50–95% saturation of the available binding sites. The reader is reminded that the treatment above assumes competitive binding with 1:1 stoichiometry and that the quantitative aspects of this work may not be useful with large, complex ligands having multiple binding sites or the capability of binding multiple substrates.

Most of our results mirror the known properties of ristocetin and vancomycin, but several of the results were unexpected until discovered during the solid-phase assay and confirmed by solution-phase titration experiments. First, D-Phe-D-Ala binds to vancomycin (but not ristocetin) more tightly than the natural substrate sequence D-Ala-D-Ala. Second, L-PheGly shows modest binding to ristocetin (but not vancomycin). Third, an analogous assay in methanol shows that all association constants are reduced, especially those of the phenylalanine-containing dipeptides. Parenthetically we note that the benzoyl dipeptides studied here generally bind more tightly than the corresponding acetyl analogues in water. These findings point to a significant hydrophobic component of the binding energy and demonstrate the utility of the method as an effective screen for finding sets of substrates that bind to a given ligand.[10]

Supplementary Material Available: Experimental details for preparing the bromoacetyl resin, for linking the ligand, and for conducting the assay; a FORTRAN computer program that evaluates binding constants from the HPLC integrations (11 pages). Ordering information is given on any current masthead page.

(10) This work was supported by NIH grant GM37255 and an SERC/NATO postdoctoral fellowship to P.W.S.

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Photocyclization Reactions of 1-Benzyl-1-pyrrolinium Salts by Diradical and Diradical Cation Pathways. Novel Photochemical Pictet–Spengler Cyclizations

Summary: Studies with a series of ortho- and meta-substituted 1-benzyl-1-pyrrolinium perchlorates have uncovered novel, electron-transfer-induced photocyclization processes leading to benzopyrrolizidines and benzindolizidines.

Sir: Mechanistic pathways for electrophilic aromatic substitution activated by single electron transfer (SET) are less common than their two-electron-transfer counterparts.[1] Yet, processes involving generation and coupling of radical cation pairs (Scheme I) could serve as mechanistic models for the design of new reactions of this type, especially in the excited-state manifold where rates of SET can be fast.

In previous efforts probing arene–iminium salt photochemistry, we uncovered isolated examples of reactions of this type. Thus, the low-yielding formation of the arylpyrrolidines **3** by irradiation of the pyrrolinium salts **1** in the presence of toluene or benzene appeared to be a consequence of radical cation pair **2** coupling which weakly competes with cage collapse or cation radical deprotonation.[2] Formation of adducts **3** by this novel pathway occurs only in polar solvents (MeOH vs MeCN) and when alternate reactions of the cation radicals (e.g. R_3Si or R_3Sn group loss) are slow.[2,3]

Scheme I

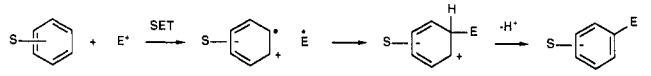
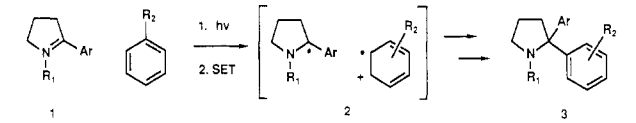


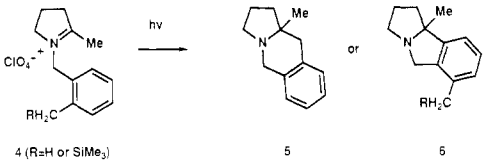
Table I. Photoproduct Distributions from Irradiation of *N*-Benzylpyrrolinium Salts

pyrrolinium salt	irradiation conditions	total yield, %	products (yield, %)
7	direct, MeCN	45	13 (11), 15 (34)
8	direct, MeCN	83	15 (21), 16 (62)
9	direct, MeCN	95	17
8	sensit., Me_2CO	97	16
9	sensit., Me_2CO	97	17
10	direct, MeCN	76	14 (18), 18 (58)
11	direct, MeCN	86	14 (19), 18 (38), 19 (29)
11	direct, MeOH	90	14 (32), 18 (55), 19 (3)
12	direct, MeCN	81	18 (13), 20 (68)
10	sensit., Me_2CO	85	14 (27), 18 (58)
11	sensit., Me_2CO	95	14 (32), 18 (42), 19 (21)
12	sensit., Me_2CO	97	20
21	direct, MeCN	99	25
22	direct, MeCN	99	24 (72), 25 (6), 26 (21)
22	direct, MeOH	99	24 (48), 25 (48), 26 (3)
23	direct, MeCN	90	25 (4), 27 (86)
23	direct, MeOH	90	25 (11), 27 (79)
21	sensit., Me_2CO	99	25
22	sensit., Me_2CO	95	24 (79), 25 (3), 26 (13)
23	sensit., Me_2CO	95	27



1 2 3

The relative rates of electrofugal group loss and radical coupling play a role in intramolecular arene–iminium salt systems. An isolated, yet instructive, example is found in the report that the *N*-xylylpyrrolinium salts **4** photocyclize to produce either the pyrrolizidines **5** or indolizidine **6** depending upon whether or not they contain TMS substitution at the benzylic position.[3,4]



4 (R=H or $SiMe_3$) 5 6

The major purpose of the current study is to explore more fully SET-induced photocyclization reactions related to those shown above. Our aim is to develop a clear understanding of the factors (e.g. excited-state multiplicity, solvent, nature, and location of substituents and nature of electrofugal groups) which influence competition between diradical and cation diradical cyclization modes. Information gained about cyclization regiochemistry and efficiency would also have synthetic implications.[5] For

(1) (a) Cf. Eberson, L.; Radner, F. *Acc. Chem. Res.* **1987**, *26*, 53. (b) Sankararaman, S.; Haney, W. A.; Kochi, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 5235 and references therein.

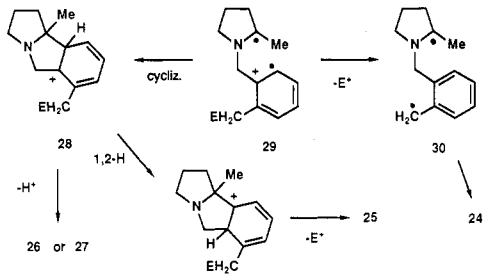
(2) Borg, R. M.; Heuckeroth, R. O.; Lan, A. J. Y.; Quillen, S. L.; Mariano, P. S. *J. Am. Chem. Soc.* **1987**, *109*, 2728.

(3) Lan, A. J. Y.; Heucheroth, R. O.; Mariano, P. S. *J. Am. Chem. Soc.* **1987**, *109*, 2738.

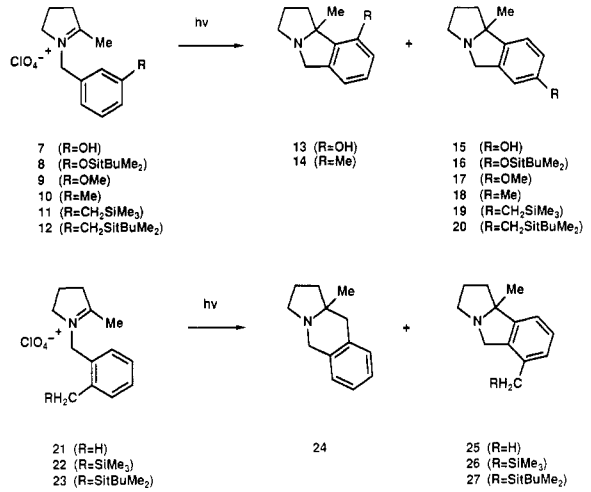
(4) (a) Competitive diradical and diradical cation cyclization pathways have been detected in allylsilane–iminium salt photocyclizations. (b) Tu, C.-L.; Mariano, P. S. *J. Am. Chem. Soc.* **1987**, *109*, 5287.

0022-3263/88/1953-1590$01.50/0

Scheme II



these purposes, a series of substituted 1-benzyl-1-pyrrolinium perchlorates were prepared by N-alkylation of 2-methyl-1-pyrroline[6] with the appropriate benzyl iodide followed by perchlorate anion exchange.[7] These salts were directly irradiated (Vycor, $\lambda > 240$ nm) in either MeCN or MeOH.[8a] Triplet-sensitized reactions were conducted by irradiation (Pyrex, $\lambda > 290$ nm) of $Me_2C{=}O$ solutions.[8b] Products were separated and purified by column chromatography (silica gel or Florisil). Photoreactions of the *m*-oxybenzyl salts **7–9** gave the corresponding benzopyrrolizidines (Table I) which were identified by their unique spectroscopic properties.[9] Similarly, the *m*-alkylbenzyl salts **10–12** provided related pyrrolizidines, and pyrrolizidines and indolizidines both arise from photoreactions of the *o*-alkylbenzyl salts **21–23**.[10]



Several interesting trends can be noticed by inspection of the data shown in the table. Photocyclizations in all series (especially acetone sensitized) are exceptionally efficient and in some cases highly chemo- and regioselective. Results from studies with the ortho-substituted salts **21–23** have the greatest mechanistic significance since cation diradical and diradical cyclization modes are clearly reflected in the respective pyrrolizidines **25–27** and indolizidine **24** produced. Indolizidine **24** predominates when Me_3Si containing salt **22** is cyclized and its proportion increases when the solvent polarity is low (MeCN vs MeOH) or when the process is acetone sensitized. The H and Me_2-*t*-Bu salts **21** and **23** give only pyrrolizidines under all conditions and the yields of silicon-containing pyrrolizidines **26** and **27** vary with solvent.

The results suggest that the relative rates of electrofugal group loss vs cyclization in the ortho-substituted cation diradicals **29** (Scheme II) are governed by electrofugal group type, solvent polarity, and diradical cation multiplicity. Earlier we demonstrated that the rates of Me_3Si group loss from cation radicals far exceed those for deprotonation[2] and are larger than for loss of the Me_2-*t*-BuSi group.[11] Thus, diradical cation **29** partitions preferentially to diradical **30**, the precursor of indolizidine **24**, when E = Me_3Si, and cyclizes to produce tricyclic cation **28** when E = H or Me_2-*t*-BuSi. Solvents of high polarity (Z(MeOH) = 83.6, Z(MeCN) = 71.3) facilitate cyclization of **29**, presumably via stabilization of the more localized cation **28**. Interestingly, stabilization by the more silophilic MeOH also leads to greater amounts of desilylation vs deprotonation of **28**. Although small, increases in the **24**/(**25**+**26**) ratio in the acetone-sensitized cyclization of **22** can be attributed to a multiplicity effect on diradical cation cyclization rates.[12,13] While distinctions between the competing pathways for photocyclizations of the meta-substituted salts cannot be made unambiguously on the basis of product analysis, interpretable trends are evident. For example, reactions of the *m*-oxy salts **7–9** favor the *p*-oxypyrrolizidines as the oxy substituent becomes more bulky. Products retaining the oxygen substituent are produced in ratios which are larger in Me_2CO vs MeCN reactions. Similarly, the para/ortho pyrrolizidine ratios in direct irradiations of **10–12** vary with the size of the R group and the silicon-containing products are more predominant for reactions run in MeCN and Me_2CO vs MeOH. Lastly, irradiation of the meta-trideuterio analogue of **10** in MeCN, MeCN + H_2O, or Me_2CO gives trideuterio analogues of **14** and **18** with 100% ^2H isotope retention.

Thus, reaction of **10** occurs exclusively by a diradical cation cyclization pathway. The MeO salt **9** and the Me_2-*t*-BuSiO salt **8** react only by this route to provide the respective pyrrolizidines **17** and **16**. Only in case of the Me_3Si salt **11** does it appear that competitive desilylation and cyclization of the intermediate cation radical occur with the former mode predominating slightly in the direct (MeCN) process and more so in the Me_2CO-sensitized reaction. Two additional points are worthy of comment. Steric effects causing increasing amounts of para-substituted products in diradical cyclization routes are a result of the highly crowded nature of an ortho-substituted tricyclic cation **31**. Lastly, the greater preferences seen for diradical cation cyclization in the *m*-oxy and *m*-alkyl systems appear to be reflective of substituent regiocontrolled stabilization of the tricyclic cations **31** and **32** relative to **28**. Thus, single electron-transfer mechanisms for electrophilic aromatic substitution have the potential of displaying regiochemical and reactivity patterns similar to their two-electron-transfer counterparts.[1b] Finally, the efficient generation of pyrrolizidines shows that the SET-induced intramolecular, electrophilic aromatic substitution

(5) For a recent synthetic application, see: Ho, G.-D.; Mariano, P. S. *J. Org. Chem.* **1987**, *52*, 704.

(6) Bielawski, J.; Brandage, S.; Lindblom, L. *J. Heterocycl. Chem.* **1978**, *15*, 97.

(7) Complete synthetic and spectroscopic data will be reported in a full paper on this subject.

(8) (a) Direct irradiations were conducted on ca. 1×10^{-3} M solutions. Workup of crude photolysates was by treatment with $NaHCO_3$ in order to liberate free amines from N-protonated forms. (b) We assume that these reactions are triplet-sensitized ($E_T(Me_2CO)$ = 81 kcal/mol, E_T(alkylbenzenes) = ca. 80 kcal/mol) since Me_2CO exclusively absorbs light under these conditions. Phenol **7** does not undergo cyclization due to efficient OH atom abstraction by Me_2CO triplets.

(9) Pyrrolizidine vs indolizidine ring and arene substitution patterns are clearly determined by ^1H and ^{13}C NMR methods.

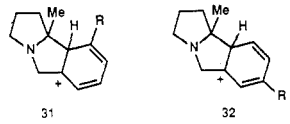
(10) That pyrrolizidines **25** and **26** arise by irradiation of **22** differs from an earlier, incorrect report (ref 3) that **24** is the exclusive product.

(11) Ohga, K.; Yoon, Y. C.; Mariano, P. S. *J. Org. Chem.* **1984**, *49*, 213.

(12) This phenomenon has been observed earlier (ref 4b). Solvent polarity ($Z(Me_2CO)$ = 65.7) might also play a role here.

(13) Direct irradiation reactions of these systems occure via the singlet manifold[2,3] and thus via singlet diradical cation intermediates. Triplet diradical cations generated in the acetone-sensitized process must undergo intersystem crossing prior to cyclization.

process, corresponding to an excited-state Pictet–Spengler cyclization, is synthetically viable.[14]



31 32

Acknowledgment. Financial support for this research by the National Science Foundation (CHE-09589) and the National Institutes of Health (GM-27251) is acknowledged. Purchase of the 400-MHz NMR spectrophotometer used in these studies was aided by an NSF grant (DMB-20157).

(14) Thermal reactions of these systems (F^--induced for SiR_3 analogues) do not yield the cyclization products observed in the photochemical processes.

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Additions and Corrections

Vol. 51, 1986

Kohji Suda,* Fumio Hino, and Chino Yijima. Mechanism of Base-Promoted Eliminative Fragmentations of 2-Alkyl-3-phenyloxaziridines.

Page 4234, the last line of the caption of Figure 1: (*Z*)-**1a** should read (*E*)-**1a**.

Herbert C. Brown,* J. V. N. Vara Prasad, and Ashok K. Gupta. Hydroboration. 78. Reinvestigation of the Hydroboration of N-Substituted-3-pyrrolines. Preparation of *N*-Benzyl-3-pyrrolidinol and (*N*-Benzyl-3-pyrrolidinyl)boronate of Very High Enantiomeric Purity.

Page 4297, eq 4, 5, and 6. The structures of the pyrrolidinols show the wrong configuration at C-3. The configuration at C-3 should be *S*, as noted in the text.

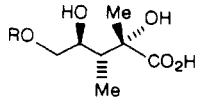
Vol. 52, 1987

Marco Alpegiani and Stephen Hanessian*. A Facile Access to (*R*)-Malic Acid.

Page 278. Column 2, lines 49 and 50 should read: (*R*)-Dimethyl Malate (**3**). A solution containing **2** (2 g, 9.08 mmol) in benzene (20 mL) and ...

Stephen Hanessian* and Peter J. Murray. A Versatile Protocol for the Stereocontrolled Elaboration of Vicinal Secondary and Tertiary Centers of Relevance to Natural Product Synthesis.

Page 1171. Scheme I. Structure **10** should be

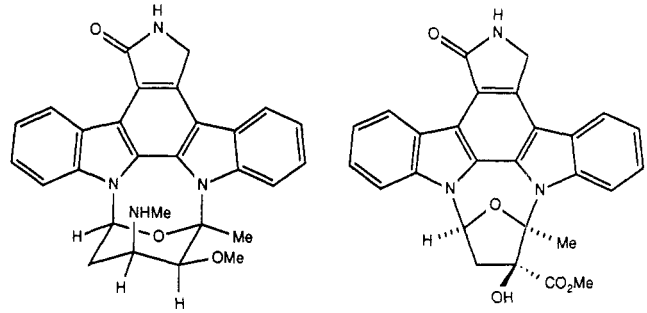


10

Page 1172. Scheme II, c. Change Pd/Al_2O_3 to Rh/Al_2O_3. Scheme II, i. Change room "temperature, 4 days, 72%" to "60 °C, 4 days, 92%".

Richard P. Joyce, James A. Gainor, and Steven M. Weinreb*. Synthesis of the Aromatic and Monosaccharide Moieties of Staurosporine.

Page 1178. The structures of staurosporine (**1**) and K252a (**2**) have been misdrawn. The correct structures are shown below.



1 **2**

Tatsuya Nakano, Shiji Irifune, Shigetoshi Umano, Akihiro Inada, Yasutaka Ishii,* and Masaysa Ogawa*. Cross-Condensation of Cycloalkanones with Aldehydes and Primary Alcohols under the Influence of Zirconocene Complexes.

Page 2244, line 8: δ 200.8 (s), 138.8 (d), 136.1 (s), 40.0 (t), 29.9 (t), 26.8 (t), 23.7 (t), 23.5 (t), 21.9 (t), 13.9 (q) must be δ 202.9 (s), 143.1 (d), 137.7 (s), 42.2 (t), 31.6 (t), 28.8 (t), 27.4 (t), 23.1 (t), 21.2 (t), 13.4 (q).

Page 2244, line 13: δ 201.1 (s), 139.4 (d), 136.6 (s), 40.2 (t), 29.9 (t), 26.9 (t), 23.8 (t), 23.5 (t), 22.6 (t), 21.7 (t), 13.9 (q) must be δ 203.2 (s), 143.4 (d), 136.9 (s), 42.0 (t), 31.1 (t), 29.1 (t), 28.0 (t), 23.6 (t), 22.7 (t), 21.0 (t), 13.7 (q).

Richard W. Thies* and Khushroo P. Daruwala. Substituent Control of Sigmatropic Periselectivity: Application to the Synthesis of (±)-Muscone.

Page 3799. The left-hand structure in Scheme I is not consistent with the anti $LiAlH_4$ reduction stereochemistry observed earlier in steroid systems (van Dijck, L. A.; Lankwerden, B. J.; Vermeer, J. G. C. M. *Recl. Trav. Chim. Pas-Bas* **1979**, *98*, 553 and references cited therein).