tion between sensitizer and D were eliminated as possibilities by observing that neither sensitizer nor D was consumed on prolonged irradiation under quenching conditions.

Because published data on singlet lifetimes of aryl ketones and rates of radiationless decay for olefins are few and of limited accuracy, a clear distinction between the proposed mechanisms cannot be made. We strongly tend to support the hypothesis of vibrational quenching, and work is continuing on this problem.

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Some Unusual Acid-Catalyzed Rearrangements of Glycidic Esters

Sir:

The acid-catalyzed rearrangement of glycidic esters usually results in the formation of pyruvic esters,[1] the only exception being an earlier report by Tiffeneau and Levy[2] who claimed to have obtained ethyl α-formylphenylacetate (IIIa) from ethyl β-phenylglycidate (Ia). However, they also reported that ethyl β-methyl-β-phenylglycidate (Ib) yielded the pyruvic ester IIb. Following these apparently anomalous results, House, *et al.*,[1] reinvestigated both reactions using boron trifluoride and convincingly proved the structure of the rearranged product from Ia to be ethyl phenylpyruvate (IIa), not the reported aldehyde IIIa. Although the rearrangement of Ib was repeated by these authors, the structure of the product was not questioned since it was in harmony with the established pattern of behavior for glycidic esters.

We wish to report that the structure for the rearranged product from Ib was in error and that an unprecedented skeletal rearrangement with carbethoxy migration had in fact taken place, yielding ethyl α-formyl-α-methylphenylacetate (IIIb).[3] In our hands, exposure of Ib to boron trifluoride resulted in a product, mol wt 206 (mass spectroscopy), having the properties reported by House, *et al.*,[1] and ascribed to IIb (2,4-dinitrophenylhydrazone melting at 161° and semicarbazone at 161–63°). The nmr spectrum in CCl_4 displayed, in addition to the aromatic and ester protons, a methyl signal at δ 1.6 as well as an aldehyde signal at δ 10.8, both appearing as sharp singlets. These signals were also present in the spectrum of the 2,4-DNP derivative at δ 1.9 and 8.0, respectively. The above data unequivocally support structure IIIb for the rearranged product from Ib.

The above rearrangement is not exceptional since we observed that β-phenylglycidic esters having α- and/or β-alkyl substituents behave similarly. For example, when ethyl α-methyl-β-phenylglycidate (Ic) was rearranged in hexane, it yielded ethyl α-phenylacetoacetate (IIIc) which was identified by nmr and mass spectroscopy and by comparing the melting point and mixture melting point of its 2,4-DNP derivative with an authentic sample. Similarly, Id gave IIId when treated with boron trifluoride in benzene.

Although the nature of the substituents at either the α or the β position does not explain why Ia behaved normally to give a pyruvate, while Ib, Ic, and Id rearranged with the migration of a carbethoxyl, it is clear that a carbonium ion character at the β position (after protonation and epoxide ring opening) accounts for these as well as all the known acid-catalyzed isomerizations of glycidic esters. The location of a carbonium ion adjacent to a carbonyl is usually prohibited, but we found that the electrostatic repulsion of adjacent positive charges can be overcome by substantially stabilizing the carbonium ion adjacent to the ester, for instance with a phenyl substituent.[6] This represents a second synthesis of esters having a β-carbonyl function from glycidic esters, this time without involving a carboethoxy migration. For instance, ethyl α-phenylglycidate (Ie) and ethyl β-methyl-α-phenylglycidate (If) gave the "abnormal" products IVe and IVf, respectively. However, the β-dimethyl-α-phenylglycidate Ig gave the normal product, the pyruvate IIg.

All these rearrangements took place very cleanly upon bubbling boron trifluoride through a benzene solution of the glycidic ester for 30 min at room temperature. After decomposition of the BF_3 complex with aqueous sodium chloride and evaporation of the solvent, a carbon tetrachloride extract of the residue gave an nmr spectrum which, with one exception,[9] was that of the compounds reported above, in pure state.

These results indicate that, while a benzylic carbonium ion adjacent to a carbethoxy is favored over an aliphatic β-carbonium ion which is primary or secondary, it is not favored over one which is tertiary. Finally, our results indicate that the migratory aptitude to a carbonium ion in this series follows the order phenyl > carbethoxy > methyl.[10] While all three groups migrate individually in preference to it, the position of hydrogen in this sequence remains to be ascertained since its transfer from the α to the β position may take place through deprotonation–protonation as well as through hydride shift.

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[1] H. O. House, J. W. Blaker, and D. A. Madden, *J. Am. Chem. Soc.*, 80, 6386 (1958).

[2] M. Tiffeneau and J. Levy, *Anales Soc. Quim. Argentina*, 16, 144 (1928).

[3] The preferential acid-catalyzed migration of a carbalkoxy group over an alkyl substituent has already been observed, but only in aromatization reactions.[4,5]

[4] S. Inayama and M. Yanagita, *J. Org. Chem.*, 27, 1465 (1962).

[5] D. E. McGreer and Y. Y. Wigfield, *Can. J. Chem.*, 47, 2095 (1969).

[6] A similar situation exists in the α,β-epoxyketone series and has been discussed by House, *et al.*,[7] However, in contrast to some epoxy ketones, all the isomeric *cis* and *trans* glycidic esters which we studied[8] yielded the same rearrangement product, thus providing additional support to the intermediacy of a carbonium ion.

[7] H. O. House, D. J. Reif, and R. L. Wasson, *J. Am. Chem. Soc.*, 79, 2490 (1957).

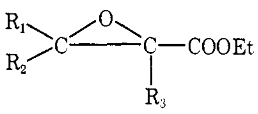
[8] Glycidic esters Ib, Ic, and Id were prepared by the Darzens reaction, while Ie, If, and Ig were obtained by epoxidation of the corresponding α,β-unsaturated esters with *m*-chloroperoxybenzoic acid.

[9] The isolated yield of IVe (as the 2,4-DNP derivative) from the rearrangement of Ie was only 20%.

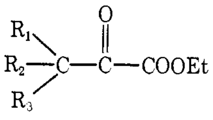
[10] The migration of dialkylphosphono group in the acid-catalyzed reaction of α,β-epoxyalkylphosphonates has recently been described.[11] The same order of migratory aptitudes was found in that series.

[11] C. E. Griffin and S. K. Kundu, *J. Org. Chem.*, 34, 1532 (1969); M. Sprecher and D. Kost, *Tetrahedron Letters*, 703 (1969), and references therein cited.

The scope and mechanism of these rearrangements of glycidic esters are being studied under acidic, thermal, and photochemical conditions.



I



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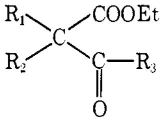
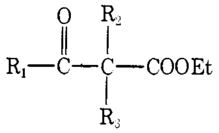


III



IV

a, $R_1 = C_6H_5$; $R_2 = R_3 = H$
b, $R_1 = C_6H_5$; $R_2 = CH_3$; $R_3 = H$
c, $R_1 = C_6H_5$; $R_2 = H$; $R_3 = CH_3$
d, $R_1 = C_6H_5$; $R_2 = R_3 = CH_3$
e, $R_1 = R_2 = H$; $R_3 = C_6H_5$
f, $R_1 = CH_3$; $R_2 = H$; $R_3 = C_6H_5$
g, $R_1 = R_2 = CH_3$; $R_3 = C_6H_5$

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An Unusual Reaction of Skatole with Tetranitromethane

Sir:

Tetranitromethane (TNM) is a reagent which selectively nitrates tyrosine residues in proteins at pH 8.[1] Because of the apparent specificity of the reagent and the mild reaction conditions, many proteins have been modified by this technique.[2]

Recently modification studies on staphylococcal nuclease[3] and papain[4] have shown that a tryptophan residue also reacts with TNM. Likewise the two vinyl groups of ferriheme at pH 8 react slowly with TNM.[5]

We have studied the mode of reaction of TNM with skatole (**1**). When equimolar proportions of reactants were mixed in diethyl ether at room temperature, orange-red needles (mp 137–141° dec, yield ~50%) separated gradually during the reaction (8–12 hr). Additional crystals (*ca.* 10%) as well as several Ehrlich-positive compounds[6] were obtained on concentration of the mother liquor.

The nmr spectrum (60 MHz, DMSO-d_6) of this product indicated no further substitution of the benzene ring and showed a slight upfield shift ($\Delta\delta = 0.15$ ppm) for the three-proton methyl singlet originally present. The ir spectrum ($CHCl_3$) indicated apparent doublets for the nitro group peaks at 1590, 1525 (asymmetric stretching) and 1333, 1313 cm^{-1} (symmetric stretching) and the absence of the indole N–H stretching band.

The ready solubility in 0.1 *N* NaOH or alkaline buffers and the strong uv absorption at $\lambda_{\max}^{\text{EtOH}}$ 395 nm[7] suggested the presence of a dinitromethylene chromophore in conjugation with an acidic proton, such as $-(-NH)-C{=}C(NO_2)_2$.[8]

The highest significant peak in the mass spectrum (Hitachi RMU-6E instrument with 250° inlet, 80-eV ionizing potential) was an ion at *m/e* 251, clearly not the molecular ion, since the combustion analysis (*Anal.* Found: C, 43.23; H, 2.99; N, 19.65) gave an incompatibly high nitrogen value. Reduced inlet temperatures, lower ionization potentials, or chemiionization techniques failed to produce the molecular ion. The thermal instability of this dinitromethylene derivative makes analysis by mass spectroscopy unfeasible.

On the basis of combustion analysis and the molecular weight (285), determined by osmometry in tetrahydrofuran, we consider $C_{10}H_8N_4O_6$ (280) (Calcd: C, 42.86; H, 2.88; N, 20.00) the most likely formula. Structure **2** would agree with the above data and the known TNM reactions in which a dinitromethylene unit is incorporated into the substrate.[9–11]

Since electrophilic substitution of 3-alkylindoles is usually initiated by attack at position 3,[12] the formation of **2** can be rationalized by the sequence **1** → **1a** → **1b** → **2** in which the reactive indolenine **1a** adds the trinitromethane anion followed by elimination of nitrous acid.

This mechanism resembles the reaction of cyclic olefins with TNM.[9] Whether or not π-complex formation precedes or accompanies the formation of **2**[13] or whether a radical pathway[14] is involved cannot be answered at this time.

Reduction of **2** in DMSO–1.0 *M* phosphate (pH 8.0), 1:10 (v/v), with excess $Na_2S_2O_4$ led to a nitrile (mp 104–105°; $\lambda\lambda_{\max}^{\text{EtOH}}$ 287, 300 (sh), 312 (sh) nm (log εε 4.21, 3.97, 3.69); *m/e* 156 (M^+), 155 (base peak); $\nu_{\max}^{CHCl_3}$ 3460, 2220 cm^{-1}; δ_{CH_3} (singlet) 2.50 ppm) in 75% yield.

This nitrile was identified as the previously unreported 2-cyano-3-methylindole (**3**) by methylation[15] to the known 1-methyl derivative (**4**)[16] (mp 69.5–71.5°; *m/e* 170 (M^+), 169 (base peak)).

This interesting and potentially useful conversion might possibly go through an enediamine which could

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(1) M. Sokolovsky, J. F. Riordan, and B. L. Vallee, *Biochemistry*, **5**, 3582 (1966).

(2) See L. A. Cohen, *Ann. Rev. Biochem.*, **37**, 698 (1968), for a brief review.

(3) P. Cuatrecasas, S. Fuchs, and C. B. Anfinsen, *J. Biol. Chem.*, **243**, 4787 (1968).

(4) K. Morihara and K. Nagami, *J. Biochem.* (Tokyo), **65**, 321 (1969).

(5) M. Z. Atassi, *Biochim. Biophys. Acta*, **177**, 663 (1969).

(6) The modified Ehrlich spray, 0.5% *p*-dimethylaminocinnamaldehyde in 1.0 *N* HCl, was used. The major product, a bright yellow spot (R_f 0.62) on silica gel G tlc (toluene–ethyl formate–formic acid, 5:3.5:1), was Ehrlich negative.

(7) The addition of base did not significantly change the uv spectrum. On the basis of a molecular weight of 280, a molar extinction coefficient of 17,200 at 395 nm in EtOH can be calculated.

(8) W. E. Thun, D. W. Moore, and W. R. McBride, *J. Org. Chem.*, **31**, 923 (1966).

(9) R. W. Bradshaw, *Tetrahedron Letters*, 5711 (1966).

(10) D. H. Reid, W. H. Stafford, and W. L. Stafford, *J. Chem. Soc.*, 1118 (1958).

(11) Reference 8 and four references cited therein.

(12) K. M. Biswas and A. H. Jackson, *Tetrahedron*, 227 (1969).

(13) D. H. Iles and A. Ledwith, *Chem. Commun.*, 364 (1969).

(14) T. C. Bruice, M. J. Gregory, and S. L. Walters, *J. Am. Chem. Soc.*, **90**, 1612 (1968).

(15) D. A. Shirley and P. A. Roussel, *ibid.*, **75**, 375 (1953).

(16) H. R. Snyder and E. L. Eliel, *ibid.*, **70**, 1857 (1948).