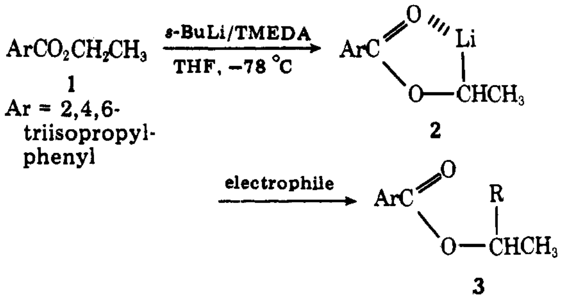
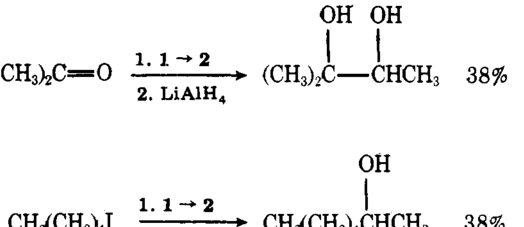
Scheme I



a, $R = HOC(CH_3)_2$	41% (64%)
b, $R = HOC(CH_2)_5$	31% (50%)
c, $R = CH_2CH{=}CH_2$	42% (79%)
d, $R = Si(CH_3)_3$	64% (94%)
e, $R = Sn(C_4H_9)_3$	53% (85%)
f, $R = HOC(CD_3)_2$	
g, $R = D$	

Scheme II



$$(CH_3)_2C{=}O \xrightarrow[\text{2. LiAlH}_4]{\text{1. }1\to 2} (CH_3)_2C(OH){-}CH(OH)CH_3 \quad 38\%$$

$$CH_3(CH_2)_4I \xrightarrow[\text{2. LiAlH}_4]{\text{1. }1\to 2} CH_3(CH_2)_4CH(OH)CH_3 \quad 38\%$$

h gives **2**, which can be trapped by addition of acetone, cyclohexanone, allyl bromide, trimethylsilyl chloride, and tri-*n*-butyltin chloride to give the expected products, **3a–e**, in the purified (and crude) yields indicated in Scheme I.[5] When hexadeuterioacetone is used as the electrophile and the composition of the products determined by NMR, the product **3f** is obtained in 67% yield, while the ethyl ester is observed to be 58% deuterated material, **3g**. This result, as well as the 85% crude yield of **3e**, suggests that metalation is satisfactorily complete under these conditions and that the relatively low yields obtained with the ketones are due to competing enolizations.

On a preparative scale the metalation can be a key step in the preparation of the α-lithioethyl alcohol synthon. Thus formation of **2** from **1** on a several gram scale, followed by addition of hexamethylphosphoric triamide (HMPA) just prior to addition of the electrophile followed by reduction with lithium aluminum hydride in THF or dimethoxyethane, yields the substituted alcohols as shown in Scheme II. The isolated yields are based on **1**.

It is reasonable that corresponding α-lithio derivatives of other primary alcohols will be available by metalation of the esters of 2,4,6-trisubstituted benzoates or closely related compounds.[6] For some situations the presence of excess *s*-BuLi/TMEDA or unmetalated ester may be inconvenient. In that case the tin compound **3d** can be reacted with methyllithium to provide **2** in high yields; subsequent additions of deuteriomethanol, methyl iodide, and methyl benzoate give the expected products in 80–100% crude yield. An imaginative alternative route to α-lithioalkyl alcohol synthons by stannylation of the corresponding aldehydes has recently been reported by Still.[7]

Activation by the benzoate carbonyl has now been shown to facilitate direct metalative preparation of primary and secondary organolithiums adjacent to oxygen, sulfur, and nitrogen.[1-3] While such organometallics can be considered dipole-stabilized carbanions, further information on that point, as well as development of the synthetic potential of these species, is being studied.

Procedure. To a solution of 1:1 *s*-BuLi/TMEDA (25.3 mmol) in THF stirring at −78 °C under nitrogen was added a solution of 3.98 g (14.4 mmol) of ethyl 2,4,6-triisopropylbenzoate (**1**) in THF. After the reaction mixture was allowed to stir at −78 °C for 6 h, 4 mL of HMPA was added, followed by 20 mL of 1-iodopentane. The reaction mixture was allowed to stir at −78 °C for 20 min, and then allowed to warm to room temperature. Ether was added and the organic phase was washed with aqueous saturated NH_4Cl, concentrated, dissolved in ether, and washed with aqueous 10% HCl and 10% NaOH. The organic layer was dried ($CaSO_4$) and concentrated under vacuum to give 4.8 g of a clear, orange oil. This material and 5.0 g (0.13 mol) of $LiAlH_4$ in 75 mL of dimethoxyethane (DME) were heated at reflux for 2.5 h. The heterogeneous reaction mixture was cooled to room temperature and treated with a minimal amount of H_2O. The insoluble salts were removed by filtration and washed with ether. The filtrates were combined, dried ($MgSO_4$), and concentrated under vacuum to give a clear, yellow oil which was distilled at atmospheric pressure to afford 0.64 g (5.51 mmol, 38%) of 2-heptanol.

Acknowledgment. We are grateful to the National Institutes of Health—Institute of General Medicine for support of this work.

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(2) P. Beak and D. B. Reitz, *Chem. Rev.*, **78**, 275 (1978).

(3) R. Schecker, D. Seebach, and W. Lubosch, *Helv. Chim. Acta*, **61**, 512 (1978).

(4) Prepared from the corresponding acid chloride and ethanol: R. C. Fuson and E. C. Horning, *J. Am. Chem. Soc.*, **62**, 2962 (1940). An alternative route from 2,4,6-triisopropylphenyllithium and diethyl carbonate is also useful.

(5) All new compounds were characterized by IR, NMR, and satisfactory combustion analysis except for **3b**, which was 0.5% low for hydrogen. Previously known compounds were identified by comparison of NMR and IR spectra with published data.

(6) For example, metalation of *n*-octyl 2,4,6-triisopropylbenzoate under similar conditions followed by separate reactions with deuteriomethanol, acetone, or allyl bromide gives the expected products in crude yields of 90, 45, and 95%, respectively.

(7) W. C. Still, *J. Am. Chem. Soc.*, **100**, 1481 (1978).

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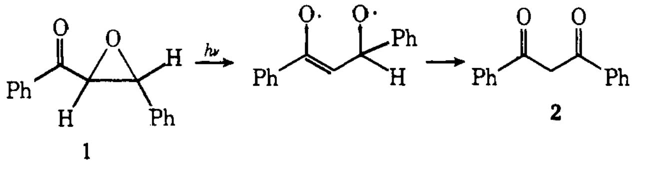
Photochemical Transformations of Chalcone Oxides

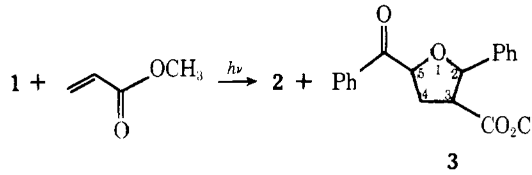
Summary: Close examination of the photobehavior of several chalcone oxides has demonstrated that aryl ring substituents control whether the C_α–O or C_α–C_β bond of the oxirane ring will be cleaved.

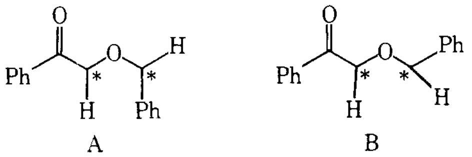
Sir: Photochemical rearrangements of α,β-epoxy ketones have received extensive study and have been the subject of several reviews.[1-4] These compounds generally display two types of photobehavior: (a) photoisomerization of arylcyclopentenone oxides to pyrylium oxides,[5,6] and (b) photoisomerization of α,β-epoxy ketones to β-diketones.[8-10] Although much data have been accumulated to show that C_α–O bond cleavage is the predominant mode of photofragmentation in α,β-epoxy ketones, Muzart and Pète[11] have demonstrated that cleavage of the oxirane C_α–C_β bond also can occur in certain optically active derivatives. Interestingly, epoxynaphthoquinones have been shown to undergo two types of photocycloaddition reactions with olefins arising either from n,π^* excited-state addition of the carbonyl group to form oxetanes, or from C–C bond fission of the oxirane ring followed by 1,3-dipolar addition to the olefin forming substituted tetrahydrofurans.[12] Because of our interest in the photochemical generation of carbonyl ylides from aryloxiranes[13,14] we have reexamined the photobehavior of chalcone oxides[8,15] to see if carbonyl ylides might also be intermediates in rearrangements of these compounds.

Irradiation[16] of *trans*-chalcone oxide (1) in acetonitrile with 313-nm radiation led to the formation of dibenzoylmethane (2) as the major product (Φ = 0.019) accompanied by an unidentified isomer[17] (Φ = 0.009). The formation of 2 from 1 was first described by Bodforss in 1918[8] and is assumed to arise from cleavage of the C_α–O bond of the oxirane followed by a 1,2 shift of the β-hydrogen to the α position.[10]

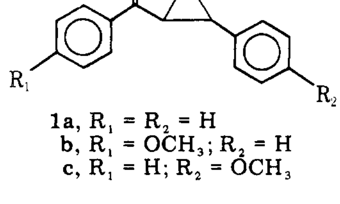


However, irradiation of 1 in the presence of a sixfold excess of methyl acrylate, an efficient dipolarophile,[13,18,19] led to the formation of substituted tetrahydrofuran adducts, 3,[17b,20] in addition to dibenzoylmethane. The configuration of the THF adducts 3 suggests that at least 83% of the intermediate carbonyl ylide precursors were formed by a disrotatory cleavage of the oxirane C_α–C_β bond,[21] producing the trans ylide A, which was subsequently trapped by methyl acrylate. These results are consonant with Woodward and Hoffmann's predictions of disrotatory electrocyclic ring opening in four-electron systems,[21] but the formation of adducts derived from the cis ylide B is an anomaly, similar to that previously observed by us[13] and by Huisgen.[14b] In attempting to determine the nature of the excited states responsible for these rearrangements, we have observed that the reaction is not quenched by 0.3 M piperylene, but is apparently sensitized by acetophenone (E_t = 74 kcal/mol) and by xanthone (E_t = 74 kcal/mol). Under conditions where both sensitizers absorbed >95% of the light, the same distribution of products was obtained. These data suggest that both C_α–O and C_α–C_β bond cleavages occur from a triplet excited state of 1 which is so short-lived that it cannot be quenched by energy transfer to piperylene.



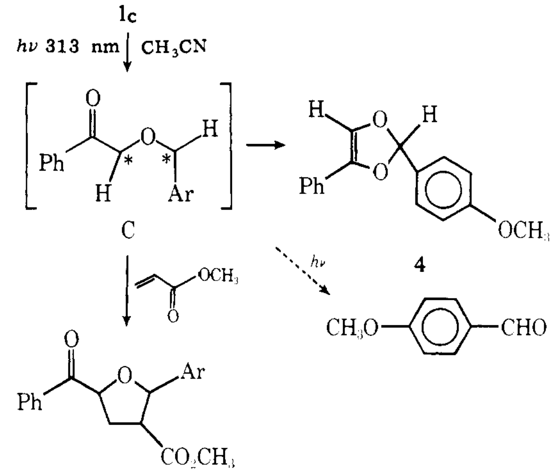


Since substituents on the oxirane ring should affect the stability of the photogenerated carbonyl ylides,[12,14b,c] we have examined the photochemistry of the methoxy-substituted chalcone oxides, 1b and 1c. Direct irradiation of a 0.03 M solution of 1b in acetonitrile led cleanly to the formation of a single product (Φ = 0.024), isolated and identified as 1-(4-methoxyphenyl)-3-phenyl-1,3-propanedione (2b).[22] Irradiation of 1b with a sixfold excess of methyl acrylate decreased the efficiency of 2b formation (Φ = 0.011), but did not lead to detectable amounts of adducts, similar to those observed from 1a. The quantitative mass balance obtained in both of the above experiments suggests that 1b undergoes photoreaction exclusively by C_α–O bond cleavage.



1a, $R_1 = R_2 = H$
b, $R_1 = OCH_3$; $R_2 = H$
c, $R_1 = H$; $R_2 = OCH_3$

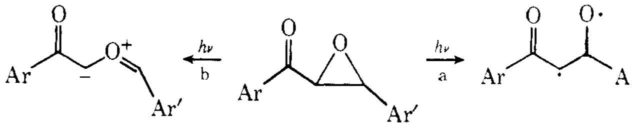
In contrast to the clean C–O bond fragmentation obtained from 1b, direct irradiation of 4-methoxychalcone oxide (1c) led to rapid formation (Φ = 0.27) of 2-(4-methoxyphenyl)-4-phenyl-1,3-dioxole[24] (4) along with a small amount (Φ = 0.03) of anisaldehyde. The formation of dioxole 4 can be rationalized by C_α–C_β bond fission to form the stabilized ylide C, which then predominantly undergoes ring closure to 4 or can suffer further photodegradation to form anisaldehyde.[26]



Ar = 4-methoxyphenyl-

We have been unable to detect any 1,3-diketone 2b, which would have arisen by C_α–O bond cleavage. Irradiation of 1c in acetonitrile containing a 15 molar excess of methyl acrylate gave a reduced yield of 4 and gave rise to the formation of THF adducts (Φ = 0.05),[27] 5. Isolation and stereochemical analysis of 5 indicates that they primarily (>90%) derive from disrotatory C–C oxirane ring cleavage of 1c (forming carbonyl ylide C), followed by 1,3-cycloaddition to methyl acrylate. Attempts to trap ylide C with other olefins, such as norbornene, have been unsuccessful. The apparent necessity of electron-deficient olefins to trap carbonyl ylides has been noted previously[5-7,13,14b] and is consistent with Houk's suggestion that alkyl and conjugated carbonyl ylides should undergo HOMO (dipole) controlled 1,3-dipolar cycloaddition reactions.[18,28]

These preliminary results illustrate the importance which substituents can play in controlling whether C_α–O or C_α–C_β bond cleavage occurs from photoexcited chalcone oxides, and suggests a new synthetic route for preparing unstable substituted dioxoles. Further work is now underway to determine the photochemical consequences of other substituents and of starting material geometry in related α,β-epoxy ketones to provide a clearer and unified mechanistic understanding of these reactions.



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(14) For examples of related work, see also (a) I. J. Lev, K. Ishikawa, N. S. Bhacca, and G. W. Griffin, *J. Org. Chem.*, **41,** 2654 (1976); (b) V. Markowski and R. Huisgen, *Tetrahedron Lett.*, 4643 (1976); (c) R. Huisgen, *Angew. Chem., Int. Ed. Engl.*, **16,** 572 (1977), and references contained therein.

(15) Previous studies on the parent chalcone oxide had failed to find any evidence for the intermediacy of carbonyl ylides; (a) A. Padwa and W. Eisenhardt, *J. Am. Chem. Soc.*, **93,** 1400 (1971); (b) D. J. Dewar and R. G. Sutherland, *J. Chem. Soc., Perkin Trans. 2*, 1522 (1977).

(16) All irradiations carried out on ~4 × 10^{-2} M solutions of the respective chalcone oxides in various solvents contained in 15 × 150 mm Pyrex test tubes. Samples were deaerated at 0 °C with argon, capped with a rubber septum and irradiated on a merry-go-round apparatus with 8-3130 Å or 8-3660 Å low-pressure Hg vapor lamps in a Srinivasan–Griffin reactor.

(17) (a) Due to the relative instability of this unknown, we have as yet been unable to adequately characterize its structure. (b) Irradiation of **1** in the presence of methyl acrylate significantly reduced the yield of this unknown.

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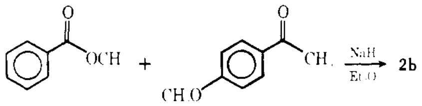
(19) R. Huisgen, *Angew. Chem., Int. Ed. Engl.*, **2,** 633 (1963); *J. Org. Chem.*, **41,** 403 (1976).

(20) The structure and stereochemistry of the adducts (**3** and **5**) are based upon spectroscopic data (^{1}H NMR, IR, *m/e*) and upon base-catalyzed (NaOMe/MeOH) epimerization of the C_3 center to give the thermodynamically favored trans orientation to the C_2–C_3 substituents.

(21) R. B. Woodward and R. Hoffmann, *J. Am. Chem. Soc.*, **87,** 395 (1965); cf. ref 12 and 13b.

(22) Spectral characteristics (^{1}H NMR, IR, *m/e*) and melting point (129–130 °C) of isolated **2b** identical with an independently prepared sample. Lit.[23] mp 132 °C.



(23) C. R. Hauser, F. W. Swamer, and J. T. Adams, *Org. React.*, **8,** 59 (1954).

(24) The structure of **4** is based upon ^{1}H NMR, IR (no C=O, 1308, 1312, 1020, 1038, and 1096 cm^{-1}, attributed to cyclic acetal[25]), and *m/e* (254 parent, 105 base) analysis and upon quantitative chemical degradation to anisaldehyde and phenacyl acetate upon treatment with AcOH/Ac_2O/*p*-toluenesulfonic acid.

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(26) G. W. Griffin, K. Ishikawa, and I. J. Lev, *J. Am. Chem. Soc.*, **98,** 5697 (1976).

(27) At higher concentrations of methyl acrylate (90 molar excess) the ratio of **5/4** = 60:40.

(28) A similar interpretation has been presented by R. Sustmann [*Tetrahedron Lett.*, 2717, 2721 (1971)] and by N. D. Epiotis [*J. Am. Chem. Soc.*, **94,** 1924, 1935, 1941, 1946 (1972)].

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