Ethyl *cis*-2-Methyl-3-phenylglycidate (*cis*-1a). A mixture of glycidic esters from the Darzens reaction which contained 53% of the cis isomer was saponified with 0.5 equiv of KOH in absolute EtOH with stirring at room temperature for 3 min. After filtration of the pure trans salt, the solution was diluted with water and extracted with ether. The extract was dried, concentrated, and distilled at 97–99° (0.5 Torr) to yield 6 g of a mixture which was 94% *cis*- and 6% *trans*-1a. Pure *cis*-1a may be obtained by using 1.1 equiv of base with respect to the trans ester in the mixture.

Thermolysis of 1a. General Procedure. The Pyrex tubes were thoroughly washed with 6 *N* NaOH, water, and acetone and flame dried. After either the ester 1a or an equimolar mixture of 1 and 2 was introduced, the tube was sealed and placed in a sand bath. Identical results were obtained when soft glass washed as described above was used instead of Pyrex, or when the tubes were washed with concentrated HCl, water, and acetone and flame dried. Just before use, 2 was washed with aqueous $NaHCO_3$ and distilled from Zn dust. The sample of **2b** was prepared according to Burgstahler, *et al.*,[9] and was pure from nmr.

A. A 250-mg sample of *trans*-1a was heated at 230° for 17 hr. Over 90% of the starting material was still present, but as a mixture of 84% trans and 16% cis isomers. Some **2a** and **3a** were also identified by glc and nmr.

B. A 250-mg sample of 1a containing 94% of the cis isomer was heated for 3.5 hr at 270°. Over 90% of 1a containing 60% of the trans isomer was recovered, in addition to small amounts of **2a, 3a,** and **5.**

C. A mixture of 1a (200 mg, *ca.* 50% trans) and **2a** (100 mg) produced 16% conversion to **3a** when heated at 235° for 2 hr, and 60% conversion to **3a** when heated at 280° for 2 hr. However, decomposition took place, and no **3a** could be isolated above 300°. The isomer of **3a** obtained in these experiments was the same as that obtained photochemically, with nmr (CCl_4) at 0.90 (t, J = 7 Hz, 3 H), 1.75 (s, 3 H), 3.65 (q, J = 7 Hz, 2 H), 4.95 (s, 1 H), 6.00 (s, 1 H), and 7.25–7.90 ppm (10 H).[10] The sample of **3c** obtained by thermolysis of 1a and **2b** was identical, except for the absence of the 4.95-ppm signal, while the signal at 6.00 was missing in **3b** from the thermolysis of 1b and **2a.**

Thermal Stability of Ethyl Pyruvate. A mixture of 0.169 of ethyl pyruvate and 0.200 g of 1a (60% cis) was heated as above for 2 hr at 275°. Nmr and gc–mass spectra showed that no ethyl pyruvate was present in this reaction mixture.

Thermolysis of 3a. A crystalline sample of **3a** did not show any change when heated in a sealed tube at 250° for 2 hr. After 0.5 hr at 300°, the nmr integration showed 50% **3a,** 25% **2a,** and 25% ethyl (*E*)-α-methylcinnamate. The assignments were confirmed by glc and glc–mass spectra against authentic samples. Neither 1a nor benzoic acid was detected.

Acknowledgment. We are indebted to the National Science Foundation for its opinion that "a study of the thermal reactions of oxiranes could have no practical applications since most laboratories are not equipped for performing reactions at the temperatures herein reported, and it will not provide answers to problems that people are interested in."

Registry No.—*cis*-1a, 7042-28-6; *trans*-1a, 7141-24-4; *cis*-1b, 52123-63-4; *trans*-1b, 52123-64-5; **2a,** 100-52-7; **2b,** 3592-47-0; **3a,** 40707-69-5; ethyl 2-bromopropionate, 535-11-5; *trans*-α-methylcinnamic acid, 1895-97-2.

References and Notes

(1) G. W. Griffin, *Angew. Chem., Int. Ed. Engl.*, **10,** 537 (1971).
(2) (a) W. J. Linn and R. E. Benson, *J. Amer. Chem. Soc.*, **87,** 3657 (1965); (b) W. J. Linn, *ibid.*, **87,** 3665 (1965); (c) W. J. Linn and E. Ciganek, *J. Org. Chem.*, **34,** 2146 (1969); (d) A. Robert, J. J. Pommeret, and A. Foucaud, *Tetrahedron Lett.*, 231 (1971); (e) A. Robert, J. J. Pommeret, E. Marchand, and A. Foucaud, *Tetrahedron*, **29,** 463 (1973); (f) H. Hamberger and R. Huisgen, *Chem. Commun.*, 1190 (1971); (g) A. Dahmen, H. Hamberger, R. Huisgen, and V. Markowski, *ibid.*, 1192 (1971).
(3) H. H. Wasserman and E. H. Barber, *J. Amer. Chem. Soc.*, **91,** 3674 (1969); W. K. Anderson and T. Veysoglu, *J. Org. Chem.*, **38,** 2267 (1973).
(4) J. Kagan, J. T. Przybytek, B. E. Firth, and S. P. Singh, *Tetrahedron Lett.*, 5133 (1972).
(5) J. Kagan, B. E. Firth, and J. T. Przybytek, unpublished results.
(6) W. B. Guenther and W. D. Walters, *J. Amer. Chem. Soc.*, **73,** 2127 (1951).
(7) C. H. DePuy and R. W. King, *Chem. Rev.*, **60,** 431 (1960).
(8) These reactions are usually acid catalyzed: C. B. Kremer and L. K. Rochen in "Heterocyclic Compounds," Vol. 6, R. C. Elderfield, Ed., Wiley, New York, N. Y., 1957, p 1. However, thermal syntheses may also take place: E. J. Jahn and H. Hibbert, *Can. J. Res.*, **8,** 199 (1933).
(9) A. W. Burgstahler, D. E. Walker, Jr., J. P. Kuebrich, and R. L. Schowen, *J. Org. Chem.*, **37,** 1272 (1972).
(10) The chemical shifts reported for **3a** in ref 4 were in error.

On the Perlactone *vs.* Dioxetanol Intermediates in the Thermal and Base-Catalyzed Autoxidation of Ethyl 2-Oxo-3-phenylbutyrate

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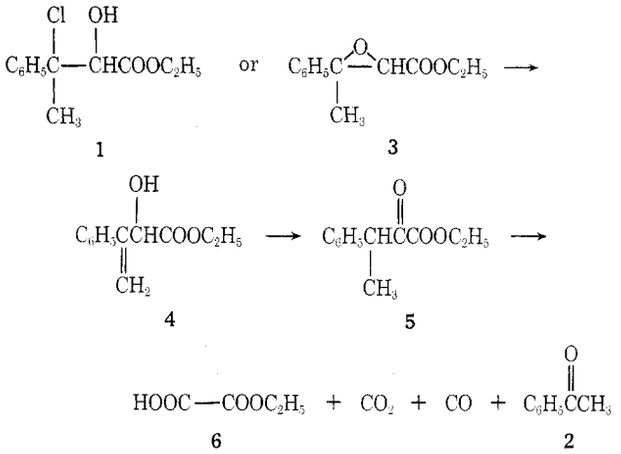
As part of a study on the mechanism of the migration of an ethoxycarbonyl group to an electron-deficient center,[1] the dehydrochlorination of ethyl 2-hydroxy-3-chloro-3-phenylbutyrate (1) at 132° was investigated. Surprisingly, acetophenone (2) was a major product.

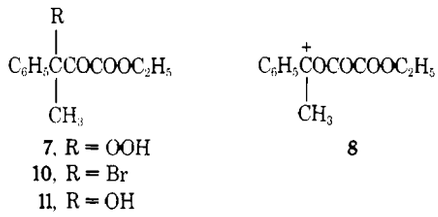
The shortest pathway from 1 to 2 involved the epoxide 3 obtained by dehydrochlorination, in which an oxygen atom was at the required position. While 3 was found to be converted into 2 under the acidic reaction conditions, nmr showed that both 1 and 3 initially yielded the allylic alcohol 4, which further isomerized into the keto ester 5 in the presence of an excess of acid. This product was the actual precursor to 2, and also yielded carbon monoxide, carbon dioxide, ethanol, and monoethyl oxalate at 132°. The conversion was accelerated by bubbling air through the solution, and was completely suppressed in the absence of oxygen. There was no oxidation with singlet oxygen, generated photochemically with rose Bengal as sensitizer, or obtained from the triphenyl phosphite–ozonide adduct.



A mechanism patterned after the well-known cumene oxidation to phenol and acetone was considered, in which a hydroperoxide is decomposed with acid, and undergoes a phenyl migration from carbon to oxygen.[2] The corresponding rearrangement in 7 with either phenyl or methyl migration could not possibly give 2, and needs no further consideration.

The migration of the acyl moiety from carbon to oxygen[3] in the decomposition of 7 would produce a tertiary, oxygen-stabilized, benzylic cation intermediate 8.

Subsequent decomposition as shown in Scheme I, incorporating the molecule of water produced in the conversion of 7 to 8, would account for the observed products. For the sake of convenience, this decomposition is written as pro-

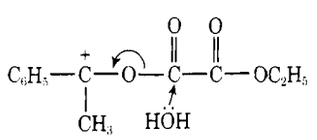


7, R = OOH
10, R = Br
11, R = OH

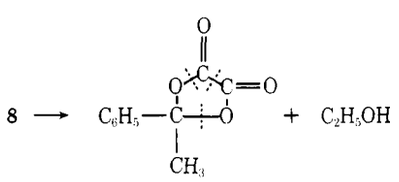
8

ceeding from the attack of water onto the carbonyl group which leads to **3** and **6**, the latter further decomposing to carbon monoxide, carbon dioxide, and ethanol. Alternatively, attack onto the other carbonyl with displacement of ethanol, and decarboxylation–decarbonylation, could also take place, but not as the exclusive pathway since it would not account for the presence of **6**. The process expressed in Scheme I may also be slightly modified to involve the cyclic intermediate **9** (Scheme II). In this case, competition with at least one other scheme producing **6** is also required. Finally, another hypothesis is that fragmentation occurred directly from **7** without prior group migration (Scheme III). Control experiments showed that the oxalate was only partially stable under the reaction conditions, and an exact determination of its contribution to the formation of carbon monoxide, carbon dioxide, and ethanol could not be obtained.

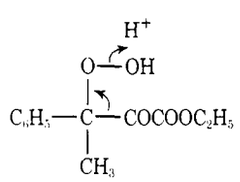
Scheme I



Scheme II



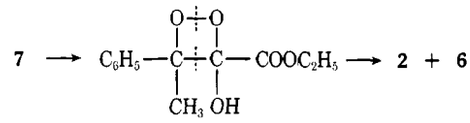
Scheme III



The synthesis of **7** was attempted, by alkaline 90% hydrogen peroxide treatment of the bromide **10**. We did not succeed in isolating the desired product down to −40°, and the formation of **2** was observed as soon as any reaction of **10** was detected. Although the nucleophile could either displace the bromide or attack one carbonyl, the former was suggested by the isolation of the substitution product **11** when water was substituted for hydrogen peroxide in this experiment. No reaction took place when this treatment of **10** was performed in acidic or neutral medium.

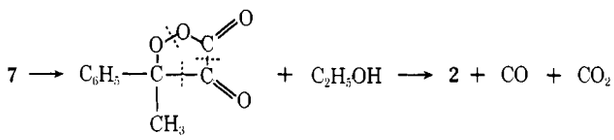
The mechanism for the conversion of **7** to **2** in basic solution need not be identical with that in acidic medium. Here the only reaction products were carbon monoxide, carbon dioxide, and ethanol. The often proposed mechanism for the degradation of α-hydroperoxy carbonyl compounds in neutral or alkaline medium does not apply,[4] since, as shown in Scheme IV, a dioxetanol intermediate would have produced monoethyl oxalate, which was proved to be stable under the reaction conditions.

Scheme IV



A mechanism which accounts for all the experimental facts in the base-catalyzed autoxidation of **5** involves cyclization of the presumed hydroperoxide intermediate **7** onto the ester carbonyl, giving an α-ketoperlactone **12** (Scheme V).

Scheme V

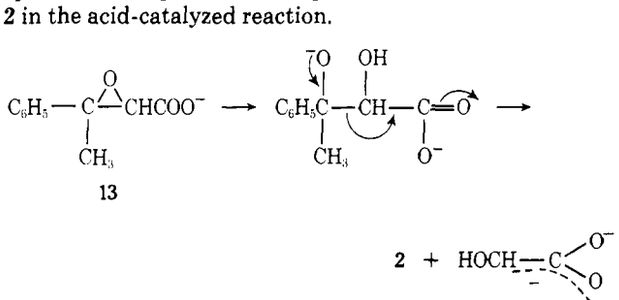


12

Although perlactones have been known since 1966,[5] and some have even been formed from β-hydroperoxy esters,[6] there is no record of any with an α-carbonyl, and this work suggests their thermal lability.

The mode of fragmentation proposed for **12** is analogous to one pathway observed in the thermolysis of simple perlactones[7] where a carbene must have been generated beside the ketone and carbon dioxide and which, understandably, required a much higher temperature than for the elimination of the stable carbon monoxide fragment. The extent to which the mechanisms expressed in Schemes IV and V contribute to the formation of **2** in the thermolysis of **1** or in the autoxidation of **5** in addition to those suggested in Schemes I–III is unknown.

Two reports of unexpected formation of acetophenone came to our attention. House and Blaker found that sodium β-phenyl-β-methylglycidate (**13**) yielded **2** beside the expected 2-phenylpropionaldehyde (**14**) when heated in aqueous solution.[8] The amount of **2** was considerably reduced (from 32 to less than 2%) when the salt was acidified at 0°. The difference was attributed to the intervention of a base-catalyzed retro-aldol reaction following opening of the epoxide. No explanation was provided for the formation of **2** in the acid-catalyzed reaction.



13

While the retro-aldol cleavage of β-hydroxy esters occurs either in base[9] or in acid,[1c] that of β-hydroxy acids is only known in acid medium.[10] The enolate ion of a carboxylic acid is only formed with great difficulty, and is therefore not expected to be a good leaving group. The autoxidation of **14** provides a more reasonable explanation for the presence of **2** in House and Blaker's experiments. The base-catalyzed treatment of **13** was repeated as described, with a control solution treated identically, but under nitrogen. The amount of **2** was found to be small in both cases (less than 3%), but the latter had about one-sixth the amount of **2** found in the former (nmr determination just following immediate work-up). As expected, the yield of **2** increased

markedly when the sample of **14** was allowed to stand in the presence of base without nitrogen protection.

The warning by House and Blaker[8] that any procedure involving heating a glycidic ester with aqueous alkali as part of the degradation to a carbonyl compound was undesirable is no longer justified. To the extent that saponification precedes glyceric ester formation (we know of no exception) the real problem rests with the protection of the initially formed carbonyl product from further autoxidation, easily solved by running the reaction under nitrogen.

Thummel and Rickborn reported the unexpected formation of **2** in the base-induced rearrangement of 1-methyl-2-phenyloxirane (**15**, 94% trans), and commented on the absence of analogy for the production of this material in the literature.[11]

A similar treatment of *trans*-1,2-diphenyloxirane had been reported to yield diphenylacetaldehyde,[12] and **14** was therefore expected from **15**. Its absence, and the failure by the authors to mention any protection from oxygen in the base-catalyzed treatment of **15**, point to the autoxidation of **14** as the most satisfactory explanation for the formation of **2** in these experiments.

Experimental Section

***threo*- and *erythro*-Ethyl 2-Hydroxy-3-chloro-3-phenylbutyrate (1).** Ether saturated with HCl (100 ml) was added to 10 g of **3**[13] frozen in liquid nitrogen. The mixture was stirred while being allowed to melt, and was then kept in a refrigerator for 23 hr. After concentration under vacuum, the residue crystallized from petroleum ether. It was recrystallized to yield 10.55 g of **1**, mp 53–59°.

Anal. Calcd for $C_{12}H_{15}O_3Cl$: C, 59.42; H, 6.22; Cl, 14.60. Found: C, 59.44; H, 6.22; Cl, 14.59.

Ethyl 2-Hydroxy-3-phenyl-3-butenoic Acid (4). A solution of 5 g of **3** in 25 ml of C_6H_5Cl was refluxed for 16.5 hr after HCl had been bubbled through for 5 min. The solvent was removed and nmr showed the crude product to be **4**, at least 90% pure. It was distilled bulb-to-bulb at 70° (0.07 Torr): nmr ($CDCl_3$) 0.95 (t, J = 7 Hz, 3 H), 4.07 (q, J = 6.75 Hz), and 4.08 (q, J = 7 Hz, total 2 H), 4.57 (s, 1 H, exchanges with D_2O), 5.28 (s, 1 H), 5.56 (s, 1 H), 5.60 (s, 1 H), 7.30 (m, 3 H), and 7.55 ppm (m, 2 H).

Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.85; H, 6.84. Found: C, 69.61; H, 7.11.

Ethyl 2-Oxo-3-phenylbutyrate (5). A solution of 10 g of **4** and 0.6 g of *p*-toluenesulfonic acid in 60 ml of C_6H_5Cl was refluxed for 30 hr. The solvent was removed under vacuum, and the residue was dissolved in ether, extracted with aqueous $NaHCO_3$, and dried over $MgSO_4$. The product, over 90% pure by nmr, was distilled and yielded **5**: bp 65° (0.07 Torr); nmr ($CDCl_3$) 1.13 (t, J = 7 Hz, 3 H), 1.80 (d, J = 7 Hz, 3 H), 4.07 (q, J = 7 Hz, 2 H), 4.38 (q, J = 7 Hz, 1 H), and 7.18 ppm (s, 5 H).

Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.92; H, 6.95.

Ethyl 2-Oxo-3-bromo-3-phenylbutyrate (10). To a refluxing solution of 7.50 g of **5** and 8.1 g of *N*-bromosuccinimide in 190 ml of CCl_4, 0.30 g of benzoyl peroxide was added over 3 hr. After another 18-hr reflux, the mixture was cooled, filtered, and concentrated under vacuum. The crude product was over 90% pure: bp 145° (3.5 Torr); nmr ($CDCl_3$) 1.15 (t, J = 7 Hz, 3 H), 2.22 (s, 3 H), 3.02 (q, J = 7 Hz, 2 H), and 7.33 ppm (m, 5 H).

Decomposition of 1. The bottom of a nmr tube containing about 0.20 g of **1** was immersed in refluxing C_6H_4Cl, contained in a flask fitted with a condenser which also cooled the top of the nmr tube. The progress of the reaction at 132° was monitored by nmr between 15 min and 54 hr. **2** was identified by comparison with an authentic sample (nmr, tlc, and glc), and **3**, **4**, and **5** were also detected by nmr.

Decomposition of 3. A sample of **1** containing a trace of HCl was heated as above. After 1.25 hr at 132°, **4** was formed in over 90% yield. In another experiment, the nmr tube containing 0.10 g of **3** and 0.01 g of **1** was sealed. After 63 hr at 132°, **5** had been formed in over 90% yield. In both cases **2** was detected by its characteristic signals at 2.5 and near 7.9 ppm in the nmr.

Decomposition of 5. The air used for the oxidation was purified through $PdCl_2$ in 0.005 M HCl, followed by solid NaOH and Linde molecular sieves. The sample of **5** was heated to 132 or 155° for 16 hr in the presence of a stream of air, which was then run into a trap cooled in liquid nitrogen. After reaction, this trap was allowed to warm up, and the gases released were passed through successive traps containing (a) NaOH and molecular sieves, (b) concentrated H_2SO_4, (c) saturated $Ba(OH)_2$, (d) aqueous $Pb(OAc)_2$, and (e) $PdCl_2$ in 0.005 M HCl.[14] The only product left in the reaction vessel was **2**, while CO_2 and CO were detected in traps c and e, respectively, and the nongaseous products left in the first trap were EtOH, monoethyl oxalate, and **2**.

Treatment of 5 with Singlet Oxygen. A. Ozone was bubbled through a solution of 1.5 g of triphenyl phosphite in 40 ml of CH_2Cl_2 at −78° until the blue color persisted. The excess of O_3 was removed by a stream of N_2, 1.0 g of **5** was added, and the solution was allowed to warm slowly to room temperature.[15] Nmr of the mixture after removal of the solvent showed that no reaction had taken place.

B. Air was bubbled through a solution of 0.479 g of **5** and 0.034 g of rose Bengal in 250 ml of CH_3CN during its irradiation at 350 nm for 2 hr in a Rayonet reactor. After removal of the solvent, nmr showed that only a trace amount of **2** had been formed.

Attempted Synthesis of Ethyl 2-Oxo-3-phenyl-3-hydroperoxybutyrate (7). A solution of 0.552 g of **10** and 0.32 ml of 90% H_2O_2 in 5 ml of acetone was stirred for 50 min after the addition of 0.145 g of K_2CO_3. The gas evolved was shown to contain CO with $PdCl_2$ in HCl. After standing for another 105 min, the mixture was filtered and the filtrate was concentrated to yield pure **2**. The solid obtained had no CH bonds as shown by nmr in D_2O. Control experiments indicated that **2**, **5**, and **6**[16] were all stable under the reaction conditions. The same results were obtained when the reaction was run at 5° in H_2O with NaOH, 24° in dioxane with K_2CO_3, and −40° in THF with K_2CO_3. A similar result was also observed at 5° in ether with K_2CO_3, but unreacted **10** was still present. At 24° in THF with HCl, no reaction took place. When the reaction in acetone with K_2CO_3 was run with H_2O rather than H_2O_2, it yielded ethyl 2-oxo-3-phenyl-3-hydroxybutyrate without decomposition.

2-Phenylpropionaldehyde (14) from 3. The published procedure was followed exactly,[8] with the exception that no stirring was used. A control reaction under N_2 was also performed. Nmr analysis showed that the amount of **2** was about 3% in the former and less than 0.5% in the latter. The crude reaction product was treated with 2,4-dinitrophenylhydrazine, and yielded the derivative from **14**, mp 135°.

Air Oxidation of 14. Air was bubbled for 1 hr through a solution of 1.25 g of **14** and 0.15 g of KO-*t*-Bu in 30 ml of *t*-BuOH. After concentration under vacuum, the nmr of the CCl_4-soluble fraction of the residue showed that over 50% of **14** had been oxidized to **2**.

Acknowledgment. We are grateful to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for financial support of this work.

Registry No.—**1**, 52217-11-5; **2**, 98-86-2; **3**, 77-83-8; **4**, 30913-58-7; **5**, 24441-66-5; **10**, 52217-12-6; **14**, 93-53-8.

References and Notes

(1) (a) S. P. Singh and J. Kagan, *J. Amer. Chem. Soc.*, **91**, 6198 (1969); (b) J. Kagan, D. A. Agdeppa, Jr., and S. P. Singh, *Helv. Chim. Acta*, **55**, 2252 (1972); (c) J. Kagan and D. A. Agdeppa, Jr., *ibid.*, **55**, 2255 (1972).
(2) R. T. Morrison and R. N. Boyd, "Organic Chemistry," 3rd ed, Allyn and Bacon, Boston, Mass., 1973, p 893.
(3) F. W. Lichtenthaler and G. Bambach, *J. Org. Chem.*, **37**, 1621 (1972).
(4) E. P. Kohler and R. B. Thompson, *J. Amer. Chem. Soc.*, **59**, 887 (1937); W. v. E. Doering and R. M. Haines, *ibid.*, **76**, 482 (1954).
(5) F. D. Greene, W. Adam, and G. A. Knudsen, Jr., *J. Org. Chem.*, **31**, 2087 (1966).
(6) R. C. P. Cubbon and C. Hewlett, *J. Chem. Soc. C*, 2983 (1968); D. H. Gibson, H. L. Wilson, and J. T. Joseph, *Tetrahedron Lett.*, 1289 (1973).
(7) W. Adam and G. Santiago Aponte, *J. Amer. Chem. Soc.*, **93**, 4300 (1971).
(8) H. O. House and J. W. Blaker, *J. Amer. Chem. Soc.*, **80**, 6389 (1958).
(9) C. S. Rondestvedt, Jr., and M. E. Rowley, *J. Amer. Chem. Soc.*, **78**, 3804 (1956).
(10) D. Ivanoff, N. Marecoff, and B. Amidjine, *Bull. Soc. Chim. Fr.*, 1214 (1963).
(11) R. P. Thummel and B. Rickborn, *J. Org. Chem.*, **37**, 3919 (1972).
(12) A. C. Cope, P. A. Trumbull, and E. R. Trumbull, *J. Amer. Chem. Soc.*, **80**, 2844 (1958).
(13) C. F. H. Allen and J. van Allan, "Organic Syntheses," Collect. Vol. III, Wiley, New York, N. Y., 1955, p 727.
(14) R. Böttger, *J. Prakt. Chem.*, **76**, 233 (1859).
(15) R. W. Murray and M. L. Kaplan, *J. Amer. Chem. Soc.*, **91**, 5358 (1969).
(16) E. Fourneau and S. Sabetay, *Bull. Soc. Chim. Fr.*, **43**, 859 (1928).