$CH_2Cl_2$, filtered, washed with $CH_3OH$ to replace the $CH_2Cl_2$ then with $H_2O$ to replace the $CH_3OH$, and then placed in 1.0-cm diameter columns. $CuSO_4$ solutions (100 mL of 0.1 N) adjusted with 1 N $H_2SO_4$ to pH 4 or with $NH_4OH$ to pH 9 were passed at a 1 mL/min rate, and then followed by pH 4 water. The effluents were combined and analyzed. The polymer was eluted using 3 N $H_2SO_4$, and this solution was analyzed also. Good agreement was obtained for results by both methods; $Cu^{2+}$ was determined using a Varian A-1000 atomic absorption spectrophotometer.

**Registry No.**—**2a,** 100-14-1; **2b,** 6694-75-3; **2c,** 66358-54-1; **2d,** 30787-43-0; **2e,** 23731-06-8; **4a,** 52761-08-7; **4b,** 62302-28-7; **4c,** 6959-48-4; **4d,** 1822-51-1; **5,** 4053-45-6; **7a,** 55912-20-4; **7b,** 57403-35-7; toluene, 108-88-3; divinylbenzene–styrene copolymer, 9003-70-7; Amberlite XE-305, 39464-91-0; Amberlite XAD-2, 9060-05-3; Amberlite XAD-4, 37380-42-0.

## References and Notes


(1) R. B. Merrifield, *J. Am. Chem. Soc.*, **85,** 2149 (1963).
(2) A. Patchornik and M. A. Kraus, *Pure Appl. Chem.*, **43,** 503 (1975); *Encycl. Polym. Sci. Tech. Suppl.*, **1,** 469 (1976).
(3) C. G. Overberger and K. N. Sannes, *Angew. Chem., Int. Ed. Engl.*, **13,** 99 (1974).
(4) C. C. Leznoff, *Chem. Soc. Rev.*, **3,** 65 (1974).
(5) R. H. Grubbs, C. Gibbson, L. C. Kroll, W. D. Bonds, and C. H. Brubaker, Jr., *J. Am. Chem. Soc.*, **95,** 2373 (1973).
(6) G. Nickless and G. R. Marshall, *Chromatogr. Rev.*, 154 (1964).
(7) V. G. Manecke and H. Heller, *Makromol. Chem.*, **55,** 51 (1962).
(8) A. Warshawsky, *Inst. Min. Metall., Trans., Sect. C,* **83,** 101 (1974).
(9) R. Kunin, E. F. Meitzner, and N. Bortnick, *J. Am. Chem. Soc.*, **84,** 305 (1962).
(10) J. A. Mikes in "Ion exchange in the Process Industries", SCI Conference, Imperial College, 1970, p 16.
(11) T. R. E. Kressman, ref 10, p 3.
(12) J. A. Petterson in "Biochemical Aspects of Reactions on Solid Supports", G. R. Stark, Ed., Academic Press, New York, N.Y., 1971, Chapter 5; J. M. J. Frechet and J. Farrall in "Chemistry and Properties of Crosslinked Polymers", Academic Press, New York, N.Y., 1977, p 59.
(13) R. Kalir, M. Fridkin, and A. Patchornik, *Eur. J. Biochem.*, **42,** 151 (1974).
(14) R. Kalir, A. Warshawsky, M. Fridkin, and A. Patchornik, *Eur. J. Biochem.*, **59,** 55 (1975).
(15) J. Rebek, D. Brown, and S. Zimmerman, *J. Am. Chem. Soc.*, **97,** 454 (1975); see also, *ibid.*, **96,** 7112 (1974).
(16) B. J. Cohen, M. A. Kraus, and A. Patchornik, *J. Am. Chem. Soc.*, **99,** 4165 (1977).
(17) A. Warshawsky, R. Kalir, and A. Patchornik, Israel Chemical Society, 43rd Meeting, Beer-Sheba, 1975, p 126.
(18) A. Patchornik, R. Kalir, M. Fridkin, and A. Warshawsky, Israeli Patent App. 43366 (1973); U.S. Patent 3 974 110 (1976).
(19) S. Sano, R. Tokunaga, and K. A. Kun, *Biochim. Biophys. Acta,* **244,** 201 (1971).
(20) G. Baum, *Biotech. Bioengin.* **17,** 253 (1975).
(21) Rohm and Haas products.
(22) S. J. Angyal, P. J. Morris, J. R. Tetaz, and J. G. Wilson, *J. Chem. Soc.*, 2141 (1950).
(23) H. Zinner and H. Fiedler, *Arch. Pharm.*, **291,** 493 (158).
(24) Degree of functionalization (D.F.) represents the conversion of Ⓟ–H to Ⓟ–$CH_2$Ar and calculated from D.F. = actual weight gain/weight gain for complete monofunctionalization.
(25) A. Patchornik, S. Ehrlich-Rogozinsky, and M. Fridkin in "Peptides", Proceedings of the 13th European Peptide Symposium, Hebrew University Press, Jerusalem, Israel, 1974, p 255.
(26) B. J. Cohen, unpublished results.


# Electrochemical and Mercury-Promoted Reduction of $\alpha,\alpha'$-Dibromophenylacetones in Acetic Acid[1]

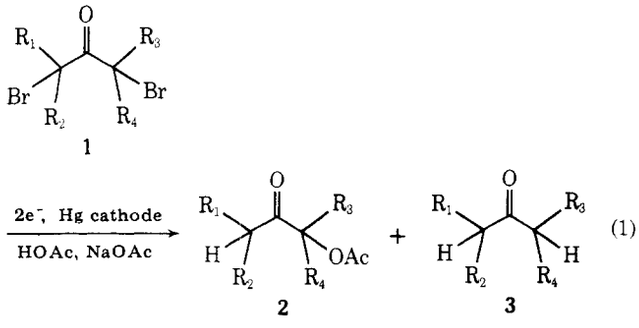

Albert J. Fry* and Jane P. Bujanauskas[2]

*Hall-Atwater Laboratories of Chemistry, Wesleyan University, Middletown, Connecticut 06457*


*Received February 6, 1978*


The factors governing the competition between formation of $\alpha$-acetoxy ketones and the doubly dehalogenated ("parent") ketones in the electrochemical and chemical reduction of $\alpha,\alpha'$-dibromo ketones in acetic acid are explored in a series of dibromophenylacetones. The degree of substitution in the dibromo ketone has a major effect upon the competition. The mass spectra of starting ketones and product $\alpha$-acetoxy ketones are discussed, and several characteristic features are observed.


We have previously described the conversion of a number of $\alpha,\alpha'$-dibromo ketones (**1**) to $\alpha$-acetoxy ketones (**2**) by electrochemical reduction in acetic acid containing sodium acetate.[3] In general (neglecting small amounts of other products), the reaction generates a mixture of **2** and the corresponding "parent" ketone **3** (eq 1), with **2** predominating when at least



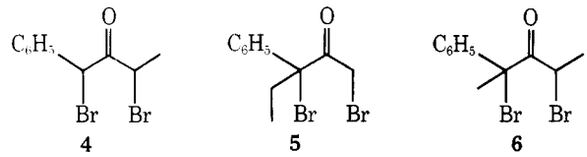

(1)

three of the substituents $R_1$–$R_4$ are alkyl and **3** predominating otherwise.[3] More recently, we have found that a very similar conversion to that shown in eq 1 can be effected by allowing the dibromo ketone **1** to react with ultrasonically dispersed mercury in acetic acid.[4] Although similar products are formed in this chemical reduction, acetoxy ketones **2** are formed in higher relative amounts than in the electrochemical reduction. In the interests of exploring further the differences between the chemical and electrochemical versions of eq 1, and to test the hypothesis that the competition between **2** and **3** depends upon the relative ease of formation of an intermediate 2-oxyallyl cation[3,4] (see Discussion), we decided to carry out a study of the reduction, by both methods, of a series of $\alpha,\alpha'$-dibromophenylacetones (**4–10**) with differing degrees of $\alpha$ substitution. We report herein the results of that study, which are consistent with our original mechanistic hypothesis.[3,4]

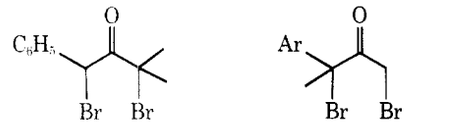
## Results

**Synthesis of Ketones and Dibromo Ketones.** Ketone **11** was commercially available; **12** was prepared by a straightforward route (phenylacetaldehyde plus isopropyl Grignard, and chromic acid oxidation of the resulting alcohol). Ketones **13–16** were all prepared by phase-transfer alkylation of the corresponding benzyl ketone, using a two-phase system consisting of aqueous sodium hydroxide and dichloromethane containing ketone, alkyl iodide, and tetrabutylammonium iodide according to the method of Brandstrom and Junggren.[5]

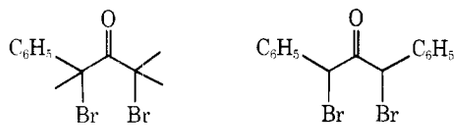
0022-3263/78/1943-3157$01.00/0 



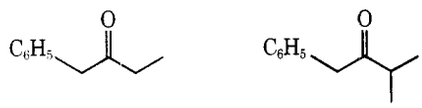
4 5 6



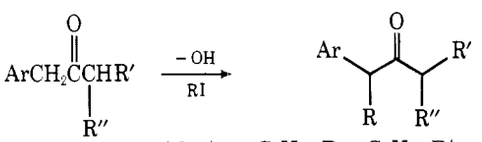
7 8, Ar = $p$-$CH_3OC_6H_4$



9 10



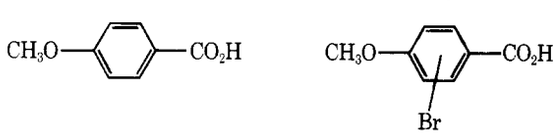
11 12



13, Ar = $C_6H_5$; R = $C_2H_5$; R′ = R″ = H
14, Ar = $p$-$CH_3OC_6H_4$; R = $CH_3$; R′ = R″ = H
15, Ar = $C_6H_5$; R = R′ = $CH_3$; R″ = H
16, Ar = $C_6H_5$; R = R′ = R″ = $CH_3$

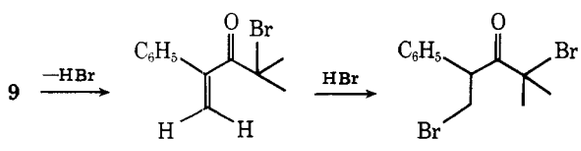
Yields were only moderate due to competing aldol condensation of the starting ketone.

Dibromides **4** and **7** could be prepared in good yield by the method of Claesson and Thalen.[6] This method was less satisfactory as a route to **5** and **6**, and to obtain these materials in a purer form the bromination of **13** and **15** was carried out in acetic acid. It was not possible to obtain dibromo ketones **8** and **9** in sufficiently pure form for further investigation. One small scale bromination of **14** in dichloromethane afforded fairly pure **8** (NMR), but when the reaction was scaled up a more complex mixture was obtained. Oxidative degradation of this mixture afforded a mixture of $p$-anisic acid (**17**) and a bromoanisic acid (**18**), demonstrating that bromination had occurred at least partially on the aromatic ring.



17 18

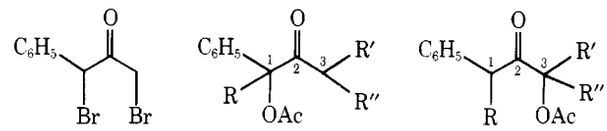
Although bromination of $\alpha,\alpha,\alpha',\alpha'$-tetraalkylacetones can be readily effected using the procedure (aqueous HBr, neat, 65 °C) of Claesson and Thalen,[6] we were unable to obtain **9** in this way. Under these vigorous bromination conditions **9** (or the corresponding monobromide, or both) apparently suffers dehydrohalogenation to **19** (NMR singlets at $\delta$ 5.84 and 5.99), and there is also some evidence for the subsequent conjugate addition of HBr to **19** to afford **20** (NMR $\delta$ 4–5).



19 20

Other bromination methods that were tried (acetic acid at room temperature, $N$-bromosuccinimide in refluxing carbon tetrachloride,[7] and photochemical bromination using molecular bromine)[8] either gave similar results under vigorous conditions or afforded mixtures of monobromides when carried out under mild conditions. Thus, the reduction experiments were carried out only on dibromo ketones **4–7**. Dibromide **10**[9] was reduced only by mercury.

**Electrochemical and Chemical Reduction of Dibromo Ketones.** The electrochemical reactions on **4–7** were carried out under previously established standard conditions[3] (acetic acid containing 1.0 M sodium acetate; mercury cathode, controlled potential). Reactions generally proceeded as in eq 1, though small amounts of other materials were also formed (usually in sufficiently small quantity to preclude isolation and characterization). All major products of the electrochemical reactions were isolated by preparative VPC and identified by NMR and mass spectroscopy. Mercury reductions on **4–7** and **10** were carried out by allowing the dibromo ketone and mercury to react at 25 °C in acetic acid containing 1.0 M sodium acetate with ultrasonic stirring.[4] Since the characterization of products had generally already been carried out on the products of the electrode reaction, the mixtures were generally simply analyzed for the relative ratios of acetoxy ketone to parent ketone. Some reductions afforded monobromo ketones; for mechanistic reasons (see Discussion), these were included with the parent ketone when calculating such ratios. The results of reduction of the various dibromo ketones under the two reduction methods are outlined in Table I. The previously reported[3] result of electrochemical reduction of dibromophenylacetone (**21**) is included for comparison. In general, two isomeric acetoxy ketones may be formed from each dibromo ketone, a 1-phenyl-1-acetoxy-2-propanone (**22**) or a 1-phenyl-3-acetoxy-2-propanone (**23**)



21 22 23

(numbering as shown). The total yields of products were generally good (≥80%) in both types of reduction, in keeping with our previous experience with the electrochemical reaction[3] but in contrast with the mercury reduction of aliphatic dibromo ketones.[4]

Several observations may be made concerning the data in Table I. First, it may be noted that the relative proportion of $\alpha$-acetoxy ketone(s) in the product mixture (last column) increases as the degree of $\alpha$-alkyl substitution in the dibromo ketone increases from **21** through **4** and **5** to **6** and **7**. Secondly, the relative proportions of **22** to **23** in the $\alpha$-acetoxylated products are quite dependent upon the structure of the dibromo ketone; 1-acetoxy ketone **22** predominates from **5** and **6**, while 3-acetoxy ketone **23** predominates from **4** and **7**. Finally, the relative proportion of acetoxy ketone from a given dibromo ketone is usually greater in the mercury reaction than in the electrochemical reduction, though the relative amounts of **22** and **23** are the same in the two reactions for a given dibromo ketone.

## Discussion

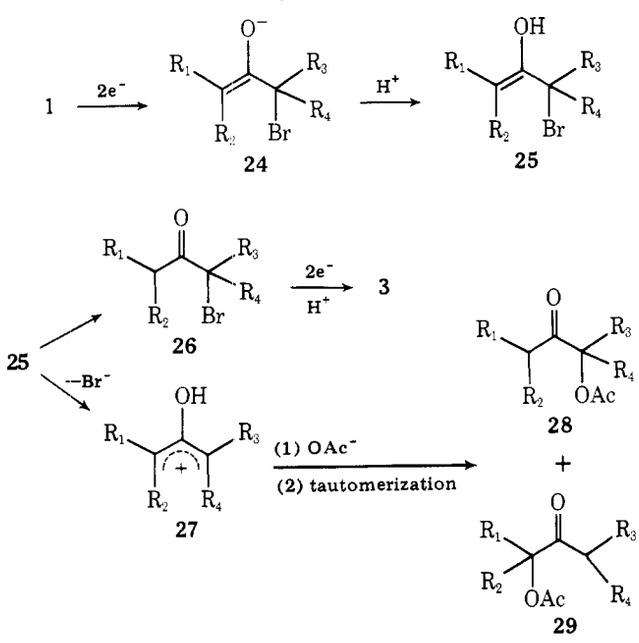
The results of this study are fully consistent with the mechanism previously proposed for the electrochemical reduction of dibromo ketones in acetic acid (Scheme I).[3,10] Prominent features of this mechanism include the following: (a) an enolate anion (**24**) is first formed but is quickly protonated in acid to form enol allylic bromide **25**; (b) this intermediate may tautomerize to bromo ketone **26**, which would

**Table I. Reduction of Dibromo Ketones in Acetic Acid**

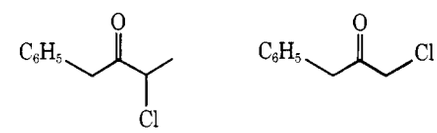
| Dibromo ketone | Reduction method | 22, % | 23, % | Parent ketone, % | Monobromo ketone, % | Other, % | Acetoxylation efficiency[a] |
|---|---|---|---|---|---|---|---|
| 21 | Electrochemical[b,c] | 0 | 0 | 100 | 0 | 0 | 0 |
| 4 | Electrochemical[b,c] | 8 | 21 | 66 | 0 | 5 | 0.4 |
| 4 | Mercury[d,e] | 12 | 66 | 16 | 0 | 6 | 4.9 |
| 4 | Mercury[e,f] | 7 | 59 | 16 | 15 | 3 | 2.1 |
| 4 | Mercury[e,g] | 11 | 48 | 21 | 9 | 11 | 2.8 |
| 5 | Electrochemical[b,e] | 43 | 11 | 38 | 0 | 8 | 2.0 |
| 5 | Mercury[c-e] | 29 | 8 | 20 | 33 | 10 | 0.7 |
| 6 | Electrochemical[b,c,e] | 64 | 15 | 14 | 0 | 7 | 5.6 |
| 6 | Mercury[c-e] | 62 | 17 | 12 | 0 | 9 | 6.6 |
| 7 | Electrochemical[b,c,e] | 3 | 83 | 8 | 0 | 6 | 10.8 |
| 7 | Mercury[c-e] | 6 | 88 | 0 | 0 | 6 | ∞[h] |
| 10 | Mercury[c-e] | 100 | | 0 | 0 | 0 | ∞[h] |

[a] (% 22 + % 23)/(% 3 + % 26). [b] Mercury cathode, 25 °C, 1.0 M NaOAc in HOAc. [c] Analysis by VPC. [d] 1.0 M NaOAc in HOAc. [e] Analysis by NMR. [f] HOAc. [g] HOAc saturated with NaOAc. [h] No parent ketone was detectable by VPC or NMR.

Scheme I



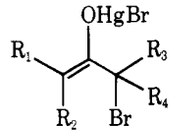

undergo subsequent reduction to parent ketone **3** by the same pathway, in known fashion; or (c) **25** may eject bromide ion to afford the 2-hydroxyallyl cation **27.** Subsequent nucleophilic attack on **27** by acetate and/or acetic acid would afford the isomeric acetoxy ketones **28** and **29.** We have argued[3] that the particular branch chosen by **25** depends mainly on the stability of cation **27** and that the path leading to acetoxy substitution will be chosen in acetic acid when at least three of the substituents ($R_1$, $R_2$, $R_3$, and $R_4$) are alkyl. (We do of course recognize the fact that highly substituted enols can be rather long-lived[11] and that therefore a high degree of alkyl substitution in **25** will probably retard the rate of conversion to **26,** as well as enhancing the rate of ionization to **27.**) We have supported our emphasis on the effect of substitution on the rate of ionization of **25** by reference to literature data which show that ionization of allylic chlorides is indeed very sensitive to the degree of alkyl substitution.[12] Since cinnamyl chloride ionizes at a rate slower than any of the dimethylallyl chlorides[12] and two alkyl groups in **25** do not apparently provide sufficient stabilization to **27** to render ionization competitive with tautomerization to **26,** we found it unsurprising that **21** should afford only the parent ketone, phenylacetone, upon reduction.[3] The mechanism in Scheme I suggests that increasing amounts of α-acetoxy substitution product should be formed as alkyl substituents are successively introduced into the two α positions of **21.** As the data in Table I indicate, this is indeed the case. Introduction of a single alkyl group into **21** (**4** and **5**) increases the yield of acetoxy ketones from 0% to 29 and 54%, and addition of a second methyl group (**6** and **7**) increases the yield of substituted materials to 79 and 86%. A second phenyl substituent (**10**) leads to clean formation of acetoxy ketone. This experiment cannot be compared directly with the electrochemical reduction of **21** because of the intrinsic tendency of the mercury reaction to favor substitution (vide infra), but a comparison of the mercury reductions of **4** and **10** clearly shows the superior carbonium ion stabilizing ability of phenyl over methyl. We had expected that **8** would give more α substitution than **5** because of the strong electron-releasing power of a $p$-$OCH_3$ substituent, but the difficulty we experienced in the preparation of this material prevented a test of this hypothesis. The effects of alkyl substituents found herein find close parallel in studies of the Favorskii rearrangement of α-halo ketones.[13,14] Chloride **30** reacts with methanolic methoxide 250 times faster than **31** and exhibits a $k_{Br}/k_{Cl}$ ratio of 1 with only




**30** **31**

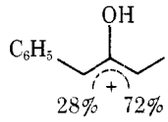
5% deuterium exchange as opposed to a $k_{Br}/k_{Cl}$ ratio of 63 and 80% deuterium exchange for **31.**[13d] These results constitute clear evidence that the enolate from **30** ionizes considerably faster than that from **31** so that the rate-determining step changes from ionization of chloride from the enolate of **30** to proton removal as rate-determining in the case of **31.**

In almost every case the acetoxylation efficiency, i.e., the ratio of acetoxylated product to parent ketone [actually, the sum of parent ketone and monobromo ketone since the latter occurs after the mechanistic branch (Scheme I) and is believed to lie on the route to parent ketone], is higher in the mercury reaction than in the corresponding electrochemical reaction. This, the fact that the ratio of **22** to **23** is the same in both electrochemical and chemical reactions for a given dibromide, and the trend toward higher acetoxylation efficiency with increasing alkyl substitution are all consistent with our previous experience with the mercury reduction of aliphatic dibromo ketones.[4] All of these factors strongly suggest similar but nonidentical mechanisms for the two kinds of reduction. We have previously suggested that the mercury reaction involves intermediate **32** rather than **25** and that the increased acetoxylation efficiency in the mercury reaction is associated with a slower conversion of **32** to monobromo ketone **26** rather than with a greater tendency of **32** to ionize compared with **25.**[4]

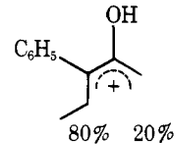



32

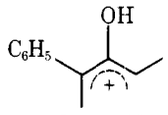
It is interesting to note that the 1-acetoxy ketone **22** predominates in the reduction of dibromo ketones **5** and **6**, while the 3-acetoxy ketone **23** is favored in the reduction of **4** and **7**. We believe that this feature of the results may be understood in terms of the competitive factors governing attack at the two possible sites of 1-phenylallyl cation **27** (or its mercury analogue). There are two principal factors to be considered: charge distribution in the cation and stability of the enol acetate resulting from nucleophilic attack on the 2-hydroxyallyl cation. We may consider the ions **33–36** derived from dibromo



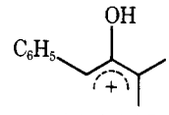

33




34



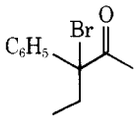

35



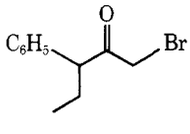

36

ketones **4–7**, respectively, and the relative amounts of attack at the two sites in each. Attack on **34, 35,** and **36** occurs principally at the tertiary site, presumably the locus of greatest charge in each case. It is interesting, however, that a substantial amount of attack does occur at the other site in **34** and **35.** This may be because a more stable enol (tetrasubstituted double bond and conjugated with the aromatic ring) is formed by attack at C-3 of **34** and **35.** Cation **33** is attacked at the site of lower charge (C-3); it may be that here the effect of obtaining preferentially that enol whose double bond is conjugated with the benzene ring is dominant when neither carbon is tertiary. (It is worth commenting here, incidentally, that we have been unable to obtain any evidence for equilibration of isomeric acetoxy ketones under our experimental conditions. The electrochemical reactions are run on a time scale of hours and the mercury reductions for days, yet the relative ratios of **22** and **23** are the same in the two reactions.) The ratios of **22** to **23** found in this work are consistent with previous studies by Bordwell et al. on positional selectivity in the reaction of halo ketones in dilute methanolic methoxide to afford $\alpha$-methoxy ketones[13] and with the limited data in the literature on the products of nucleophilic attack on substituted cinnamyl cations.[15] The analogy to Bordwell's work is to be expected since intermediates **24, 25,** and **27** are also proposed by Bordwell as the precursors to $\alpha$-methoxy ketones in that reaction.[13]

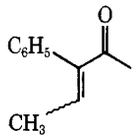
Monobromides have occasionally been observed by us in reductions of dibromo ketones by mercury. It was quite surprising, however, to find that the monobromide formed in the reduction of **5** is the benzylic bromide **37** (NMR) rather than its isomer **38** since reduction of the benzyl bromine of **5** ought




37

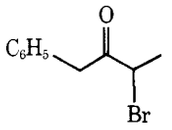



38




39

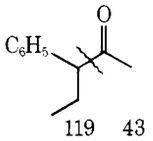
to be markedly easier.[16] It is possible that the initially formed bromide might actually have been **38** but that isomerization to **37** by known routes[17] then occurred on standing. This interpretation is supported by the observation that after 2 months the product mixture began to decompose rapidly to afford the new unsaturated ketone **39** (NMR) component(s). The monobromide formed in the reduction of **4** was the expected **40.**



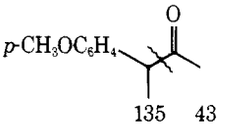

40

**Mass Spectra.** We previously found mass spectroscopy to be quite useful for assignment of structures to isomeric $\alpha$-acetoxy ketones.[3] For that reason we paid careful attention to the mass spectral cracking patterns of the substituted phenylacetones prepared during this study in order to identify common features.

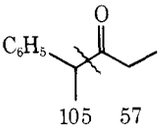
The ketones **13–16** fragmented, as previously observed[17]



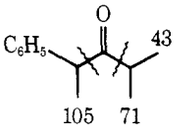

13




14




15



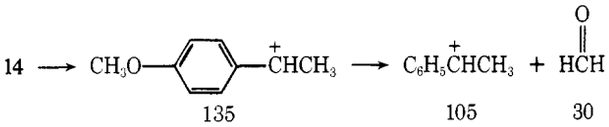

16

for benzyl alkyl ketones, predominantly between the benzyl and carbonyl carbons.

The benzylic fragments formed in this manner exhibited a variety of fragmentation pathways. Common fragments in all ketones were at *m/e* 43, 77, and 91. The origin of a number of such secondary ions was established by analysis of metastable ions[18] observed in the various spectra using a computer program written for this purpose.[19] For example, a metastable ion peak at *m/e* 69.6 in the spectrum of **13** was shown to be the conversion of an ion of mass 119 to one of 91 with extrusion of a fragment of mass 28 (eq 2).

$$\underset{119}{13} \xrightarrow{-43} \underset{91}{C_6H_5C^+HCH_2CH_3} \rightarrow \underset{91}{C_7H_7^+} + \underset{28}{CH_2{=}CH_2} \quad (2)$$

On the other hand, a metastable ion peak at *m/e* 81.7 in the spectrum of **14** was shown to be associated with the process 135 → 105 + 30, probably as in eq 3




(3)

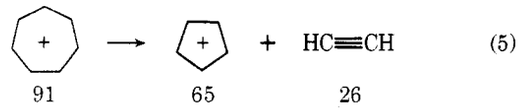
(anisole has previously been shown to expel formaldehyde in the mass spectrometer).[20]

A metastable peak at *m/e* 101 in the mass spectra of **14, 15,** and **16** was found to arise from the process 105 → 103 + 2, possibly via eq 4.

$$\underset{105}{C_6H_5C^+HCH_3} \rightarrow \underset{103}{C_6H_5{}^+C{=}CH_2} + \underset{2}{H_2} \quad (4)$$

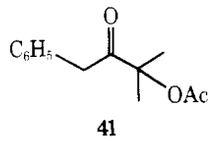
The fragment of mass 91 in all of the spectra is presumably the tropylium ion. Every spectrum showed a metastable peak

at *m/e* 46.4 due to the process 91 → 65 + 26, probably[21] as in eq 5.

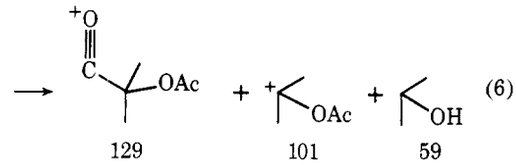



(5)

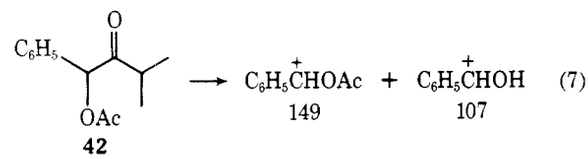
The mass spectra of the various acetoxy ketones exhibit the same major cleavage paths as the parent ketones. In every case there is at least one major fragment by which isomers can be distinguished. For example, acetate **41** exhibits fragments at *m/e* 129, 101, and 59 (eq 6) which distinguish it from its isomer **42**, which has fragments at *m/e* 149 and 107 (eq 7).




**41**



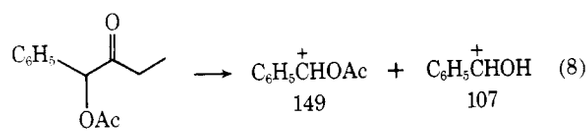

(6)




(7)

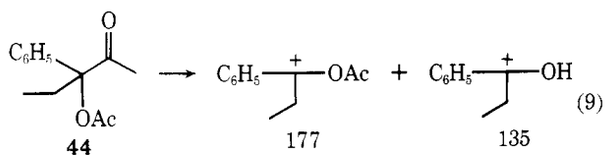
**42**

The mode of cleavage shown here is quite general and was also observed for acetoxy ketones **43–45** (eq 8–10).



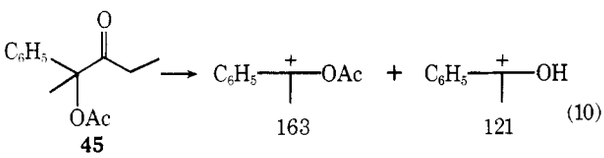

(8)

**43**




(9)

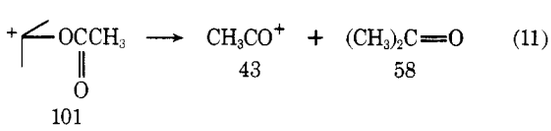
**44**




(10)

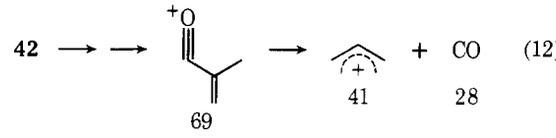
**45**

We obtained no evidence from metastable ion analysis concerning whether the second ion in each of these cases is derived from the first (by loss of the elements of ketene) or by an independent pathway. A metastable ion at *m/e* 18.3 in the mass spectrum of **41** demonstrated another decomposition path for the fragment of mass 101 observed in that spectrum (eq 11).



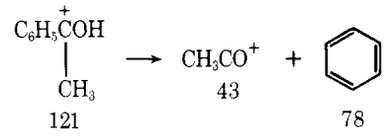

(11)

An interesting metastable peak at *m/e* 24.4 in the spectrum of acetate **42** arises from a fragment of *m/e* 69 decomposing to a daughter of *m/e* 41, perhaps by eq 12.




(12)

There is a metastable peak at *m/e* 15.3 in the spectrum of **48** corresponding to 121 → 43 + 78 (eq 13).




(13)

These types of processes may be common to all of the spectra, but of varying degrees of importance so that the appropriate metastable ions to establish their existence are not always of sufficient intensity to be observed.

## Experimental Section

**General.** Melting points were determined on a Mel-Temp capillary apparatus and are uncorrected. Nuclear magnetic resonance (NMR) spectra were recorded on a Varian A60-A spectrometer in $CDCl_3$ containing internal tetramethylsilane ($Me_4Si$) unless otherwise noted. Mass spectra were recorded at 70 eV on a Perkin-Elmer Hitachi RMU-6L spectrometer and were calibrated against the spectrum of perfluorokerosene; relative intensities are indicated for new compounds. VPC separations were made using a Varian Model 1720 dual column thermal conductivity instrument, equipped with a temperature programmer, on a 0.25 × 8 ft column packed with 60% (sic) SE-30 on Chromosorb P. Electrochemical experiments were carried out using a Princeton Applied Research Model 170 electrochemistry system. Elemental analyses were performed by Chemalytics, Inc., Tempe, Ariz.

**3-Methyl-1-phenyl-2-butanone (12).** 3-Methyl-1-phenyl-2-butanol was prepared in 70% yield by the addition of phenylacetaldehyde (0.18 mol) to a solution of 0.21 mol of isopropylmagnesium bromide in ether. The crude alcohol was oxidized directly by chromium trioxide in acetic acid to afford the desired ketone in 58% yield. This route is more convenient than that employed by Bordwell.[13c]

**3-Phenyl-2-pentanone (13)** was prepared by the method of Brandstrom and Junggren.[5] Tetrabutylammonium iodide (44.32 g, 0.12 mol) was dissolved in 100 mL of dichloromethane. To this mixture was added phenylacetone (13.42 g, 0.1 mol) and 37.43 g (0.24 mol) of ethyl iodide. To the flask was added a solution of 9.6 g of sodium hydroxide (0.24 mol) in 120 mL of water. The two-phase mixture was stirred vigorously magnetically and heated to reflux. The reaction was terminated after 41 h, at which time VPC analysis showed that less than 10% of the starting phenylacetone remained. The aqueous layer was extracted twice with dichloromethane and combined with the original organic layer, and the combined organic extracts were washed with $H_2O$, 5% HCl, and $H_2O$. After evaporation of the dichloromethane, tetrabutylammonium iodide was precipitated by the addition of ether and removed by filtration for reuse. Evaporation of the ether and distillation afforded 12.5 g of 3-phenyl-2-pentanone (**13**) (77% yield; >95% pure by VPC): bp 55–56.5 °C (1.3 mm); NMR δ 0.75 (t, 3 H), 1.7 (m, 2 H), 1.95 (s, 3 H), 3.25 (t, 1 H), and 7.16 (s, 5 H); mass spectrum, *m/e* (relative intensity) 162 (15, $M^+$), 119 (49), 118 (7), 105 (6), 103 (6), 92 (8), 91 (100), 77 (12), 65 (6), 51 (9), 43 (38), and 41 (15).

The 2,4-dinitrophenylhydrazone, mp 130–131 °C, was purified by repeated recrystallization from ethanol.

Anal. Calcd for $C_{17}H_{18}N_4O_4$: C, 59.64; H, 5.30. Found: C, 59.66; H, 5.23.

**3-(4-Methoxyphenyl)-2-butanone (14).** Using the same procedure as described for the synthesis of 3-phenyl-2-pentanone, anisylacetone (16.4 g) (Research Organic Chemical Corp.) was allowed to react with methyl iodide for 125 h until the anisylacetone had completely disappeared (VPC). Distillation afforded 8.05 g (45% yield; >95% pure by VPC) of ketone **14**: bp 60–61 °C (0.03 mm) [lit.[23] bp 267 °C (755 mm)]; NMR δ 1.35 (d, 3 H), 1.98 (s, 3 H), 3.68 (q, 1 H), 3.73 (s, 3 H), and 6.83 and 7.08 (AB quartet, $J$ = 8.5 Hz); mass spectrum, *m/e* 178 ($M^+$), 136, 135 (base), 123, 120, 105, 103, 91, 79, 77, 65, 51, and 43.

**2-Phenyl-3-pentanone (15).** Methylation of 12.3 g of 1-phenyl-2-butanone (Aldrich Chemical Co.) was carried out as in the synthesis of 3-phenyl-2-pentanone. The reaction was terminated after 148 h,

at which time the starting ketone had completely reacted (VPC). A 5.6-g amount of distilled ketone (42% yield; >95% pure by VPC) was obtained: bp 27–28 °C (0.025 mm) [lit.[22] bp 225–228 °C (760 mm)]; NMR δ 0.93 (t, 3 H), 1.48 (d, 3 H), 2.36 (q, 2 H), 3.75 (q, 1 H), and 7.22 (s, 5 H); mass spectrum, *m/e* 162 ($M^+$), 141, 133, 119, 106, 105 (base), 104, 103, 91, 79, 78, 77, 63, 57, 51, and 43.

**2-Methyl-4-phenyl-3-pentanone (16).** Methylation of ketone **12** (9 g) by the procedure used in the synthesis of 3-phenyl-2-pentanone was difficult to follow by VPC because the starting material and product had the same VPC retention time. The reaction was stopped after 316 h when the organic layer had become very dark yellow. Workup and distillation afforded ketone **16:** 3.7 g (38%; >95% pure by VPC); bp 34 °C (0.05 mm) [lit.[22] bp 256–257 °C (760 mm)]; NMR δ 0.91 (d, 3 H), 1.05 (d, 3 H), 1.37 (d, 3 H), 2.65 (m, 1 H), 3.92 (q, 1 H), and 7.26 (s, 5 H); mass spectrum, *m/e* 176 ($M^+$), 141, 106, 105, 104, 103, 91, 79, 78, 77, 71, 70, 51, and 43 (base).

**1,3-Dibromo-1-phenyl-2-butanone (4).** Bromination of ketone **11** was carried out according to the method of Claesson and Thalen. NMR spectroscopy showed the crude product to be an 87:13 mixture of dibromide **4** and a tribromide [δ 6.35 (1 H)]. The dibromide **4** was a mixture of diastereomers in the ratio 57:43. Repeated recrystallization from heptane afforded **4** as a white solid, mp 34–45 °C, still a mixture of diastereomers: NMR δ 1.7 (d, 3 H), 1.77 (d, 3 H), 4.47 (q, 1 H), 4.98 (q, 1 H), 5.88 (s, 1 H), 6.04 (s, 1 H), and 7.2–7.7 (m, 5 H).

Anal. Calcd for $C_{10}H_{10}Br_2O$: C, 39.25; H, 3.29. Found: C, 39.07; H, 3.31.

**1,3-Dibromo-3-phenyl-2-pentanone (5).** Bromination of ketone **13** in acetic acid at room temperature afforded a 90:10 mixture of dibromide **5** and a tribromide (NMR δ 5.98). This mixture was used as obtained because of its decomposition upon attempted vacuum distillation: NMR δ 0.83 (t, 3 H), 2.15–2.4 (m, 2 H), 3.99 and 4.34 (AB quartet, $J$ = 14.0 Hz), and 7.3 (s, 5 H).

**2,4-Dibromo-2-phenyl-3-pentanone (6).** Bromination of ketone **15** in acetic acid afforded dibromide **6** in ≥96% purity (NMR) (90% yield) as a viscous liquid consisting of almost equal amounts of erythro and threo diastereomers: NMR δ 1.52 (d, 2 H), 1.85 (d, 2 H), 2.19 (s, 3 H), 2.23 (s, 3 H), 4.63 (q, 1 H), 4.82 (q, 1 H), and 7.3–7.7 (m, 5 H).

**1,3-Dibromo-3-methyl-1-phenyl-2-butanone (7).** Ketone **12** was brominated according to the method of Claesson and Thalen.[6] Two distillations at oil pump pressure and a final recrystallization from heptane afforded a white solid: mp 58.8–59.8 °C; NMR δ 1.8 (s, 3 H), 2.0 (s, 3 H), 6.1 (s, 1 H), and 7.2–7.8 (m, 5 H).

Anal. Calcd for $C_{11}H_{12}Br_2O$: C, 41.28; H, 3.78. Found: C, 41.57; H, 3.91.

**Bromination of 3-(4-methoxyphenyl)-2-butanone** in dichloromethane at 0 °C afforded a mixture containing some of the desired dibromide [NMR δ 2.34 (s), 3.82 (s), 4.12 (s), and 6.93 and 7.42 (AB pattern)] but also a considerable amount of other material. The material was suspended in water at 70 °C and vigorously stirred, and an aqueous solution of potassium permanganate was added over an hour interval with a second hour of stirring and heating. Manganese dioxide was removed by filtration, and the filtrate was acidified with 5% HCl. A white precipitate formed and was isolated by filtration. The NMR spectrum of this material indicated the presence of anisic acid and a bromoanisic acid in a ca. 2:1 ratio: δ 3.82 (s), 3.94 (s), 7.01 and 7.92 (AB quartet), and 7.1–8.2 (m); mass spectral peaks (inter alia) at *m/e* 230 and 232 ($C_8H_7BrC_3$) and 152 ($C_8H_8O_3$).

**Electrochemical reductions** were carried out as previously described.[3] Acetoxy ketones were isolated for spectral characterization by preparative VPC. Microanalyses were carried out on most acetoxy ketones, except when the substances were formed in very small amounts or were unstable (as noted below). When VPC conditions could not be found to separate a pair of isomeric acetoxy ketones, spectral characterization and microanalysis were carried out on the mixture. Mixtures were analyzed by VPC (cut and weigh) or NMR integration, or a combination of these, as appropriate.[25]

**Reductions by ultrasonically dispersed mercury** were carried out as previously described.[4] Workup and analysis were carried out as with the electrochemical reactions.

**Acetoxy Ketones.** Characterization data for the various acetoxy ketones are summarized below. Only the largest mass spectral lines are listed.

**2-Acetoxy-2-methyl-4-phenyl-3-butanone (41):** mp 41.5–42.5 °C from heptane; NMR δ 1.5 (s, 6 H), 2.09 (s, 3 H), 3.77 (s, 2 H), and 7.24 (s, 5 H); mass spectrum, *m/e* (relative intensity) 220 (1.5, $M^+$), 162 (4), 160 (3), 130 (2), 129 (34), 119 (8), 101 (32), 92 (8), 91 (60), 69 (5), 65 (16), 59 (54), and 43 (100).

Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.88; H, 7.32. Found: C, 70.89; H, 7.46.

**1-Acetoxy-1-phenyl-3-methyl-2-butanone (42):** Mass spectrum, *m/e* (relative intensity) 220 (5, $M^+$), 160 (54), 149 (38), 107 (100), 91 (69), and 71 (22).

**1-Acetoxy-1-phenyl-2-butanone (43)** and **3-acetoxy-1-phenyl-2-butanone (46)** were inseparable by VPC and hence were collected as a single fraction by preparative VPC. The NMR spectra of the mixture exhibited absorptions at δ 0.94 (t, $J$ = 6.8 Hz),* 1.25 (d, $J$ = 7 Hz), 1.99 (s), 2.09 (s),* 2.22 (q, $J$ = 6.9 Hz),* 3.66 (s), 5.81 (s),* and 5.02 (q, $J$ = 7 Hz), together with an aromatic multiplet from δ 7.1–8.0; the mass spectrum of the mixture exhibited prominent peaks at *m/e* (relative intensity) 206 (6, $M^+$),* 160 (8),* 149 (15),* 122 (20), 115 (24), 107 (30),* 105 (35), 103 (20), 91 (43), 87 (22), 77 (25), 57 (13),* 51 (13), and 43 (100)* (the peaks in the NMR and mass spectra attributable with certainty to isomer **43** are marked with an asterisk; the relative intensities of the NMR absorptions are consistent with the assignments given).

Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 68.50; H, 6.73.

**3-Acetoxy-3-phenyl-2-pentanone (44):** NMR δ 0.6 (t, 3 H), 1.79 (s, 3 H), 2.19 (s, 3 H), 2.4 (m, 2 H), 7.13 (broad s, 2 H), and 7.22 (broad s, 3 H); mass spectrum, *m/e* (relative intensity) 220 (3, $M^+$), 177 (22), 160 (7), 136 (1), 135 (100), 119 (30), 117 (13), 115 (7), 105 (8), 91 (30), 77 (13), 57 (21), and 43 (53).

**1-Acetoxy-3-phenyl-2-pentanone (47):** NMR δ 1.00 (t, 3 H), 1.8 (m, 2 H), 2.01 (s, 3 H), 3.47 (t, 1 H), 4.50 and 4.30 (AB quartet, $J$ = 16.7 Hz, 2 H), and 7.12 (broad s, 5 H); mass spectrum; *m/e* (relative intensity) 220 (8, $M^+$), 158 (8), 119 (68), 117 (13), 115 (10), 101 (47), 91 (100), 77 (8), 73 (14), and 43 (49).

Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.88; H, 7.32. Found: C, 70.83; H, 7.65.

**2-Acetoxy-2-phenyl-3-pentanone (45)** and **4-acetoxy-2-phenyl-3-pentanone (48)** (the latter as a mixture of erythro and threo diastereomers) were obtained as an inseparable mixture. The ratio of **45** to **48** was established by the ratio of the singlet at δ 1.85 (**45**) to the two overlapping doublets at δ 1.4 (the two diastereomers of **48**) in the NMR spectrum of the crude product. Upon preparative VPC **45** mostly decomposed to 2-phenyl-3-keto-1-pentene (**49**) (singlets at δ 5.75 and 6.00), which was eluted mixed with unreacted **45** and **48.** The mass spectrum of this mixture exhibited peaks at *m/e* (relative intensity) 220 (1, $M^+$),* 163 (18),* 160 (19),* 131 (7),* 122 (8), 121 (80),* 115 (15), 105 (29), 104 (10), 103 (55), 91 (3), 87 (8), 77 (21), 57 (27.6),* 51 (11), and 43 (100)* (peaks marked with an asterisk are associated with **45**).

**1-Acetoxy-1,3-diphenyl-2-propanone (50).** The crude product from mercury reduction of a mixture of *dl*- and *meso*-**10** in acetic acid was essentially pure **50**:[26] NMR δ 1.87 (s, 3 H), 3.41 and 3.45 (AB quartet, $J$ = 15 Hz), 5.80 (s, 1 H), and 6.8–7.2 (m, 5 H).

**Acknowledgment.** Financial support was provided by the National Science Foundation, Wesleyan University, and Sigma Xi. The electrochemical reduction of 1-phenyl-1,3-dibromo-2-propanone was carried out by Mr. John O'Dea. The reduction of 1,3-diphenyl-1,3-dibromo-2-propanone by mercury was carried out by Mr. Gilbert Shuster. Computer time was provided by the Wesleyan University Computer Center.

**Registry No.**—erythro-**4,** 56764-08-0; *threo*-**4,** 56764-00-2; **5,** 66551-77-7; *erythro*-**6,** 66551-78-8; *threo*-**6,** 66551-79-9; **7,** 37988-51-5; **8,** 66551-80-2; *dl*-**10,** 51513-35-0; *meso*-**10,** 51513-34-9; **11,** 1007-32-5; **12,** 2893-05-2; **13,** 1528-39-8; **13** DNP, 66551-81-3; **14,** 7074-12-6; **15,** 16819-77-5; **16,** 20474-49-1; **17,** 100-09-4; **18,** 66552-46-3; **41,** 66551-82-4; **42,** 66551-83-5; **43,** 66551-84-6; **44,** 66551-85-7; **45,** 66551-86-8; **46,** 66551-87-9; **47,** 66551-88-0; *threo*-**48,** 66551-89-1; *erythro*-**48,** 66551-90-4; **49,** 66551-91-5; **50,** 66551-92-6; 3-methyl-1-phenyl-2-butanol, 705-58-8; phenylacetaldehyde, 122-78-1; isopropyl bromide, 75-26-3; phenylacetone, 103-79-7; ethyl iodide, 75-03-6; anisylacetone, 122-84-9; methyl iodide, 74-88-4.

## References and Notes

(1) Abstracted in part from the M.A. Thesis of Jane Bujanauskas, Wesleyan University, November, 1976.
(2) Current address: Allied Chemical Corp., Morristown, N.J. 07960.
(3) A. J. Fry and J. J. O'Dea, *J. Org. Chem.*, **40,** 3625 (1975).
(4) A. J. Fry and D. Herr, *Tetrahedron Lett.*, 1721 (1978).
(5) A. Brandstrom and U. Junggren, *Tetrahedron Lett.*, 473 (1972).
(6) G. Claesson and A. Thalen, *Acta Chem. Scand.*, **17,** 1172 (1963).
(7) H. O. House, "Modern Synthetic Reactions", 2nd ed, W. A. Benjamin, New York, N.Y., 1972, p 459ff.
(8) V. Calo and L. Lopez, *J. Chem. Soc., Chem. Commun.*, 212 (1975).
(9) R. Breslow, T. Eicher, A. Krebs, R. A. Peterson, and J. Posner, *J. Am. Chem.*

Soc., **87**, 1320 (1965).
(10) J. P. Dirlam, L. Eberson, and J. Casanova, *J. Am. Chem. Soc.*, **94**, 240 (1972).
(11) (a) A. R. Miller, *J. Org. Chem.*, **41**, 3599 (1976), and references therein; (b) H. M. R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, **12**, 819 (1973); (c) E. A. Schmidt and H. M. R. Hoffmann, *J. Am. Chem. Soc.*, **94**, 7832 (1972).
(12) C. A. Vernon, *J. Chem. Soc.*, 423 (1954).
(13) (a) F. G. Bordwell, *Acc. Chem. Res.*, **3**, 281 (1970); (b) F. G. Bordwell and M. W. Carlson, *J. Am. Chem. Soc.*, **92**, 3370, 3377 (1970); (c) F. G. Bordwell and J. Almy, *J. Org. Chem.*, **38**, 575 (1973); (d) F. G. Bordwell, M. W. Carlson, and A. C. Knipe, *J. Am. Chem. Soc.*, **91**, 3949 (1969).
(14) (a) It is conceivable that the key intermediate in the formation of the α-acetoxy ketones is not oxyallyl cation **27** but rather an allene oxide,[14b] though we regard the latter as unlikely for reasons similar to those advanced by Bordwell;[13b] nevertheless, we are presently carrying out an experimental search for such intermediates;[14c] (b) B. S. Ong and T. H. Chan, *Tetrahedron Lett.*, 3257 (1976); (c) Y. Migron, research in progress.
(15) (a) R. A. Sneen, *J. Am. Chem. Soc.*, **83**, 900 (1961); (b) R. H. De Wolfe and W. G. Young, *Chem. Rev.*, **56**, 753 (1956).
(16) A. J. Fry, "Synthetic Organic Electrochemistry", Harper and Row, New York, N.Y., 1972, Chapter 5.
(17) H. Budzikiewicz, C. Djerassi, and D. Williams, "Mass Spectrometry of Organic Compounds", Holden-Day, San Francisco, Calif., 1967, p 168.
(18) F. W. McLafferty, "Interpretation of Mass Spectra", 2nd ed, W. A. Benjamin, 1973.
(19) Program written by A.J.F.
(20) Reference 17, p 237.
(21) Reference 17, p 443.
(22) J. Levy and P. Jullien, *Bull. Soc. Chim. Fr.*, **45**, 941 (1929).
(23) A. Sosa, *Ann. Chim. (Paris)*, [11], **14**, 100 (1940).
(24) "Handbook of Chemistry and Physics", 47th ed, Chemical Rubber Publishing Co., Cleveland, Ohio, 1966, p C-194.
(25) A referee has commented that thermal conductivity detector response factors were not established, thus introducing some inaccuracies into the data of Table I; while this is correct, it is unlikely that conclusions reached herein would be affected in any substantive way if this omission was corrected. In point of fact, whenever analyses were feasible by both NMR and VPC, the results agreed quite closely (±2–5%).
(26) C. Prevost and A. Sommiere, *Bull. Soc. Chim. Fr.*, **2**, 1151 (1935).

# 3,5-Dinitroperoxybenzoic Acid. A Crystalline, Storable Substitute for Peroxytrifluoroacetic Acid

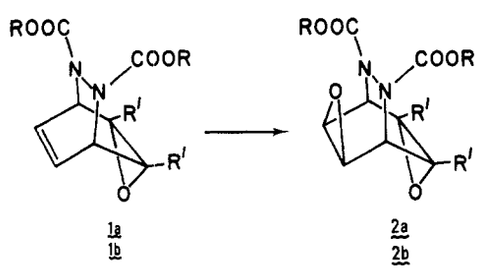
William H. Rastetter,* Thomas J. Richard, and Michael D. Lewis

*Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139*

*Received January 27, 1978*

Epoxidations and Baeyer-Villiger oxidations by 3,5-dinitroperoxybenzoic acid (3,5-DNPBA) are described. A preparation of 3,5-DNPBA is also given.

In the course of our syntheses of *sym*-oxepin oxides[1a-d] we were required to effect the difficult epoxidations of olefins **1a** and **1b**. Neither peroxytrifluoroacetic acid epoxidation nor high-temperature epoxidation by *m*-chloroperoxybenzoic acid proved preparatively useful in these systems. Under optimized conditions only low conversions of **1a** and **1b** to the corresponding epoxides could be achieved with peroxytrifluoroacetic acid. Buffered ($Na_2CO_3$ or $Na_2HPO_4$) peroxytrifluoroacetic acid reaction mixtures gave, at best, intractable mixtures of starting material, desired epoxide, and unidentified by-products.[2] Treatment of the parent system **1a** with 4,4′-thiobis(6-*tert*-butyl-3-methylphenol) (tbp)[3] stabilized *m*-chloroperoxybenzoic acid at elevated temperatures led to tarry reaction mixtures and low yields of diepoxide **2a**.[1a] Clean, efficient epoxidation of **1a** was achieved using *p*-nitroperoxybenzoic acid, stabilized by tbp,[3] in 1,2-dichloroethane at 90 °C (yield of crystalline **2a**, 65%).[1a] With the substituted derivative **1b**, however, the optimized yield utilizing *p*-nitroperoxybenzoic acid did not exceed 37%.[2] We have found that 3,5-dinitroperoxybenzoic acid (3,5-DNPBA) is an efficient reagent for achieving the conversion **1b** → **2b** (vide infra).[4] Herein we report on the synthetic utility of 3,5-DNPBA for difficult epoxidations and Baeyer-Villiger oxidations.




**1a**, **1b** **2a**, **2b**

**1a** and **2a**, R = $CH_2CCl_3$; R′ = H
**1b** and **2b**, R = $CH_2CCl_3$; R′, R′ = $-CH_2CH_2CH_2-$

## Results and Discussion

To test the utility of 3,5-DNPBA we have chosen as substrates **1a**, **1b**, and several other olefins or ketones for which literature oxidation procedures exist. Our results and a summary of literature oxidations are presented in Table I. An inspection of the table suggests that 3,5-DNPBA is not as reactive as peroxytrifluoroacetic acid (e.g., compare concentrations and reaction times for ethyl crotonate) but shows that yields for oxidations by these two peroxy acids are comparable.

It should be noted that similar weights of precursor per mole of peroxy acid are needed for 3,5-DNPBA and peroxytrifluoroacetic acid. The procedure for generation of methylene chloride solutions of peroxytrifluoroacetic acid[5] utilizes trifluoroacetic anhydride (mol wt 210.03) and hydrogen peroxide; buffers are routinely utilized to remove the trifluoroacetic acid which is also formed. By our procedure, crystalline samples of 3,5-DNPBA with active oxygen content >90% can be easily made from 3,5-dinitrobenzoic acid (mol wt 212.12).

Advantages of 3,5-DNPBA over peroxytrifluoroacetic acid are (1) no buffers are needed in 3,5-DNPBA oxidations and (2) 3,5-DNPBA can be stored for long periods without significant loss of active oxygen content. We have routinely stored 3,5-DNPBA in a freezer (<−10 °C) for periods up to 1 year without noticeable loss of reactivity. A more quantitative measure of the loss of active oxygen content from samples of 3,5-DNPBA and peroxytrifluoroacetic acid is given in Table II. At least some loss of active oxygen content from peroxytrifluoroacetic acid solutions is due to evaporation of the volatile peroxy acid. At ambient temperature sufficient evaporation occurs from an approximately 0.2 M solution of peroxytrifluoroacetic acid in methylene chloride to give an immediate, positive KI/starch test at the top of an ice–water cooled spiral condenser attached to a flask of the solution. Our studies of loss of active oxygen content from peroxytrifluo-

0022-3263/78/1943-3163$01.00/0 