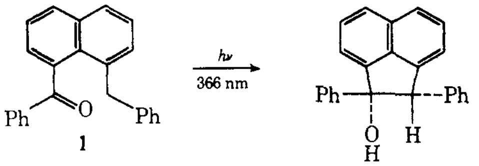
and *trans*-stilbene (1.02×10^{-1} *M*) in benzene gave a stilbene photostationary state of 68.8% *cis*-stilbene.[20] A tenfold decrease in the stilbene concentration (1.02×10^{-2} *M*) gave a photostationary state of 78.0% *cis*-stilbene. Clearly, the excitation energy of the Michler's ketone is transferred at the same rate to both ketone **1** and *trans*-stilbene in these experiments. Additional experiments show that, relative to 0.1 *M* benzophenone, the quantum yields for stilbene isomerization are the same at both high and low concentrations of Michler's ketone and thioxanthone The same relative quantum yield was also found for high concentrations of Michler's ketone in the presence of ketone **1**. Thus, sensitizer inefficiency *via* eq 1 does not seem to be an important process in the photoreaction of ketone **1**. We suggest that the concentration-dependent sensitizer quenching observed for **1** is due to a reaction between ground-state sensitizer and the $^3(\pi-\pi^*)$ state of the ketone yielding the vibrationally excited ground states of the sensitizer and ketone **1** (eq 2).[21] Interestingly,

$$^3\text{ketone } \mathbf{1}^* + \text{sens} \longrightarrow {}^0\text{ketone } \mathbf{1}^{\nu} + {}^0\text{sens}^{\nu} \qquad (2)$$

the quenching phenomena observed for **1** shows no correlation with sensitizer lifetimes as found by Chapman and Wampfler in their system.[18]

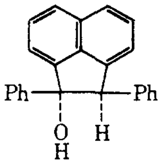
A singlet-state reaction analogous to eq 2 has recently been reported.[22] Vibrational quenching of a triplet state has also been suggested to account for the reduced efficiency of the sensitized isomerization of *cis*-piperylene in the presence of 1,4-cyclohexadiene.[23]

Further work on the intriguing implications of the process described in eq 2 are currently being investigated.



1

2



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(20) 99.8% of the incident light is absorbed by Michler's ketone under these conditions.

(21) A referee has suggested that charge-transfer exciplex quenching may also account for these concentration effects.

(22) R. S. Cooke and G. S. Hammond, *J. Amer. Chem. Soc.*, **90**, 2058 (1968), and references cited therein.

(23) A. M. Braun, W. B. Hammond, and H. G. Cassidy, *ibid.*, **91**, 6196 (1969).

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Thallium in Organic Synthesis. XIX. Photochemical Phenylation. An Effective Synthesis of Unsymmetrical Biphenyls from Arylthallium Ditrifluoroacetates[1]

Sir:

Unsymmetrical biaryls are customarily prepared by the Gomberg reaction and variations thereof,[2] or by arylations by free radicals generated through the decomposition of peroxy intermediates.[2] However, symmetrical biaryls as well as mixtures of isomeric unsymmetrical biaryls are formed, and in yields usually well below 50%. The most attractive alternate procedure is photolysis of aromatic iodides in benzene solution, giving yields which range from 40 to 80%.[3]

We report a new aromatic phenylation reaction which involves photolysis of the readily accessible arylthallium ditrifluoroacetates[4] in benzene. Products are formed in high yield and in a high state of purity. Thus, 0.01 mol of an arylthallium ditrifluoroacetate is suspended in 600 ml of benzene in a quartz vessel, nitrogen bubbled through for 15 min, and the suspension then irradiated (Rayonet photochemical reactor, 3000-Å tubes) for 18 hr.[5] The benzene solution is evaporated to dryness; the residue is taken up in 100 ml of 1:1 ether–hexane and extracted twice with 30-ml portions of water. The dried organic layer is decolorized with charcoal, filtered through a short column of silica gel, and evaporated to yield the unsymmetrical biphenyl. Representative conversions are listed in Table I.

The above results are in agreement with a free-radical pathway which we suggest is initiated by a photolytically induced homolysis of the aryl C–Tl bond.[6] Capture of the resulting aryl radical by benzene would lead to the observed unsymmetrical biphenyl; spontaneous disproportionation of the initially formed Tl^{2+} species [$\cdot Tl(OCOCF_3)_2$] to thallium(I) trifluoroacetate (isolated) and trifluoroacetoxy radicals,[8] followed by reaction of the latter with aryl radicals, would account for the small amounts of aryl trifluoroacetates formed.[10]

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(1) Part XVIII: A. McKillop, J. D. Hunt, and E. C. Taylor, *J. Organometal. Chem.*, in press.

(2) See, for example: (a) W. E. Bachmann and R. A. Hoffman, *Org. React.*, **2**, 224 (1944); (b) O. C. Dermer and M. T. Edison, *Chem. Rev.*, **57**, 77 (1957); (c) D. R. Augood and G. H. Williams, *ibid.*, **57**, 123 (1957).

(3) W. Wolf and N. Kharasch, *J. Org. Chem.*, **30**, 2493 (1965).

(4) (a) A. McKillop, J. S. Fowler, M. J. Zelesko, J. D. Hunt, E. C. Taylor, and G. McGillivray, *Tetrahedron Lett.*, 2423 (1969); (b) E. C. Taylor, F. Kienzle, R. L. Robey, and A. McKillop, *J. Amer. Chem. Soc.*, **92**, 2175 (1970).

(5) Most of the suspended solid dissolves after 1 hr. In some cases a considerably shorter irradiation time appears to be sufficient, but prolonged photolysis has no adverse effect upon the eventual yield of biaryls formed.

(6) The photolytic synthesis of aromatic nitriles from arylthallium ditrifluoroacetates in aqueous potassium cyanide solution has also been found to be a free-radical process.[7]

(7) E. C. Taylor, H. W. Altland, R. H. Danforth, G. McGillivray, and A. McKillop, *J. Amer. Chem. Soc.*, **92**, 3520 (1970).

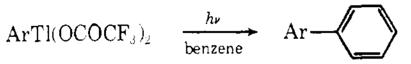
(8) Thallium(III) carboxylates upon photolysis are known to yield intermediate thallium(II) carboxylates, which decompose spontaneously to thallium(I) carboxylates and carboxylate radicals.[9]

(9) J. K. Kochi and T. W. Bethea, III, *J. Org. Chem.*, **33**, 75 (1968).

(10) Trifluoroacetoxy radicals would be expected to decompose rapidly to trifluoromethyl radicals and CO_2.[9] There was no evidence, however, for the formation of any trifluoromethylated aromatic hydrocarbons. The water extracts (see the experimental procedure described above) were strongly acidic, suggesting that the necessary hydrogen abstraction from the radical species formed by addition of the aryl radicals to benzene might have been effected by trifluoroacetoxy radicals.

In an attempt to extend this phenylation reaction,[11] phenylthallium ditrifluoroacetate was photolyzed in pyridine. We had hoped that complex formation between the pyridine nitrogen atom and thallium[4b] might result in specific α phenylation. However, the mixture of isomeric phenylpyridines obtained (50% overall yield; isomer distribution $\alpha:\beta:\gamma$, 54:32:14) was identical in composition with that observed in other free-radical phenylations of pyridine.[12]

Table I. Photolysis of Arylthallium Ditrifluoroacetates in Benzene



Ar[a]	Yield (%) of crude biphenyl[b]
Phenyl	90
p-Tolyl	91[c]
p-Ethylphenyl	84[d]
m-Xylyl	83[e]
p-Xylyl	82[f]
p-Chlorophenyl	87[g]
Mesityl	80[h]
o-Bromo-*p*-tolyl	78[i]

[a] Unrecrystallized arylthallium ditrifluoroacetates rich in the predominant isomer were used (ref 4b). The presence of small amounts of the other positional isomers accounts for the isomeric biaryls found. [b] Purity of products was determined by glc. The identity of products was established by chromatographic comparison with authentic samples or by preparative glc followed by spectral analysis. [c] Composition: 93% *p*-methylbiphenyl, 5% *o*-methylbiphenyl, 1.5% biphenyl, 0.5% *p*-cresol. [d] Composition: 93% *p*-ethylbiphenyl, 2% of an unidentified ethylbiphenyl, 1.5% biphenyl, 3.5% *p*-ethylphenyl trifluoroacetate. [e] Composition: 98% 2,4-dimethylbiphenyl, 0.5% 2,6-dimethylbiphenyl, 1% biphenyl. [f] Composition: 99% 2,5-dimethylbiphenyl, 1% biphenyl. [g] Composition: 89% *p*-chlorobiphenyl, 8% *o*-chlorobiphenyl, 3% biphenyl. [h] Composition: 63% 2,4,6-trimethylbiphenyl, 27% mesitylene, 7% mesityl trifluoroacetate, 3% biphenyl. [i] Based on recovered starting material (20%); irradiation was carried out for only 6 hr with 3500-Å light. Composition: 93% 2-bromo-4-methylbiphenyl, 2.5% biphenyl, 2.5% 2-bromo-4-methylphenyl trifluoroacetate, 2% *m*-bromotoluene.

In the above unsymmetrical biphenyl synthesis, replacement of thallium by a phenyl group takes place cleanly without contamination by positional isomers; the same specificity of replacement was previously observed in the synthesis of aryl iodides from arylthallium ditrifluoroacetates.[13,14] Since the position of thallation can be controlled,[4b] the complementary photolytic reactions in benzene of arylthallium ditrifluoroacetates and of aryl iodides provide a simple synthesis of unsymmetrical biphenyls of predetermined orientation.

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(11) Photolysis in benzene of the thallation derivatives of benzoic and phenylacetic acids (ref 4b) yielded unidentified, benzene-insoluble, brown solids, in addition to smaller amounts of crude biphenyls. For example, the mixture of biphenyls (30%) obtained from benzoic acid consisted of *o*-phenylbenzoic acid (72%) and biphenyl (18%); benzoic acid (10%) was also present. Similarly, phenylacetic acid, under the above conditions, yielded a mixture of *o*-phenylphenylacetic acid (77%), an unidentified isomer thereof (5%), *o*-methylbiphenyl (0.5%), biphenyl (8.5%), and unchanged phenylacetic acid (8%).

(12) K. Schofield, "Hetero-Aromatic Nitrogen Compounds," Butterworths, Washington, D. C., and London, 1967, p 253.

(13) A. McKillop, J. S. Fowler, M. J. Zelesko, J. D. Hunt, E. C. Taylor, and G. McGillivray, *Tetrahedron Lett.*, 2427 (1969).

(14) This is also the case in the photochemical conversion of aromatic iodides to chlorides;[15] similar observations have been made by Kharasch.[3]

(15) F. Kienzle and E. C. Taylor, *J. Org. Chem.*, **35**, 528 (1970).

(16) NRCC Postdoctoral Fellow, 1968–1970.

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Identification of the Rate-Limiting Step in the Chymotrypsin-Catalyzed Hydrolysis of *N*-Acetyl-L-tryptophanamide

Sir:

The identification of the chemical changes associated with observed rate processes in enzyme-catalyzed reactions has not kept pace with the elucidation of the number and rates of such processes. In the case of the α-chymotrypsin-catalyzed hydrolysis of furylacryloyltryptophanamide,[1] the existence of no less than two intermediates prior to the acyl enzyme intermediate has been demonstrated. However, in this and in other cases[2,3] the natures of the various reaction steps have been determined only in a general way. We have previously shown[4,5] that heavy atom isotope effects in enzymatic reactions can be used to compare the rate of a step in which a bond to an isotopic atom is broken with the rates of prior steps in the enzymatic reaction sequence. In such a reaction, a heavy atom isotope effect is observed to the extent that the bond-breaking step is slow relative to steps prior to it. We have now measured the amide nitrogen isotope effect on the α-chymotrypsin-catalyzed hydrolysis of acetyl-L-tryptophanamide. The isotope effect is $k^{14}/k^{15} = 1.010$ at 25° in pH 8.0 phosphate buffer and indicates that the slowest step in the acylation of the enzyme is the step in which the carbon–nitrogen bond is broken.

For each experiment two portions of a freshly prepared solution of 0.01 *M* *N*-acetyl-L-tryptophanamide in 0.05 *M* potassium phosphate buffer at pH 8.0 were equilibrated at 25° for 30 min and an amount of desalted chymotrypsin sufficient to hydrolyze 10% of the substrate in 5–15 min was added to one of the samples and 5–10 times that amount of enzyme was added to the other. A small amount of the first sample was withdrawn for spectrophotometric monitoring at 306 mμ. After a time corresponding to approximately 10% reaction, the reaction in the first solution was stopped by the addition of Norit. The solution was filtered twice, ultra-filtered (Dia-Flo UM-2 filter), and steam distilled in all-glass apparatus. The distillate was concentrated to about 3 ml and the ammonia

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(1) G. P. Hess, J. McConn, E. Ku, and G. McConkey, *Phil. Trans. Roy. Soc. London, Ser. B*, **257**, 89 (1970).

(2) M. R. Hollaway, *Annu. Rep. Progr. Chem.*, **65**, 601 (1968); M. L. Bender, M. J. Gibian, and D. J. Whelan, *Proc. Nat. Acad. Sci. U. S.*, **56**, 833 (1966); M. L. Bender, G. E. Clement, F. J. Kezdy, and H. d'A. Heck, *J. Amer. Chem. Soc.*, **86**, 3680 (1964); A. Himoe, P. C. Parks, and G. P. Hess, *J. Biol. Chem.*, **242**, 919 (1967).

(3) L. Parker and J. H. Wang, *ibid.*, **243**, 3729 (1968).

(4) M. H. O'Leary, *J. Amer. Chem. Soc.*, **91**, 6886 (1969); M. H. O'Leary and D. W. Hendrickson, *Fed. Proc., Fed. Amer. Soc. Exp. Biol.*, **29**, 407 (1970).

(5) M. H. O'Leary, D. T. Richards, and D. W. Hendrickson, *J. Amer. Chem. Soc.*, **92**, 4435 (1970).