The mother liquors were combined and chromatographed on 1 g of activity I Woelm alumina. The resulting colorless oil (0.227 g, 29%) had the same tlc R_f value as **2**, but would not crystallize. The nmr spectrum ($CDCl_3$) displayed two methinyl singlets at 6.18 ppm and 6.05 as well as two methyl singlets at 2.25 and 2.17. Apparently this oil is a mixture of *o*-, *p*-, and perhaps *m*-tolylphenylmethyl phenyl ketone. Both the crystalline substance and the mother liquor residue were examined by mass spectrometry. In both samples the base peak had *m/e* 105 which corresponds to the benzoyl carbonium ion, whereas the *m/e* 119 (*p*-methylbenzoyl carbonium ion), if present at all, was less than 1% of the base peak. This would seem to exclude the possibility of a tolyloyl compound being present to any significant extent in the reaction mixture.

Solvolysis of Benzoic Tosylate (1) in Benzene with and without Added Toluenesulfonic Acid. A solution of 0.5566 g (0.00152 mol) of **1** in 10 ml of benzene was refluxed for 2 days without affecting the starting material. A solution of 0.5618 g (0.00296 mol) of toluenesulfonic acid monohydrate was boiled in 5 ml of benzene to remove the water, while additional benzene was added to maintain the 5-ml level. A concentrated benzene solution of 1.00 g (0.00274 mol) of **1** was then added dropwise at a rate such that boiling continued and the 5-ml level was maintained (addition required 15 min). The solution was allowed to boil for 5 min after addition was complete, then extracted with a sodium carbonate solution and washed with water, and the residual water was azeotroped with benzene. After removal of the benzene, the residue was recrystallized from dichloromethane–methanol to give 0.6296 g (85%) of 2,2-diphenylacetophenone, mp 133–137° (lit.[10] 136–137°). Another recrystallization from the same solvent system gave 0.5756 g of material, mp 135.5–138°. This reaction is also catalyzed with boron trifluoride etherate in place of toluenesulfonic acid.

Solvolysis of Benzoin in Benzene–Toluenesulfonic Acid. A solution of 3.935 g (0.0207 mol) of toluenesulfonic acid monohydrate was evaporated by boiling until all of the acid had dissolved, and the volume of the solution adjusted to 25 ml. To this refluxing solution was added a slurry of 3.118 g (0.0147 mol) of benzoin in about 5 ml of benzene. After refluxing 2.5 hr the reaction mixture was cooled, extracted with sodium carbonate solution, and dried by filtration through magnesium sulfate. The residue remaining after evaporation of the filtrate was recrystallized twice from dichloromethane–methanol and once from dichloromethane–*n*-hexane to yield 2.59 g (65%) of 2,2-diphenylacetophenone, mp 135.5–138°.

In a similar reaction, that was interrupted after 20 min and processed in the aforementioned manner, a mixture of three components resulted, one of which was neither starting material nor product. This substance was isolated by tlc and found to be benzoin tosylate, mp and mmp 107–110, nmr spectra identical with that of an authentic sample.

Solvolysis of Benzoin Acetate in Benzene–Toluenesulfonic Acid. In a manner similar to the foregoing examples a solution of 1.028 g (0.0054 mol) of toluenesulfonic acid monohydrate and 1.149 g (0.0045 mol) of benzoin acetate in 10 ml of benzene was refluxed for 49 hr. The usual purification yielded 0.6410 g (52%) of 2,2-diphenylacetophenone, mp 135–137.5°.

Solvolysis of Benzoin-d_1 Tosylate (5) in Benzene–Toluenesulfonic Acid. A 15-ml solution of 0.5339 g (0.00145 mol) of benzoin-d_1 tosylate (**5**) and 0.2830 g (0.00153 mol) of toluenesulfonic acid monohydrate in benzene prepared in the usual way was refluxed. Three-milliliter aliquots were removed after 0.5, 1.5, and 2 hr. Each aliquot was neutralized with several drops of 2,4,6-collidine, the solution was separated from the precipitated collidine salt, and the components of the mixture were separated by preparative tlc.

The deuterium content of the 2,2-diphenylacetophenone was determined by mass spectrometry and that of the recovered benzoin tosylate by nmr as shown in Table I.

Table I

Time, hr	% reaction	Deuterium content, % Benzoin tosylate	Deuterium content, % 2,2-Diphenylacetophenone
0.5	42	96–91	42
1.5	81		34
2	90		31

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[7] All melting points were uncorrected and were taken on a Reichert hot-stage microscope. The infrared spectra were determined with a Perkin-Elmer Model 237 grating spectrophotometer. The nmr spectra were determined at 60 Mc with a Varian Model A-60 spectrometer. Solvents were removed under reduced pressure unless stated otherwise.

[8] As per the general procedure of W. D. Emmons and A. F. Ferris, *J. Amer. Chem. Soc.*, **75**, 2257 (1953).

[9] H. O. House and W. F. Berkowitz, *J. Org. Chem.*, **28**, 307 (1963).

[10] H. Biltz, *Ber.*, **26**, 1952 (1893).