

and D. D. Newkirk and G. J. Gleicher, *J. Amer. Chem. Soc.*, **96**, 3543 (1974).

- (19) The benzylic hydrogens of the two toluenes were integrated relative to *tert*-butylbenzene.
- (20) E. L. Eliel, P. H. Wilken, F. T. Fang, and S. H. Wilen, *J. Amer. Chem. Soc.*, **80**, 3303 (1958); K. M. Johnston and G. H. Williams, *J. Chem. Soc.*, 1446 (1960).
- (21) (a) Since only 0.24 M docosane is produced, and since  $k_d/k_c$  for primary radicals is 0.15,<sup>22</sup> only 0.036 M, or 20%, of the undecane is produced in disproportionation reactions. This undecane does not interfere because we follow substrate disappearance, not product appearance. (b) The average decrease in the concentration of the substituted toluenes, 12% (0.1 M), is less than the amount of undecane formed (0.18 M). We cannot account for all of the excess undecane, but ca. 0.03 M of it arises from disproportionation. (c) In a solution of 0.8 M toluene in benzene, the amount of undecylbenzene formed (0.024 M) is less than half that formed by thermolysis of 0.6 M LPO in neat benzene (0.053 M). Shelton, in his study of homolytic aromatic cyclohexylation, reports a similar change in addition product (arylcyclohexane) yield when the solvent was changed from toluene to benzene. J. R. Shelton and C. W. Uzelmeier, *J. Amer. Chem. Soc.*, **88**, 5222 (1966), especially p 5223. (d) Important termination reactions are U• combinations to give docosane and benzyl radical combination to form bibenzyls.
- (22) M. J. Gibian and R. C. Corley, *Chem. Rev.*, **73**, 441 (1973).
- (23) Preliminary studies of methyl radical addition to substituted benzenes indicate a  $\rho \approx 0$  and an abstraction to addition ratio for toluene greater than ten.<sup>24a</sup> Other studies of addition/abstraction ratios have been reported: (1) Pryor's compilation of his work<sup>24b</sup> and that of Szwarc<sup>24c</sup> for methyl radicals predicts a relative reactivity of toluene to benzene of 2:1. Since these workers obtained data at different temperatures, this ratio may not be very accurate. (2) Eliel approximates a ratio of rate of methyl radical abstraction from the side chain of toluene to rate of abstraction of hydrogen from the toluene ring of 7.5.<sup>24d</sup> (3) In his study of homolytic aromatic cyclohexylation,<sup>21c</sup> Shelton reports that addition to toluene is a minor process compared to abstraction of benzylic protons. Thus, although the precise magnitude of the addition/abstraction ratio is uncertain, it is evident that alkyl radicals abstract benzylic hydrogens in preference to addition to the aromatic ring. Therefore, addition occurs to a lesser extent than abstraction in our system. Furthermore, some addition does not prevent our nmr analysis from determining the amount of toluene which undergoes abstraction.
- (24) (a) W. A. Pryor, W. A. Davis, Jr., and J. H. Gleaton, unpublished data; (b) W. A. Pryor, D. L. Fuller, and J. P. Stanley, *J. Amer. Chem. Soc.*, **94**, 1632 (1972); (c) M. Szwarc and J. H. Binks, "Theoretical Organic Chemistry," Kekule Symposium, 1958, Butterworths, London, 1958, p 262; (d) S. H. Wilen and E. L. Eliel, *J. Amer. Chem. Soc.*, **80**, 3309 (1958).
- (25) The nmr method is also insensitive to other reactions which do not affect the benzylic proton peak such as abstraction of methoxy protons from the methylanisoles. These methoxy protons are about as reactive as the benzylic protons. See note 24 in ref 8.
- (26) R. W. Henderson and R. D. Ward, Jr., *J. Amer. Chem. Soc.*, **96**, 7556 (1974).
- (27) NOTE ADDED IN PROOF. A. A. Zavitsas has informed us (private communication) that he has obtained a rho of about +0.4 for this reaction.

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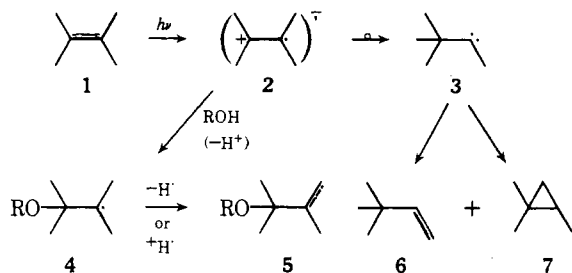
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### Photochemistry of Alkenes. III. Formation of Carbene Intermediates<sup>1</sup>

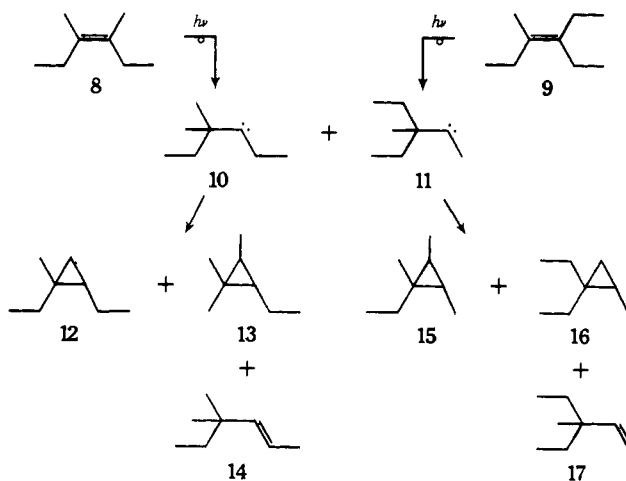
Sir:

Recent reports from these laboratories have shown that tri- and, especially, tetrasubstituted alkenes display a novel behavior on direct irradiation in hydroxylic media which leads principally to the formation of a mixture of saturated

#### Scheme I



#### Scheme II



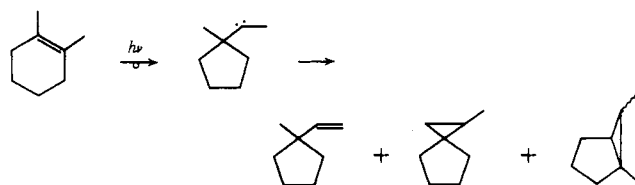
and unsaturated ethers, as depicted in Scheme I for the conversion of 2,3-dimethyl-2-butene (**1**) to the mixture of ethers **5**.<sup>1</sup> By contrast, in nonhydroxylic media, such as ether or octane, rearrangement to a 1.03:1 mixture of the 1-butene **6** and the cyclopropane **7** occurs.<sup>2</sup> Moreover, in alcoholic solvents of low nucleophilicity substantial amounts of **6** and **7** are formed in competition with the ethers **5**; thus the ratio **5**:(**6** + **7**) decreases in the order methanol > ethanol > 1-propanol > 1-butanol.

The formation of ether products **5** has been interpreted in terms of nucleophilic trapping of the  $\pi, R(3s)$  Rydberg excited state (**2**).<sup>1</sup> It is attractive to interpret the formation of **6** and **7** in terms of competing rearrangement of the excited state **2** to the carbene intermediate **3**, especially since **3** is known to undergo rearrangement to afford **6** and **7** in the same ratio when generated by other means.<sup>3</sup> We wish now to report additional evidence which strongly supports the generation of carbene intermediates and indicates that the process is general for most tetrasubstituted alkenes on direct irradiation in nonnucleophilic media.

Thus, as shown in Table I, 3,4-dimethyl-3-hexene (**8**) is converted on irradiation in pentane solution to a mixture of the cyclopropyl and olefinic products **12**–**17**,<sup>4</sup> as would be expected from initial photorearrangement to the two possible carbene intermediates **10** and **11** (Scheme II). Moreover, the isomeric olefin **9**, which should undergo rearrangement to the same two carbene intermediates, affords a mixture of the same products **12**–**17**. Furthermore, although the carbene intermediates **10** and **11** are apparently formed in different relative amounts from olefins **8** and **9**, the three products **12**–**14** are formed in similar ratios from each olefin and by independent generation of carbene **10** from the corresponding tosylhydrazone. Likewise the products **15**–**17** are formed in similar ratios on irradiation of either olefin or on independent generation of carbene **11**.<sup>5</sup>

We have observed photoarrangement of a number of other tetrasubstituted alkenes to carbene-derived products, as exemplified in Scheme III for 1,2-dimethylcyclohexene.<sup>6</sup> Although the proposal that the carbene intermediates arise via rearrangement of the  $\pi, R(3s)$  excited state requires fur-

#### Scheme III



**Table I.** Comparison of Photoproducts from Olefins **8** and **9** and Products from Independent Generation of Carbenes **10** and **11**

Origin	Yield, % <sup>a</sup>						
	Starting Olefin	12	13	14	15	16	17
Olefin <b>8</b> <sup>b</sup>	25	4	1	9	9	5	13
Olefin <b>9</b> <sup>b</sup>	21	6	2	30	9	4	5
Carbene <b>10</b> <sup>c</sup>		7	3	83			
Carbene <b>11</b> <sup>c</sup>					51	27	22

<sup>a</sup> Determined by chromatography through silver nitrate impregnated alumina followed by gas chromatographic analysis. <sup>b</sup> Irradiations were conducted on 115-ml pentane solutions containing 2.58 g of olefin using a 450-W Hanovia mercury arc and quartz immersion well. <sup>c</sup> Generated by treatment of the corresponding tosylhydrazone with sodium hydride in diglyme at 170°.

ther study, it is consistent with the fact that these olefins all afford a mixture of saturated and unsaturated ethers on irradiation in methanol,<sup>1,7</sup> a behavior attributable to reaction *via* a low-lying  $\pi, R(3s)$  excited state.<sup>1</sup> If the proposal is correct, rearrangement to carbenes represents the second observed chemical behavior of the  $\pi, R(3s)$  Rydberg excited state in solution, along with nucleophilic trapping in hydroxylic media.<sup>1</sup>

Additional studies are in progress to elucidate further the nature, relative energies, and chemical properties of the various excited states of alkenes.

**Acknowledgment.** Support of this research by the U.S. Army Research Office is gratefully acknowledged.

## References and Notes

- (1) For part II see P. J. Kropp, E. J. Reardon, Jr., Z. L. F. Gaibel, K. F. Williard, and J. H. Hattaway, Jr., *J. Amer. Chem. Soc.*, **95**, 7058 (1973).
- (2) Also formed in both hydroxylic and nonhydroxylic media is the isomer 2,3-dimethyl-1-butene. Simple double bond shifts without concomitant skeletal rearrangement are ubiquitous in olefin photochemistry and will be the subject of a separate report. All of the olefins reported in this communication undergo positional isomerization in competition with the described photochemical behavior.
- (3) L. Friedman and H. Shechter, *J. Amer. Chem. Soc.*, **81**, 5512 (1959).
- (4) Products were identified by direct comparison with commercial specimens or with material independently synthesized. Satisfactory analytical data were obtained for all novel compounds.
- (5) Due to poor resolution, the photoproduct yield data from olefins **8** and **9** are only approximate. Moreover, since relative product yields from carbenes are highly dependent on solvent, temperature, and the mode of generation, precise quantitative comparisons between the photochemical data and the data from independent generation of the carbenes are probably not meaningful.
- (6) The formation of carbene-derived products from benzene-photosensitized rearrangement of 3-phenylcycloheptene was recently reported; see S. J. Cristol and C. S. Ilenda, 167th American Chemical Society National Meeting, Los Angeles, Calif., April 1974, Abstract ORGN 113. It is not clear what relation, if any, this has with the photobehavior of the tetrasubstituted alkenes reported here, none of which afforded carbene-derived products on sensitization with *p*-xylene.
- (7) P. J. Kropp and H. G. Fravel, in preparation.
- (8) Alfred P. Sloan Research Fellow.

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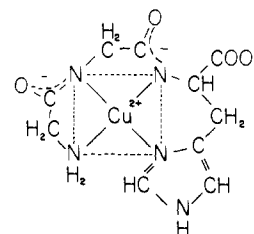
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## Ligand Displacement of Glycylglycyl-L-histidine from Its Copper(II) Complex. A Proton-Assisted Mechanism Initiated at a Nonterminal Position

Sir:

The presence of L-histidine as the third amino acid residue in tri- and tetrapeptides enhances their ability to bind copper.<sup>1</sup> We find that coordination by the imidazole group

causes large differences in the stability, in the pH response, in the electronic spectrum, and in the kinetics behavior of Cu<sup>II</sup> when it is bound to glygly-L-his (structure I) rather



than to glyglygly. This work concerns the reactions of Cu(H<sub>2</sub>glygly-L-his)<sup>-</sup>, which is the main species present in solution between pH 5 and 10. (An additional loss of a proton from the pyrrole nitrogen to form Cu(H<sub>3</sub>glygly-L-his)<sup>2-</sup> has a pK<sub>a</sub> value of 10.7.<sup>2</sup>) Histidine is the third amino acid residue in serum albumin (human, bovine and rat) and it has been proposed that Cu<sup>II</sup> binds to serum albumin using the same nitrogen donors shown in I.<sup>3-6</sup> We find that the kinetics of transfer of Cu<sup>II</sup> from glygly-L-his to triethylenetetramine (trien) or to EDTA closely parallels the transfer of Cu<sup>II</sup> from bovine serum albumin to EDTA<sup>7</sup> or from human serum albumin to trien or EDTA. The mechanism of the Cu(H<sub>2</sub>glygly-L-his)<sup>-</sup> reaction (and the parallel reactions of Cu<sup>II</sup> in serum albumin) is unusual because the displacement process for this tripeptide starts at a central donor group (a peptide nitrogen) rather than at one of the terminal donor groups (the imidazole or the amino nitrogen).

Previous studies<sup>8-11</sup> of the displacement reactions of Cu<sup>II</sup> from glycyl, L-alanyl, and L-leucyl tripeptide complexes have shown the existence of two main reaction pathways: (1) proton transfer to a peptide nitrogen followed by rapid solvent or ligand displacement, but with no rate dependence on the attacking ligand, and (2) nucleophilic attack by chelating ligands which show a high degree of steric selectivity. The nucleophilic pathway, when it is not sterically hindered, predominates over the proton-transfer mechanism even in neutral solutions. As a result the rates of displacement of Cu<sup>II</sup> (and Ni<sup>II</sup>) from the tripeptide complexes increase with increasing pH because the less-protonated chelating ligands are better nucleophiles. Thus, for the trien reactions with the gly, L-ala, and L-leu tripeptides, the reactivity is H<sub>2</sub>trien<sup>2+</sup> ≪ Htrien<sup>+</sup> < trien. On the other hand, a ligand such as EDTA, with sterically hindered tertiary nitrogens, is a relatively poor nucleophile, so that solvent dissociation and various catalyzed pathways become important. The rate contribution of HEDTA<sup>3-</sup> with (Cu(H<sub>2</sub>glyglygly)<sup>-</sup>) is not significant and the rate constant for EDTA<sup>4-</sup> is quite small (600 M<sup>-1</sup> sec<sup>-1</sup>) compared to the rate constant for trien (1.1 × 10<sup>7</sup> M<sup>-1</sup> sec<sup>-1</sup>) with Cu(H<sub>2</sub>glyglygly)<sup>-</sup>.

The kinetics behavior of Cu(H<sub>2</sub>glygly-L-his)<sup>-</sup> is very different from the glycyl, L-alanyl, and L-leucyl tripeptides. Table I compares the rate constants for a number of reactions of the copper complexes of glyglygly and glygly-L-his. The presence of histidine as the third group in the tripeptide reduces the rate of the acid dissociation pathway by a factor of 25 and reduces the rate of solvent dissociation by a factor of 160. (The solvent and acid pathways cause partial dissociation of the tripeptides from copper and are followed by rapid reaction of additional acid or other complexing agents.) However, the most striking difference is in the rate of direct attack by trien which is a factor of 2 × 10<sup>7</sup> slower for glygly-L-his. This is consistent with the behavior of other reactions of peptide complexes which show the importance of the accessibility of equatorial sites for nucleophilic