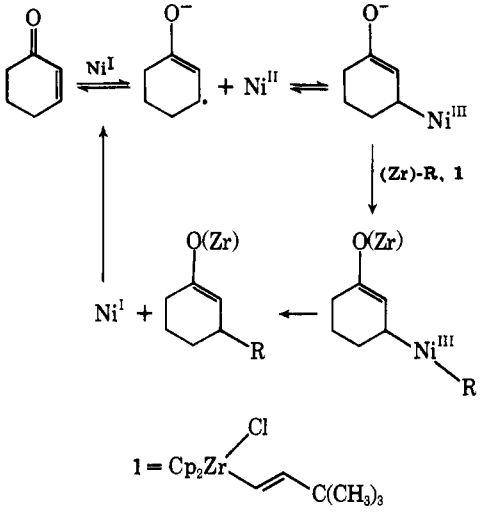
Scheme I. Proposed Mechanism for Conjugate Addition



immediately upon mixing $Ni(acac)_2$ with 1 equiv of Dibah. This is followed by a much slower evolution of an additional 0.5 equiv of isobutane. Or, reaction between $Ni(acac)_2$ and Dibah results in a rapid oxidation-state change from Ni(II) to Ni(I) followed by gradual reduction to Ni(0). When compared with this isobutane evolution data, it becomes clear that the reduction of Ni(II) to Ni(0) is associated with the *loss* of catalytic activity for the system.

On the basis of the data presented, Ni-catalyzed conjugate addition of alkenylzirconium compounds to enones likely involves initial electron transfer from a Ni(I) species to the unsaturated ketone (Scheme I). Attack of ketyl upon the Ni(II) species thus generated yields an organonickel(III) intermediate which could undergo transmetalation with the alkenylzirconium compound and reductive elimination to give the observed zirconium enolate and regenerate Ni(I). It is interesting to note here that Kochi has recently determined that the transformation Ni(I) → Ni(III) → Ni(I) is responsible for efficient catalysis in nickel-mediated aryl coupling reactions.[9]

The CV experiments described above suggest that catalysis of conjugate addition occurs through a family of nickel species, the members of which possess different lifetimes and different oxidation potentials. The fact that a *single* reduction wave couples the three reducing waves observed in the anodic scan indicates that a *single* oxidation state describes the Ni species in this family (it may be that the various species observed reflect clustering in which aggregation numbers or geometries for Ni atoms in the various members of the family are different). The fact that *none* of the reducing species observed (in the presence of the supporting electrolyte) are strong enough reducing agents to add an electron to an *isolated* α,β-enone suggests that complexation between that unsaturated organic molecule and the reactive Ni species may be important.[10,11] Preliminary attempts were made at isolating an active nickel catalyst by allowing reduction of $Ni(acac)_2$ with Dibah in THF to proceed for 24 h. Evacuation of solvent left a black solid material which exhibited a CV anodic wave at −1.30 V and a cathodic wave at −1.75 V. The black material successfully catalyzed the conjugate addition of **1** to cyclohexen-1-one. Further investigations using this material hopefully will shed more light on the nature of these coupling reactions.

Acknowledgments. The authors acknowledge generous support for this research provided by the National Science Foundation, Grant No. CHE 79-00996, and by the National Institutes of Health, Grant No. PHS HL22612. They also thank Professor M. F. Semmelhack for the use of his electrochemical equipment.

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(9) Tsou, T. T.; Kochi, J. K. *J. Am. Chem. Soc.* **1979**, *101*, 7547.
(10) House[3] has postulated a similar complexation requirement for cuprate conjugate addition.
(11) For cyclohexen-1-one, the reduction potential in THF, 0.42 M n-Bu_4NClO_4, is −2.18 V vs. SCE.

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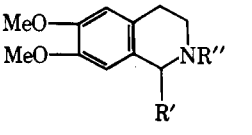
Photohydrolysis of Sulfonamides via Donor–Acceptor Ion Pairs with Electron-Donating Aromatics and Its Application to the Selective Detosylation of Lysine Peptides

Sir:

The importance of exciplexes in photochemistry is now well recognized through a number of recent theoretical and mechanistic studies,[1] because they have opened the possibility of "endothermic photosensitization" in classical energy transfer.[2] As part of our photochemical studies[3] we report an improved photochemical removal of an *N*-tosyl protecting group from *p*-toluenesulfonamides with the assistance of electron-donating aromatic compounds.[4] This reaction is of mechanistical interest and also may provide a useful method in organic synthesis, especially in peptide chemistry.

In 1969, Umezawa et al. reported that, on irradiation in the presence of $NaBH_4$, 1-substituted 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline *N*-tosylates (**1a–d**) were readily cleaved to the corresponding tetrahydroisoquinolines (**2a–d**) in high yields.[5] The photolysis was proceeded via intramolecular formation of an excited donor–acceptor pair between the electron-donating dimethoxybenzene group and the electron-withdrawing tosyl group.[6] Extension of this photolysis to intermolecular reactions may provide a general method for the cleavage of sulfonamides.



1a, R′ = H; R″ = Ts	**2a**, R′ = R″ = H
b, R′ = Me; R″ = Ts	**b**, R′ = Me; R″ = H
c, R′ = Ph; R″ = Ts	**c**, R′ = Ph; R″ = H
d, R′ = CH_2Ph; R″ = Ts	**d**, R′ = CH_2Ph; R″ = H

When an EtOH solution of *N*-tosylmethylphenethylamine (**3**, 10 mM) and veratrol (**12**, 30 mM) was irradiated with a 100-W high-pressure mercury lamp, methylphenethylamine (**5**) was isolated in 66% yield. Irradiation in the presence of a large excess of $NaBH_4$ (0.1 M) in 80% aqueous EtOH improved the yield to 86%.[7] Similarly, **4** and **7** readily gave **6** and **8**, respectively (Table I).

In Table II the $k_q\tau$ values calculated from linear Stern-Volmer plots of fluorescence quenching of dimethoxybenzenes (**12, 13**) by *N*-tosylmethylamine,[8] relative quantum yields for disappearance of **3** (ϕ), and oxidation potentials [$E_{1/2}$ (ox)]

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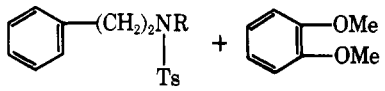
Table I. Photolysis of Sulfonamides in the Presence of Electron Donors[a]

sulfonamide (mM)	donor (mM)	$NaBH_4$, M	solvent	filter	amine (yield, %)[b]
3 (10)	**12** (30)		EtOH		**5** (66)
3 (10)	**12** (30)	0.1	80% EtOH		**5** (86)
4 (10)	**12** (30)	0.1	80% EtOH		**6** (87)
7 (10)	**12** (30)	0.1	80% EtOH		**8** (87)
3 (10)	**13** (30)	0.1	80% EtOH		**5** (82)
4 (10)	**13** (30)	0.1	80% EtOH		**6** (89)
3 (10)	**14** (40)	0.1	80% EtOH		**5** (91)
3 (4.2)	**18** (7.6)	0.04	80% MeCN	Pyrex	**5** (70)
3 (4.2)	**18** (7.6)	0.04	80% THF	Pyrex	**5** (78)
3 (4.2)	**18** (7.6)	0.04	90% EtOH	Pyrex	**5** (84)[c]
9 (3)	**18** (3)	0.015	90% EtOH	Pyrex	**10** (75)
11 (4.6)		0.04	90% EtOH	Pyrex	**6** (64)
11 (4.6)	**13** (46)	0.04	90% EtOH	Pyrex	**6** (88)

[a] Irradiation with a 100- or 200-W high-pressure mercury lamp for 1 h. [b] Isolated yield as HCl salts. [c] The disappearance quantum yields of **3** were determined to be 0.037 when a 97% EtOH solution of **3** (4.2 mM), **18** (6.4 mM), and $NaBH_4$ (42 mM) was irradiated with 322-nm light.

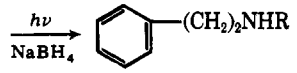
are shown. Compound **13** is clearly more effective than **12** and the k_q value is very close to the diffusion-controlled rate constant.[9] Some preparative data using **13** are also shown in Table I.

Compound **3** was recovered unchanged when irradiated with

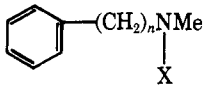


3, R = Me
4, R = H

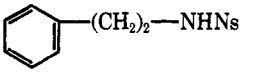
12



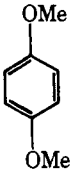
5, R = Me
6, R = H



7, *n* = 1; X = Ts
8, *n* = 1; X = H
9, *n* = 0; X = Ts
10, *n* = 0; X = H



11, Ns: β-naphthalenesulfonyl



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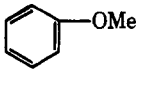

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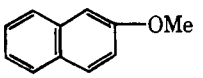

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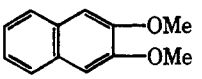

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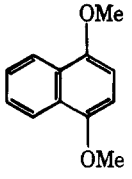

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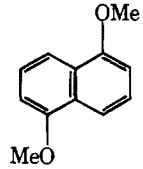

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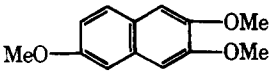

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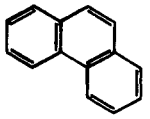

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Table II. Fluorescence Quenching ($k_q\tau$), Relative Disappearance Quantum Yields of **3** (ϕ), Oxidation Potentials [$E_{1/2}$(ox)], Excited Singlet Energies ($E_{0\text{-}0}$), and Calculated Enthalpy Changes (ΔG)

fluorophor (donor)	$k_q\tau$,[a] M^{-1}	k_q, 10^9 M^{-1} s^{-1}	relative ϕ[b]	$E_{1/2}$(ox), V	$E_{0\text{-}0}$, kcal mol^{-1}	ΔG, kcal mol^{-1}
12	9.9		1.00[c]	1.45[d]	101.7[e]	−15.7
13	16.5	8.25	1.61[c]	1.35[d]	95.0[e]	−11.4
				1.15[f]		−17.1
14				1.78[d]	103[g]	−8.46
15	0			1.52[h]	86.8[e]	+0.74
16	0		0.11[i]	1.39[h]	88.5[e]	−3.95
17	8.1	1.04[j]	1.00[i]	1.10[h]	83.9[e]	−6.04
18	9.1	0.72[j]	1.97[i]	1.28[h]	87.8[e]	−5.79
19	0.8		0.43[i]			
20	0			1.50[k]	82.9[g]	+4.18

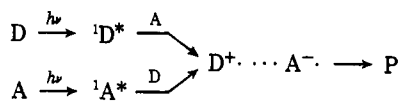
[a] For an EtOH solution (10^{-3}–10^{-5} M), quenched by *N*-tosylmethylamine. [b] Solution of a donor (30 mM), **3** (10 mM), and $NaBH_4$ (0.1 M). Disappearance of **3** was followed by GLC analysis. [c] 80% EtOH solution, 100-W lamp. [d] A. Zweig, W. G. Hodgson, and W. H. Jura, *J. Am. Chem. Soc.*, **86**, 4124 (1964). [e] Obtained from the 0-0 bands of excitation spectra when the fluorescence spectra of donors were measured at 77 K. [f] S. Andreades and E. W. Zahnow, *ibid.*, **91**, 4181 (1969). [g] S. L. Murov, "Handbook of Photochemistry", Marcel Dekker, New York, 1974, pp 5-10. [h] A. Zweig, A. H. Maurer, and B. G. Roberts, *J. Org. Chem.*, **32**, 1322 (1967). [i] A. Zweig, W. G. Hodgson, and W. H. Jura, *J. Am. Chem. Soc.*, **86**, 4124 (1964). [j] Measured with a phasefluorometer modulated at 10.7 MHz (He-Cd laser). [k] E. S. Pysh and N. C. Yang, *J. Am. Chem. Soc.*, **85**, 2124 (1963).

light above 300 nm in the presence and absence of $NaBH_4$. Interestingly, addition of dimethoxynaphthalenes resulted in the smooth cleavage of **3** except in the case of 2,3-dimethoxy compound **16** which has a higher oxidation potential (Table II). Again fluorescence quenching and relative reaction quantum yields were measured (Table II). Near-diffusion-controlled rate constants were found for the fluorescence quenchings of **17** and **18**.[10] Although naphthalenes (**17** and **18**) were somewhat less effective than **13**, they are more useful practically because their strong light absorption above 300 nm[11] avoids the direct photolysis of sulfonamide groups.[4]

Some preparative data using **18** are shown in Table I. Although the direct photolysis of *N*-tosylaniline is known to give the rearranged sulfone as well as aniline in very poor yield,[4a] **9** in the presence of **18** gave only **10** in a good yield.

The β-naphthalenesulfonamide (**11**) gave **6** in 64% yield when irradiated in the presence of $NaBH_4$ with light above 300 nm, and, interestingly addition of 1,4-dimethoxybenzene (**13**) improved the yield to 88%.

These results show that the initial step of the present photolysis must be the formation of a radical ion pair through excitation either by a donor or an acceptor (in the case of **11**).



D: donor (dimethoxybenzenes, dimethoxynaphthalenes)
A: acceptor (tosylamides, β-naphthalenesulfonamide)
$D^{+\cdot} \cdots A^{-\cdot}$: solvated radical ion pair
P: products

This electron-transfer mechanism is further supported by the negative values of calculated free enthalpy changes (ΔG) involved in the electron-transfer processes (Table II).[12] Although the ΔG of **18** is less negative than that of **17**, **18** was actually more effective than **17** in the photolysis of tosylamides, probably because of a longer lifetime of the excited singlet state of **18**. Compounds **15**, **16**, and **20** having more positive ΔG values were ineffective in this photolysis.

Since the radical anion ($A^{-}\cdot$) is identical with the known species generated in the initial step of Na-NH_3 (liquid),[13] Na-naphthalene,[14] and electrochemical reductions[15] of sulfonamides, the first step of its decomposition can be described as shown in eq 1. Equations 2-5 presumably show further principal processes in the photohydrolysis in the presence (eq 2, 3) and absence (eq 4, 5) of $NaBH_4$ on the basis of the following evidence, though a more detailed description of the mechanism must await further work. (1) Most of the donors in these photoreactions, especially in the presence of $NaBH_4$, were recovered unchanged. (2) When an ethanol solution of **3** (10 mM) and **18** (5 mM) in the presence of $NaBH_4$ (50 mM) was irradiated with light above 300 nm, toluenesulfinic acid (71%), as its methyl and ethyl esters, as well as the amine (**5**, 89%) and the recovered donor (**18**, 95%), were readily isolated. (3) On irradiation in the presence of NaOEt (6 mM) instead of $NaBH_4$, an ethanol solution of **3** (7 mM) and **18** (5 mM) gave **5** (62%), **18** (77%), and ethyl toluenesulfonate (45%). There was no detectable formation of toluenesulfinic acid and its ester. (4) When an anhydrous acetonitrile solution of **3** and **18** was irradiated under argon, no reaction occurred, though the fluorescence of **3** was quite efficiently quenched by *N*-tosylmethylamine.[10]

$$ArSO_2NRR'^{-}\cdot\ (A^{-}\cdot) \rightarrow RR'N^{-} + ArSO_2\cdot \quad (1)$$

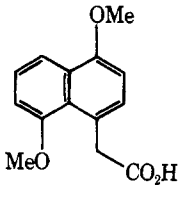
$$RR'N^{-} + ArSO_2\cdot \xrightarrow[H_2O]{NaBH_4} RR'NH + ArSO_2H^{-}\cdot \quad (2)$$

$$ArSO_2H^{-}\cdot + D^{+}\cdot \rightarrow ArSO_2H + D \quad (3)$$

$$RR'N^{-} + ArSO_2\cdot \xrightarrow{H_2O} RR'NH + ArSO_3H^{-}\cdot \quad (4)$$

$$ArSO_3H^{-}\cdot + D^{+}\cdot \rightarrow ArSO_3H + D \quad (5)$$

The ϵ-*N*-tosyl group has been used as the most stable side-chain protection of lysine in peptide synthesis,[16] and the reduction with Na-NH_3 (liquid) is practically the only useful method for removing the tosyl group. However, a number of serious side reactions such as the reductive fission of proline peptides have been reported.[13b,17] The photohydrolysis of tosylamides presented here can be expected to be a selective method for the detosylation of lysine peptides since it avoids the side reactions which occur in Na-NH_3 reductions, because only the *N*-tosyl group in usual protected peptides can form an ion pair with an excited electron donor. As preliminary experiments some model ϵ-*N*-tosyl lysine peptides in water or 50% DMF were irradiated with a 100-W lamp (Pyrex filter) in the presence of a large excess of $NaBH_4$ and 0.3-1 equiv of a water-soluble donor (**21**). The isolated yields of detosylated



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peptides from the corresponding ϵ-*N*-tosyl-protected compounds are as follows: Z-Lys (90%), Z-Gly-His-Lys (68%), Z-Gly-Pro-Lys (76%), and Z-Gly-Lys-Gly (81%). No cleavage of the peptide bonds was observed. Experiments to determine further applications are now in progress.

Acknowledgment. We thank Professor H. Kokubun (Tohoku University) for helpful discussions and fluorescence lifetime measurements.

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(4) The yields of direct photolyses of sulfonamides, sometimes accompanied by photorearrangements, are usually poor: (a) H. Nozaki, T. Okada, R. Noyori, and M. Kawanishi, *Tetrahedron*, **22**, 2177 (1966); (b) L. D'Souza and R. A. Day, *Sciences*, **160**, 882 (1968); (c) M. Somei and M. Natsume, *Tetrahedron Lett.*, 2451 (1974); (d) L. J. Kricka, M. C. Lambert, and A. Ledwith, *J. Chem. Soc., Perkin Trans. 1*, 52 (1974); (e) J. C. Arnould, J. Cossy, and J. P. Pête, *Tetrahedron Lett.*, 3919 (1976).
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(6) T. Hamada, A. Nishida, and O. Yonemitsu, *Heterocycles*, **12**, 647 (1979).
(7) Photolysis of **3** in the presence of $NaBH_4$ has been reported to give **5** in 49% yield: O. Hoshino, S. Sawaki, and B. Umezawa, *Chem. Pharm. Bull.*, **18**, 182 (1970).
(8) No quenching by *N*-mesylmethylamine was observed.
(9) The fluorescence lifetime of **13** has been reported to be 2 ± 1 ns: M. T. McCall, G. S. Hammond, O. Yonemitsu, and B. Witkop, *J. Am. Chem. Soc.*, **92**, 6991 (1970).
(10) The reported τ of **17** is 5.7[a] and 8.474 ns.[b] (a) F. H. Quina, Z. Hamlet, and F. A. Carroll, *J. Am. Chem. Soc.*, **99**, 2240 (1977); (b) D. R. Arnold and A. J. Maroulis, *ibid.*, **99**, 7356 (1977). The fluorescence of **17** was also quenched by *N*-tosylmethylamine in benzene and acetonitrile with k_q = 6.3 × 10^8 and 7.4 × 10^8 M^{-1} s^{-1}, respectively, though no exciplex emission was observed.
(11) This is very important in peptide chemistry because some amino acid residues such as Trp, Tyr, and His sometimes decompose when irradiated with light below 300 nm: A. D. Mc Laren and D. Shugar, "Photochemistry of Proteins and Nucleic Acids", Pergamon, Oxford, 1964.
(12) The ΔG values were calculated by the Weller equation:[a,b]

$$\Delta G\ (\text{kcal/mol}) = 23.06[E(D/D^{+})_V - E(A/A^{-})_V - e^2/\epsilon R] - E_{0-0}\ (\text{kcal/mol})$$

Although the equation was originally valid in acetonitrile, it can be successfully applied to the estimation of ΔG values in ethanol when oxidation and reduction potentials in ethanol are used. The half-wave reduction potential of *p*-toluenesulfonamide in ethanol is −2.36 V.[c] For oxidation potentials, the data in acetonitrile were used because they are little affected by alteration of solvents:[d,e] (a) D. Rehm and A. Weller, *Isr. J. Chem.*, **8**, 259 (1970); (b) Y. Taniguchi, Y. Nishida, and N. Mataga, *Bull. Chem. Soc. Jpn.*, **45**, 764 (1972); (c) L. Horner and R. J. Singer, *Justus Liebigs Ann. Chem.*, **723**, 1 (1969); (d) N. L. Weinberg, D. H. Marr, and C. N. Wu, *J. Am. Chem. Soc.*, **97**, 1499 (1975); (e) L. Eberson and K. Nyberg, *ibid.*, **88**, 1686 (1966).
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Difluoromethylene Chain-Extension Reactions. Preparation of Fluorinated Alkenes and Alkadienes from Olefin Precursors

Sir:

Chain-extension or homologation reactions are well documented in many areas of organic synthesis. In the field of organofluorine chemistry, however, a notable lack of effort and success for similar conversions has been achieved. Alkylation of fluoro olefins via *F*-alkyl carbanions,[1] nucleophilic addition-elimination reactions of fluoro olefins by Grignard or lithium reagents,[2] or alkylation of fluoro olefins with phosphonium ylides[3] (followed by hydrolysis) permits chain extension of the *F*-alkene within a limited framework. Insertion

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