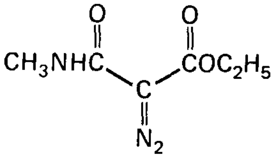
Tetrahedron Letters,Vol.24,No.3,pp 233-236,1983 0040-4039/83/030233-04$03.00/0
Printed in Great Britain

PHOTOLYSIS STUDIES OF α-DIAZOAMIDES
THE EFFECT OF CARBOXAMIDE SUBSTITUENTS ON SELECTIVITY RATIOS

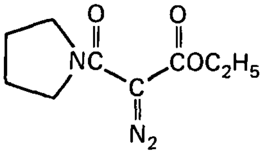
John Wydila and Edward R. Thornton*
Department of Chemistry
University of Pennsylvania
Philadelphia, Pa. 19104

Summary: Photolysis of several α-diazoamide compounds in mixed solvent systems has resulted in unusually large OH:CH insertion selectivity ratios of 10^3-10^4:1.

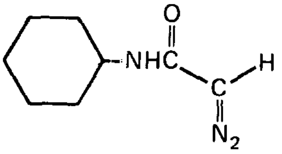
Substituents alpha to the diazo carbon have been shown to influence the selective behavior of the photochemical intermediates in photolysis reactions of diazo compounds.[2-3] In order to probe the effect of the carboxamide substituent on the photochemistry of the diazo group,[4] compounds 1, 2,[5] and 3 have been prepared.



1



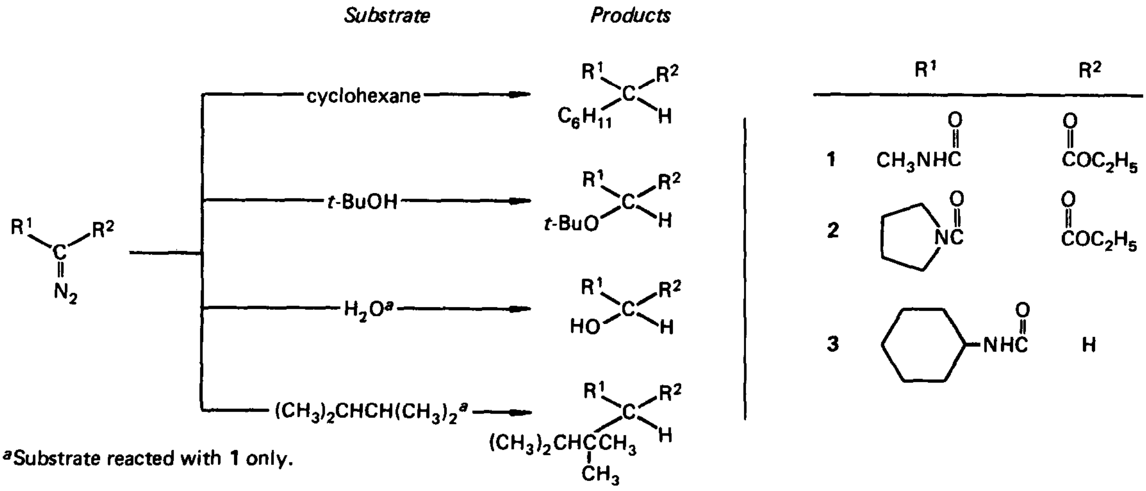
2



3

Photolysis of these α-diazoamides in several hydroxylic or aliphatic solvents at 254 nm, 33° C has yielded the corresponding OH and CH insertion products depicted in Scheme I. The structure of each of the photoproducts has been confirmed by ^{1}H NMR, ^{13}C NMR, IR and elemental microanalysis.

SCHEME I



ᵃSubstrate reacted with 1 only.

Reaction of **1** in t-butyl alcohol and 2,3-dimethylbutane yielded the respective OH and 3° CH insertion products with no isolated 1° CH insertion product in either case, indicating a very discriminating intermediate(s). In order to establish a quantitative measure of α-diazoamide photochemical behavior, selectivity ratios were determined by photolyzing **1** through **3** individually in selected binary mixtures of the substrates given in Scheme I.[6] The relative substrate concentrations were varied over a wide range and the product ratios were calculated for each substrate mixture by comparing the integration of the appropriate malonyl proton in the case of **1** and **2** and the amide proton in the case of **3** in the 250 MHz ^{1}H NMR spectra of the photoproduct mixture. In each case the integrated peak was fully resolved and corresponded exactly to the authentic purified product. The product ratios were plotted as a function of the relative substrate concentrations and the selectivity ratios were obtained from the slope of a linear least-squares correlation of the data. The results appear in Table I.

Table I

α-Diazoamide Selectivity Ratios[a]

compound	OH:2° CH[b]	OH:OH[c] (HOH:ROH)	3° CH:2° CH[d]
1	1.0×10^4	1.9	1.7
2	5.4×10^3	-	-
3	1.1×10^3	-	-

a) The data have been statistically corrected for the number of available reactive sites on each substrate molecule. For further details, cf: J. Wydila, Ph.D. Dissertation in Chemistry, University of Pennsylvania, 1982. b) Reaction solvent consisted of mixtures of t-butyl alcohol and cyclohexane. c) Reaction solvent consisted of mixtures of t-butyl alcohol and water. d) Reaction solvent consisted of mixtures of cyclohexane and 2,3-dimethylbutane.

The data in Table I indicate that the high OH:CH selectivity ratio is maintained by each of the three α-diazoamide compounds. In order to compare these results with the effect of α-alkoxycarbonyl substituents on diazo photochemistry, the selectivity ratios for diazoacetate esters have been calculated using the data of Do Minh *et al.*[7]

Table II: Diazoacetate Selectivity Ratios[a]

ester	OH:1° CH
methyl	7.2
ethyl	17
isopropyl	48

[a] substrate: t-butyl alcohol

Comparing the OH:CH selectivity ratios of the diazoacetate esters with the OH:CH selectivity ratio of compound **3**, the α-diazoamide selectivity ratio is found to be between one to two orders of magnitude higher than those of the corresponding α-diazoesters. Thus the carboxamide substituent is shown to increase the yield of OH insertion product relative to the ester group.

It is proposed that the influence of the carboxamide substituent is an electronic effect upon the photoreaction intermediates. It is not the result of an interaction between the alcohol and the α-diazoamide prior to irradiation. This contention is supported by our investigation. The UV spectrum of compound 1 in t-butyl alcohol is virtually identical to the UV spectrum of 1 in cyclohexane. This tends to rule out any direct interaction between the hydroxyl group and the diazo moiety. Further, 2 which was synthesized to preclude any hydrogen bond interaction between the amide proton of 1 and the oxygen of the hydroxy group of the alcohol yielded a OH:CH selectivity ratio upon photolysis that was equal to the selectivity ratio of 1 within a factor of two. It must be concluded that the source of the high OH:CH selectivity ratio cannot be attributed to a preferential association between the alcohol and the diazo compound. Photolysis of 1 in H_2O/t-butyl alcohol mixtures demonstrated a slight preference of the carbene for the water hydroxyl residue which was anticipated on the basis of relative acidities.[8]

The $3^o:2^o$ CH selectivity ratio, 1.7:1, obtained for 1 was close to the 1.5:1 ratio calculated for ethyl diazomalonate from the data of Doering and Knox.[9] Regarding the $3^o:1^o$ CH selectivity ratio, no 1^o CH insertion product could be detected by MPLC when 1 was photolyzed in 2,3-dimethylbutane, suggesting that this ratio may be very large for α-diazoamide compounds. Photolysis of the corresponding alkyl diazomalonate esters in 2,3-dimethylbutane resulted in a $3^o:1^o$ CH selectivity ratio of 13:1.[9,10]

In summary, the influence of the carboxamide substituents on the photochemistry of diazo compounds has been found to be consistent with an increased electrophilic character of the reaction intermediates in regard to OH insertion and more discriminative behavior with regard to CH insertion. The use of mixed solvent systems permitted the quantification of the high selectivity factors determined in this study and the technique would be applicable to gauging other effects in photochemical reactions (e.g., the effect of steric hindrance on the 3^o CH insertion could be studied using mixtures of 2,3-dimethylbutane and isobutane). Although complete characterization of all photochemical intermediates involved in these studies is not yet possible, the selectivity ratios are nevertheless useful for their predictive function and may prove to be valuable assets to biological photolabeling investigations.[11]

References

1. This work has been supported by National Institutes of Health Grants GM-22,647 and NS-16,826 and by National Science Foundation Grant BNS 77-04019. Previous paper: D. T. T. Su and E. R. Thornton, J. Am. Chem. Soc. 100, 1871 (1978).

2. W. von E. Doering, L. H. Knox, and M. Jones, Jr., J. Org. Chem., 24, 136 (1959).

3. a) D. Seyferth, W. A. Mai, and M. E. Gordon, J. Org. Chem., 55, 1993 (1970).
b) H. Tomioka, W. Itoh, S. Yamakawa, and Y. Izawa, J. Chem. Soc., Perkin Trans. 2, 603 (1980).

4. a) H. Chaimovich, R. J. Vaughan, and F. H. Westheimer, J. Am. Chem. Soc., 90, 4088 (1969). b) R. Rando, J. Am. Chem. Soc. 92, 6706 (1970). c) R. Rando, J. Am. Chem. Soc., 94, 1620 (1972). d) H. Tomioka, H. Kitagawa, and Y. Izawa, J. Org. Chem., 44, 3072 (1979).

5. G. Lowe and J. Parker, J. Chem. Soc., Chem. Commun., 577 (1971).

6. Yields for the CH insertion products ranged from 9.0% for the 2 cyclohexane insertion product to 60% for the 1 cyclohexane insertion product. Yields for the OH insertion products ranged from 40% for the 3 t-butyl alcohol insertion product to 75% for the 1 t-butyl alcohol insertion product.

7. T. Do Minh, O. P. Strausz, and H. E. Gunning, J. Am. Chem. Soc., 91, 1261 (1969).

8. W. J. Baron, M. R. Decamp, M. E. Hendrick, M. Jones, Jr., R. H. Levin, and M. B. Sohn, Chapter 1 in "Carbenes," Vol. 1, R. A. Moss and M. Jones, Jr., Eds., Wiley-Interscience, New York, 1973.

9. W. von E. Doering and L. H. Knox, J. Am. Chem., Soc., 83, 1989 (1961).

10. M. Jones, Jr., W. Ando, M. E. Hendrick, A. Kulczyk, Jr., P. M. Howley, K. M. Hummel, and N. S. Malauent, J. Am. Chem. Soc., 94, 7469 (1972).

11. V. Chowdhry and F. H. Westheimer, Ann. Rev. Biochem. 48, 293 (1979).

(Received in USA 25 August 1982)