treatment of ZGly(N-DHMB)PheOEt gave 83.3% ZGlyPheOEt and 11% HGlyPheOEt; the half-time for DHMB cleavage is 12 min in Tfa and in 3:1 Tfa–CH_2Cl_2.[10] The N-DHMB group is resistant to hydrogenation (Pd, 1 atm, 3 hr).[9]

Other Issues. 1. Racemization. Scheme I is expected to minimize normal racemization processes or other side reactions which occur at the acyl site,[11] but it is potentially vulnerable to epimerization at the amino site of **2**. To test the extent of this problem, we applied our isotopic dilution assay.[11] Reaction of **1** (R = Z-2-^{14}C-Gly) with H-L-PheGlyOEt was followed by conversion to **4** and treatment with Tfa, without purification of intermediates. Reaction times for **1** → **2** of 1.5 and 14 hr (0.2 *M*, CH_3CN) gave 0.1 and 0.3% DL tripeptide, respectively.[12] **2. Diketopiperazines.** The sequence HGlyProX readily forms diketopiperazines.[13] A similar problem is observed for HGly(N-DHMB)XY. When ZGly(N-DHMB)PheOEt was hydrogenolyzed (3 hr, Pd, HOAc), 62% diketopiperazine was isolated. The tripeptide HGly(N-DHMB)-L-LeuGlyOH formed diketopiperazine and HGlyOH slowly in DMSO solution. **3. Solubility.** As noted by Weygand,[9] substitution of *N*-benzyl groups on the amide backbone markedly increases peptide solubility. Unlike their counterparts which lack the N-DHMB group, ZGly(N-DHMB)-L-LeuGlyOH is soluble in chloroform and HGly(N-DHMB)-L-LeuGlyOH is soluble in DMSO. The solubilizing effect in these two cases appears to be at least an order of magnitude. **4. Protection of 1.** In order to be useful as a "safety catch" activated group, **1** must be convertible to an unreactive derivative. Reaction of **1** (R = ZGly) with NaH/DMF and benzyl bromide, followed by acidic ethyl orthoformate, generates 4-methoxy-3-ZGlyO-2-benzyloxybenzaldehyde diethyl acetal, which aminolyzes very slowly with peptide nucleophiles (with HGlyOEt in CH_3CN, $k_2 = 5 \times 10^{-6}$ sec^{-1}, 25°) and which is reconverted to **1** by treatment with Tfa for 1 hr.

Summary. The potential virtues of amide formation by prior amine capture and intramolecular acylation have been summarized previously.[1] Several of these (diminished steric effects on rate, first-order acylation rate, solubilization) have been demonstrated in this system; others are likely but remain to be proved. Although its feasibility awaits testing, the following scheme can be envisaged from the results here obtained. The amino acid ester of **1**, blocked by benzylation and acetal formation, could be introduced at the C terminus of a medium-sized peptide acid by conventional amide-forming reagents. Liberation of **1** at some later stage by Tfa treatment would permit a fragment condensation to yield a peptide bearing the solubilizing N-DHMB group at an N site of its amide backbone. A critical question concerns the minimum ratio of DHMB amide to secondary amide which is required for useful solubility effects. Until these questions are resolved, the importance of Scheme I is the demonstration of the feasibility of a new approach to amide synthesis.

Acknowledgment. Financial support from the National Institutes of Health (GM 13453) is gratefully acknowledged.

References and Notes

(1) D. S. Kemp and F. Vellaccio, Jr., *J. Org. Chem.*, **40**, 3003 (1975).
(2) R. Green and P. Alexander, *Aust. J. Chem.*, **18**, 329 (1965); R. Green and E. Le Mesurier, *ibid.*, **19**, 229 (1966); R. Green and R. Sleet, *ibid.*, **19**, 2101 (1966), **22**, 917 (1969).
(3) Prepared by DCCI coupling of ZGlyOH with 4-methoxy-2,3-dihydroxybenzaldehyde: H. Gross, A. Reiche, and G. Mattley, *Chem. Ber.*, **96**, 308 (1963); K. Campbell, P. Hooper, and B. Campbell, *J. Org. Chem.*, **16**, 1736 (1951).
(4) J. Billman and J. McDowell, *J. Org. Chem.*, **26**, 4137 (1961).
(5) Although **3** is a catechol monoester, it is hindered. No aminolysis of the more activated **2** was observed over 24 hr in the presence of excess amine, nor were concentration effects on aminolysis seen. Rate constants were obtained from NMR measurements.
(6) Strikingly, this result is the opposite of that seen for intermolecular phenyl ester aminolysis.
(7) D. S. Kemp and F. Vellaccio, Jr., *J. Org. Chem.*, preceding paper.
(8) Unless otherwise noted, yields were obtained by isotopic dilution.
(9) F. Weygand, W. Steglich, J. Bjarnason, R. Akhtar, and N. Khan, *Tetrahedron Lett.*, **No. 29**, 3483 (1966); F. Wegand, W. Steglich, J. Bjarnason, R. Akhtar, and N. Chytil, *Chem. Ber.*, **101**, 3623 (1968).
(10) E. Schnabel, H. Klostermeyer, and H. Berndt, Proc. *Eur. Pept. Symp., 11th, 1973*, 69 (1973).
(11) D. Kemp, S. Wang, S. Busby, and G. Hugel, *J. Am. Chem. Soc.*, **92**, 1043 (1970).
(12) Since the optical purity of the amine is unknown, the racemization in 1.5 hr must be taken to lie in the range of 0.02 to 0.1%.
(13) E. Schroder and K. Lubke, "The Peptides", Academic Press, New York, N.Y., 1965, p 148.

Department of Chemistry
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139

D. S. Kemp*
James A. Grattan
James Reczek

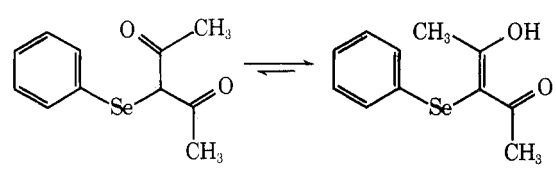
Received August 15, 1975

Heteroatom Directed Photoarylation. Photochemistry of an Organoselenide

Summary: Aryl selenide **1** undergoes photocyclization–rearrangement to give benzoselenophene **4**.

Sir: While the existence of carbonyl and thiocarbonyl ylides has been established,[1] the generation of selenocarbonyl ylides has not been reported.[2] In this paper, we communicate preliminary results concerning possible generation and rearrangement of a selenocarbonyl ylide and describe the first preparative organoselenium photoreaction.[3]

Recent success with photogeneration of carbonyl[4] and thiocarbonyl ylides[5] from 2-aryloxyenones and 2-thioaryloxyenones, with subsequent rearrangement to dihydrofurans and dihydrothiophenes, suggested that selenocarbonyl ylides might be generated from similarly structured 2-selenoaryloxyenones. Because of the known propensity of selenides to eject elemental selenium on exposure to light,[6] we initiated the investigation with aryl selenide **1**, which via enolic form **1b** was expected to give a relatively stable photoproduct, i.e., **4**.

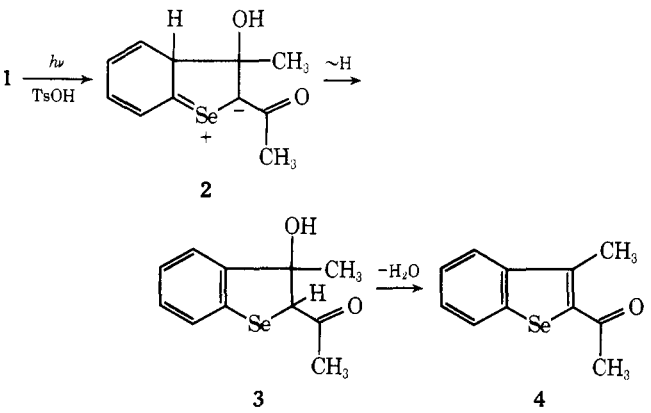


1a **1b**

The elegant method for α-arylselenenylation of ketone enolates developed principally by Sharpless[7] and Reich[8] was used to prepare **1**. Reaction of a suspension of the sodium enolate of acetylacetone in tetrahydrofuran with benzene selenyl bromide gave the required phenyl selenide (**1**), which exists predominately in enolic form **1b** (NMR analysis, 4 *M* **1** in $CDCl_3$, ratio of **1a**:**1b** = 1:9).

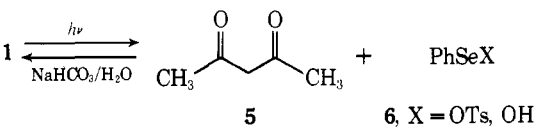
Preparative-scale Pyrex-filtered irradiation of **1** in benzene solution (0.05 *M*) saturated with *p*-toluenesulfonic acid at ~15° while purged with argon gave 2-acetyl-3-methylbenzo[*b*]selenophene (**4**) in 60% isolated yield (mp 93–95°, lit.[9] mp 94°). The mechanism[10] for the transformation **1** → **4** presumably involves photocyclization of **1b** to selenocarbonyl ylide (**2**), which undergoes rearrangement

to β-hydroxy ketone 3; acid-catalyzed dehydration of 3 would give benzoselenophene (4).



That 3 actually is an intermediate in the conversion of 1 → 4 was demonstrated by photolysis of 1 in benzene-d_6 containing acetic acid (1 equiv) in a degassed[11] NMR tube; extended irradiation led to a mixture of products (vide supra), a major component (~30%) of which gave NMR singlets at δ 1.92 (3 protons), 2.31 (3 protons), and 4.86 (1 proton) and has been assigned structure 3 on the basis of chemical reactivity. Thus, treatment of the photolysis mixture with a catalytic amount of *p*-toluenesulfonic acid resulted in rapid disappearance of the three NMR singlets attributable to 3 together with an enhancement of absorptions due to the methyl resonances of benzoselenophene 4 (δ 2.60 and 2.73).

The photochemistry of 1 also includes cleavage of carbon–selenium bonds. Photoreaction of 1 in benzene-d_6 with *p*-toluenesulfonic acid was carefully monitored by NMR spectroscopy;[11] after brief irradiation, NMR analysis above δ 6.00 revealed that 1 (19%), benzoselenophene (4, 54%), and acetylacetone (5, 27%) were present. Interestingly, treatment of the crude photoreaction with aqueous sodium bicarbonate solution resulted in the disappearance of acetylacetone with concomitant formation of selenide 1. Thus, a portion of photoexcited 1 must undergo carbon–selenium bond cleavage to generate acetylacetone (5) and PhSeX (6); on treatment with base, 1 is regenerated from 5 and 6.[12] Formation of considerable acetylacetone occurred when 1 was irradiated in benzene–acetic acid solution, and in pure benzene photocleavage was the predominant reaction.



The high yield obtained in the conversion of 1 → 4 suggests that analogous photoreactions may be useful for synthesis of a variety of aryl annelated selenophenes. Perhaps more importantly, it is clear that appropriately structured organoselenium compounds may undergo interesting and synthetically useful photoreactions. Work in this area will continue.

Acknowledgment. This work was supported by the National Institutes of Health (Grant No. GM 21159-01).

References and Notes

(1) T. Do-Minh, A. M. Trozzolo, and G. W. Griffin, *J. Am. Chem. Soc.*, **92**, 1402 (1970); D. R. Arnold and L. A. Karnischky, *ibid.*, **92**, 1404 (1970); J. Buter, S. Wassenaar, and R. M. Kellogg, *J. Org. Chem.*, **37**, 4045 (1972).
(2) Preparation of highly stabilized selenonium ylides (three substituents attached to selenium) has been reported. For example, see R. D. Hughes and K. I. Kuriyan, *J. Chem. Soc.*, 1609 (1935); D. Lloyd and M. I. C. Singer, *Chem. Commun.*, 390 (1967); and J. Stackhouse, G. H. Senkler, B. E. Maryanoff, and K. Mislow, *J. Am. Chem. Soc.*, **96**, 7835 (1974).
(3) Previous reports of solution-phase photochemistry of organoselenium compounds are W. Stanley, M. R. VanDeMark, and P. L. Kumler, *Chem. Commun.*, 700 (1974) and D. L. Ross, J. Blanc, and F. J. Matticoli, *J. Am. Chem. Soc.*, **92**, 5750 (1970).
(4) A. G. Schultz and R. D. Lucci, *J. Org. Chem.*, **40**, 1371 (1975).
(5) A. G. Schultz, *J. Org. Chem.*, **39**, 3185 (1974).
(6) "Organic Selenium Compounds: Their Chemistry and Biology", D. L. Klayman and W. H. H. Günther, Ed., Wiley-Interscience, New York, N.Y., 1973, Chapter 6.
(7) K. B. Sharpless, R. F. Lauer, and A. Y. Teranishi, *J. Am. Chem. Soc.*, **95**, 6137 (1973).
(8) H. J. Reich, J. M. Renga, and I. L. Reich, *J. Org. Chem.*, **39**, 2133 (1974).
(9) L. Christiaens and M. Renson, *Bull. Soc. Chim. Belg.*, **77**, 153 (1968).
(10) A. G. Schultz and M. B. DeTar, *J. Am. Chem. Soc.*, **96**, 296 (1974).
(11) These photoreactions were performed in clear Pyrex NMR tubes degassed by four freeze–pump–thaw cycles with an oil-diffusion-pump vacuum and were examined periodically with a Varian a-60A NMR spectrometer (TMS external standard).
(12) It is of interest to note that ketones undergo an efficient acid-catalyzed selenenylation with ArSeX in ethyl acetate solution; see ref 7. With β diketones, however, the equilibrium is reversed and acid-catalyzed selenenylation is not possible: private communication, K. B. Sharpless.

Department of Chemistry **Arthur G. Schultz**
Cornell University
Ithaca, New York 14853

Received September 23, 1975

Asymmetric Synthesis and Absolute Stereochemistry of Some Cis and Trans Diols

Summary: A general method for the preparation of optically active cis and trans diols by asymmetric reduction of α-acetoxy ketones using a 2:1 Darvon–lithium aluminum hydride complex, is described. The absolute stereochemistry of these diols has been established by chemical methods.

Sir: In the course of some studies on the absolute stereochemistry of a variety of metabolites, cis dihydrodiols[1a] obtained from the microbial metabolism of aromatic substrates and trans dihydrodiols prepared by enzymatic hydration of arene oxides,[1b] we encountered difficulties in obtaining sufficient quantities of these compounds. Therefore, we have developed chemical methods for preparing optically active dihydro derivatives of several metabolites. The absolute stereochemistry of these compounds has been determined by chemical transformations to substances of known absolute stereochemistry.

We first chose the asymmetric synthesis of 1, a dihydro derivative of a metabolite of biphenyl[2] by a species of *Beijerinckia*. Our approach focused on the chiral reduction of