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STUDIES IN CLAISEN REARRANGEMENT—VI
ORTHO CLAISEN REARRANGEMENT OF DISSYMMETRICAL 1,4-DIARYLOXY-*TRANS*-2-BUTENES

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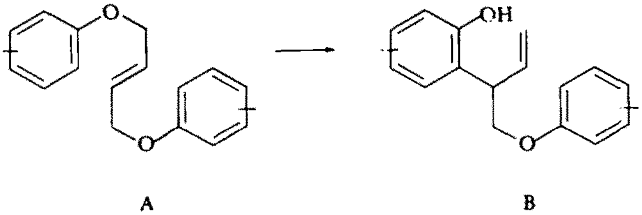
Abstract—The *ortho* Claisen rearrangement of dissymmetrical, 1,4-diaryloxy-*trans*-2-butenes has been studied. Degradative evidence was provided to determine the migratory aptitude of the aryl moieties. An *ortho* substituent on the aryl ring induced greater ease of migration. *Para* chloro and *para* methyl functions induced nearly equal migratory aptitude.

IN A recent communication[1] on the *ortho* Claisen rearrangement of *symmetrical* 1,4-diaryloxy-*trans*-2-butenes, it was reported that 1,4-diaryloxy-*trans*-2-butenes underwent only a single Claisen rearrangement as shown below:



The butenyl ether (B) did not tautomerize under the experimental conditions, precluding thereby a second Claisen migration. Encouraged by this observation, we have investigated the behaviour of 16 different dissymmetrical ethers with a view to determine their relative migratory aptitudes.

Synthesis of the dissymmetrical 1,4-diaryloxy-*trans*-2-butenes was achieved by a bimolecular displacement of an 1-aryloxy-4-chloro-*trans*-2-butene with a different

TABLE 1. 1-ARYLOXY-4-CHLORO-*trans*-2-BUTENES

Ar = . . .	b.p.	°C/mm Yield	
1. Phenoxy	130/5	*	
2. *o*-Methylphenoxy	110/0·5	*	
3. *o*-Chlorophenoxy	165/12	51	This study
4. *m*-Methylphenoxy	138/5	48	This study
5. *p*-Chlorophenoxy	158/4	45	This study
6. *p*-Methylphenoxy	140/4	43	This study

* B. W. Horrow and H. E. Zaugg, *J. Am. Chem. Soc.* **79**, 1754 (1957).

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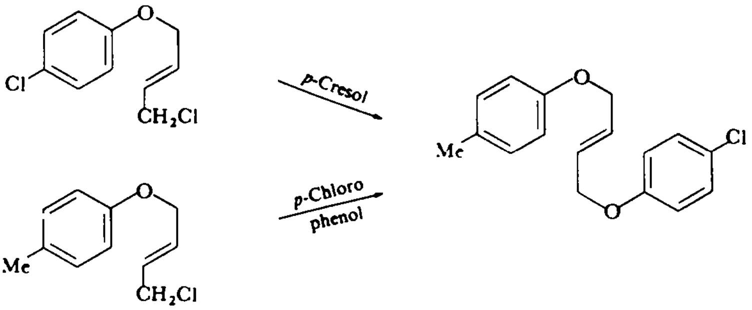
[1] B. S. Thyagarajan, K. K. Balasubramanian and R. Bhima Rao, *Tetrahedron* **23**, 3205 (1967).

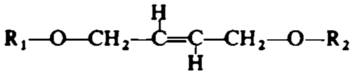
phenol in the presence of alkali. Two such monoethers were already known in the literature and four more were synthesized. These are listed in Table 1.

In order to ensure that no SN'_2 displacement had occurred during introduction of the second aryl moiety, the 1-(*p*-chlorophenoxy)4-(*p*-methylphenoxy)*trans*-2-butene was prepared starting from either mono aryl ether as illustrated below:



As identical derivatives were obtained from either starting material it was clearly established that the ethers were truly dissymmetrical 1,4-diaryloxy-*trans*-2-butenes. The NMR spectra of the ethers corroborated these conclusions by showing only three types of protons, *viz.* the O-methylene protons, the vinyl protons and the aromatic ring protons. The ethers are listed in Table 2.

TABLE 2. DISSYMMETRICAL 1,4-DIARYLOXY-*trans*-2-BUTENES



R_1—O—CH_2—$\overset{H}{C}$=$\underset{H}{C}$—CH_2—O—R_2

	R_1	R_2	B.p. °C/mm	M.p. °C
I.	Phenyl	*o*-Chlorophenyl	160/0·5	
II.	Phenyl	*p*-Methylphenyl		72
III.	Phenyl	*p*-Chlorophenyl		69
IV.	Phenyl	*p*-Nitrophenyl		102
V.	Phenyl	β-Naphthyl		112
VI.	*o*-Methylphenyl	*m*-Methylphenyl	148/0·7	
VII.	*o*-Methylphenyl	*p*-Methylphenyl		72
VIII.	*m*-Methylphenyl	*p*-Methylphenyl	180/0·9	
IX.	*m*-Methylphenyl	*p*-Chlorophenyl	180/1·0	
X.	*p*-Methylphenyl	*o*-Chlorophenyl		65
XI.	*p*-Methylphenyl	*o*-Methoxyphenyl		76
XII.	*p*-Methylphenyl	*p*-Nitrophenyl		110
XIII.	*p*-Chlorophenyl	*o*-Methoxyphenyl		81
XIV.	*p*-Chlorophenyl	*p*-Nitrophenyl		113
XV.	*p*-Chlorophenyl	*p*-Methylphenyl		104
XVI.	*p*-Chlorophenyl	β-Naphthyl		100

As in the earlier study,[1] the ethers were subjected to Claisen rearrangement in refluxing diethylaniline. Although the ethers were liquids or solids of low, m.p., rearrangement without solvent caused considerable decomposition and reversal to the starting phenols.

In every instance, the product was a high boiling liquid obtainable in good yields (55–82%). However, most of the products proved to be inseparable mixtures. To an extent, this was anticipated because of the close similarity in chemical properties between the products arising by the two different modes of rearrangement. In addition, one has complications arising from concomitant ring closure of the products to benzopyran or benzofuran derivatives. The b.p. of the products and relative yields are listed in Table 3.

Table 3. Rearrangement products of dissymetrical butenyl ethers

Starting compound *vide* earlier Table	Product	B.p. °C/mm	Yield %
I	XVII	158/0·6	60
II	XVIII	180/1	66
III	XIX	192/1	82
V	XX	(m.p. 122°)*	—
VI	XXI	164/0·6	72
VII	XXII	196/1·0	70
VIII	XXIII	160/0·4	64
IX	XXIV	174/0·5	55
X	XXV	160/0·5	62
XI	XXVI	190/0·6	67
XIII	XXVII	164/0·4	68
XV	XXVIII	175/0·7	62
XVI	XXIX	(m.p. 122°)*	—

* This solid was identified as β-naphthol. Ethers IV, XII and XIV did not yield characterizable products from the rearrangement.

All the rearranged products exhibited the following common features: 1, a strong OH absorption in the IR; 2, facile formation of a *mono*-acetate; 3, elements of unsaturation by the ready uptake of bromine water and aqueous permanganate; 4, UV spectra (*vide* Tables 4 and 5) that showed no enhanced conjugation from the starting ether so that the newly created unsaturation was not in conjugation with either aryl unit.

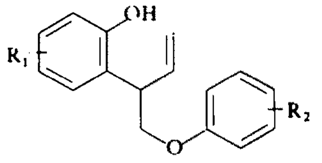
Table 4. UV data of dissymmmetrical ether

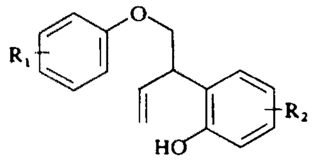
Starting ether No.	λ_{max}^{EtOH} mμ (log ε)
I	219 (4·29), 274 (3·56), 280 (3·56)
VII	226 (4·33), 281 (3·50)
XI	220 (4·19), 278 (3·33), 284 (3·46)
XV	226 (4·35), 280 (3·48)

The NMR spectra of all the rearranged products also showed characteristic signals, especially three sets of multiplets in the regions 4·1, 5·2 and 6·2 ppm in the ratio 3:2:1 respectively. These were similar to those obtained in the rearrangement products from the corresponding symmetrical ethers.[1] The synthetic and degradative evidence adduced earlier relating to the rearrangement of symmetrical ethers and the combination of chemical and physical evidence presently available indicate either of the following two formulations for the rearrangement products:

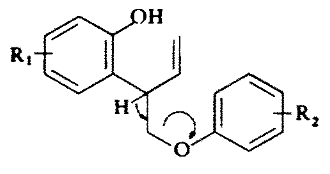
TABLE 5. UV DATA OF THE REARRANGEMENT PRODUCTS OF DISSYMMETRICAL ETHERS

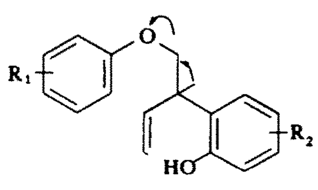
Product No.	λ_{max}^{EtOH} mμ (log ε)
XVII	220 (4·19), 276 (3·58)
XXII	220 (4·02), 280 (3·42)
XXIV	225 (4·18), 278 (3·57)
XXVIII	208^{sh} (4·19), 228 (4·35), 282 (3·61)





The earlier study indicated the facile cleavage of these derivatives either by alkali or by anhydrous aluminium chloride to the respective phenols. In the present instance, cleavage to the phenol would occur only on that aryl ring which did not suffer migration. Whereas simple *ortho* allyl phenols undergo only an isomerization to the propenyl derivatives under the action of alkali, the stability of the phenolate anion as a leaving group and the enchanced acidity of the benzyl-allylic proton favours the smooth β-elimination.





Such a cleavage was applied to the five cases where elemental analyses and VPC analyses of the phenols (or their acetates) guaranteed their purity and homogeneity. The resulting phenols were estimated by VPC. The results are summarized in Table 6.

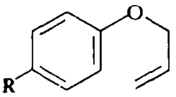
In the two mixed ethers derived from *p*-cresol–guiacol and from *p*-chlorophenol–guiacol, the guiacol residue shows preferential migration to the extent of more than 10:1. This suggests that a single *ortho* substituent enhances the rate of migration of that aryl moiety in comparison with the *para* substituted aryl ring in the competitive

TABLE 6. PHENOLS OBTAINED BY CLEAVAGE OF REARRANGEMENT PRODUCTS

Starting Compound	Product	Phenols obtained R_1	R_2	Relative ratio R_1/R_2
VI	XXI	*o*-Cresol	*m*-Cresol	1:4
XI	XVI	*p*-Cresol	Guiacol	11:1
XIII	XVII	*p*-Chlorophenol	Guiacol	10:1
XV	XVIII	*p*-Chlorophenol	*p*-Cresol	1·1:1
XV	acetate of XVIII	*p*-Chlorophenol	*p*-Cresol	1·2:1

Claisen rearrangement. Only recently the same conclusion was indicated by kinetic analysis of the rates of re-arrangement of simple aryl allyl ethers.[2] Thus product analyses in the present study amply bear out the results of the kinetic investigations.

The case of the 1-(*p*-chlorophenoxy)4-(*p*-methylphenoxy)*trans*-2-butene emphasizes this feature even more strongly. The rearranged phenol and its acetate showed excellent elemental analyses. The solid acetate showed a single spot on TLC. Nevertheless, alkali cleavage of both the acetate and the phenol resulted in the formation of nearly equal amounts of the two different phenols (*vide* Table 6). This clearly indicated that although the solid crystalline acetate showed a single spot on TLC, the product was a mixture involving the migration to nearly equal extent of either aryl moiety. Earlier kinetic studies[3] showed the following data:



$k_0 \times 10^5$/sec
R = Cl 1·70
R = Me 2·08

EXPERIMENTAL

1-*Aryloxy-4-chloro-*trans-2-*butenes*

General procedure. To *trans*-1,4-dichloro-2-butene (1·5 moles) in EtOH (200 ml), in a 2-necked flask fitted with an efficient stirrer, the required phenol (1 mole) was added in the form of potassium aryloxide (prepared by dissolving 1 mole of phenol and 1 mole of KOH in 150 ml EtOH). The addition was carried out over a period of 5 hr with stirring at room temp. Next day it was filtered, the residue was washed well with EtOH, which contained mostly KCl and a little bis ether.

The ethanolic filtrate was completely distilled off, the residue taken up in ether and the ether soln washed with dilute alkali. It was then washed with water and dried ($MgSO_4$) and evaporated. The liquid

TABLE 7. 1-ARYLOXY-4-CHLORO-*trans*-2-BUTENES

No.	Ar = . . .	Formula	Analysis % Calc. C	H	Found C	H
3.	*o*-Chlorophenoxy	$C_{10}H_{10}OCl_2$	55·30	4·60	55·14	4·48
4.	*m*-methylphenoxy	$C_{11}H_{13}OCl$	67·52	6·14	67·37	6·55
5.	*p*-Chlorophenoxy	$C_{10}H_{10}OCl_2$	55·30	4·60	55·30	4·74
6.	*p*-methylphenoxy	$C_{11}H_{13}OCl$	67·52	6·14	67·47	6·36

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[2] E. N. Marvel, B. J. Burreson and T. Crandall, *J. Org. Chem.*, 30, 1030 (1965).

[3] H. L. Goering and R. R. Jacobsen, *J. Am. Chem. Soc.* 80, 3277 (1958).

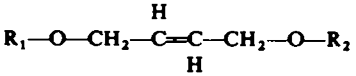
obtained was fractionally distilled *in vacuo*. The first fraction distilling over at 70–90° at 40 mm was discarded, and consisted mostly of unreacted excess dichlorobutene. The second fraction distilling over at a constant temp at 5 mm, was the desired 1-aryloxy-4-chloro-*trans*-2-butene. The pot residue on cooling to room temp yielded some bis ether which was combined with the earlier ppt and crystallized from EtOH after eliminating KCl. The yield of mono ether was about 50%. Tables 1 and 7 summarize the properties of the mono ethers:

Preparation of dissymmetrical ethers

The desired phenol (0·125 mole) and KOH (0·125 mole) were dissolved in EtOH (50 ml). The soln was refluxed with stirring for about 15 min. Then the desired 1-aryloxy-4-chloro-*trans*-2-butene (0·1 mole) was added slowly and refluxing with stirring was continued for about 6 hr, and the mixture left overnight. It was then filtered, the residue washed well with water to remove KCl and crystallized from either pet. ether–benzene or EtOH. The ethanolic filtrate on concentration furnished some more material, yields were about 65 to 75% in each case.

The ethers thus obtained are listed in Tables 2 and 8.

TABLE 8. DISSYMMETRICAL 1,4 DIARYLOXY-*trans*-2-BUTENES

No.	 $R_1{-}O{-}CH_2{-}\overset{H}{C}{=}\underset{H}{C}{-}CH_2{-}O{-}R_2$		Formula	Analysis %			
				Calc.		Found	
	R$_1$	R$_2$		C	H	C	H
I.	Phenyl	*o*-Chlorophenyl	$C_{16}H_{15}O_2Cl$	69·95	5·8	70·01	5·27
II.	Phenyl	*p*-methylphenyl	$C_{17}H_{18}O_2$	80·28	7·13	79·70	7·16
III.	Phenyl	*p*-Chlorophenyl	$C_{16}H_{15}O_2Cl$	69·95	5·8	69·81	5·74
IV.	Phenyl	*p*-Nitrophenyl	$C_{16}H_{15}O_4N$	67·36	5·3	67·25	5·3
V.	Phenyl	β-naphthyl	$C_{20}H_{18}O_2$	82·37	6·25	83·07	6·04
VI.	*o*-methylphenyl	*m*-methylphenyl	$C_{18}H_{20}O_2$	80·56	7·51	80·50	7·62
VII.	*o*-methylphenyl	*p*-methylphenyl	$C_{18}H_{20}O_2$	80·56	7·51	80·40	7·19
VIII.	*m*-methylphenyl	*p*-methylphenyl	$C_{18}H_{20}O_2$	80·56	7·51	80·61	7·34
IX.	*m*-methylphenyl	*p*-Chlorophenyl	$C_{17}H_{17}O_2Cl$	70·70	5·89	69·93	6·03
X.	*p*-methylphenyl	*o*-Chlorophenyl	$C_{17}H_{17}O_2Cl$	70·70	5·89	70·69	5·68
XI.	*p*-methylphenyl	*o*-methoxyphenyl	$C_{18}H_{20}O_3$	76·06	7·04	75·94	6·87
XII.	*p*-methylphenyl	*p*-Nitrophenyl	$C_{17}H_{17}O_4N$	68·22	5·72	68·00	5·60
XIII.	*p*-Chlorophenyl	*o*-methoxyphenyl	$C_{17}H_{17}O_3Cl$	66·90	5·55	66·88	5·64
XIV.	*p*-Chlorophenyl	*p*-Nitrophenyl	$C_{16}H_{14}O_4ClN$	60·09	4·38	59·74	4·48
XV.	*p*-Chlorophenyl	*p*-methylphenyl	$C_{17}H_{17}O_2Cl$	70·70	5·89	70·87	5·90
XVI.	*p*-Chlorophenyl	β-naphthyl	$C_{20}H_{17}O_2Cl$	73·95	5·20	74·32	5·56

Rearrangement of dissymmetrical butenyl ether

The rearrangement of these ethers was done in refluxing N,N-diethylaniline (5 ml for 1 gm ether) for 10 to 12 hr and removing the $PhNEt_2$ *in vacuo* (5 mm) and distilling the residue at a still lower press (0·5 to 1·0 mm). None of the nitro ethers could be rearranged to give any characterizable product. The two β-naphthoxy ethers V and XVI afforded only β-naphthol as the identifiable product. The IR spectra of all the rearrangement products showed the presence of a OH function (2·8 mμ) and a weak band (6·1 mμ) for the newly created unsaturation.

Tables 3 and 9 give the data on the rearrangement products:

TABLE 9. REARRANGEMENT PRODUCTS OF DISSYMMETRICAL ETHERS

Starting compound *vide* earlier Table	Product	Analysis % Calc. C	Analysis % Calc. H	Analysis % Found C	Analysis % Found H
VI	XXI	80·56	7·51	80·60	7·87
VIII	XXIII	80·56	7·51	80·92	7·85
XV	XXVIII	70·71	5·89	71·24	6·16

Preparation of the acetate derivatives

The phenolic product (5 g) was refluxed for 6 hr in AC_2O (25 ml) to which pyridine (15 ml) was added. It was then decomposed with ice pieces, extracted with ether, washed with $NaHCO_3$aq and water. The liquid acetates were distilled *in vacuo* while the solid acetate was crystallized from pet. ether (40–60°) or alcohol. The physical constants and analytical data are listed in Table 10. IR spectra of all the acetates showed the absence of OH peak and the presence of the acetyl group (5·72 mμ).

TABLE 10. ACETATE DERIVATIVES OF REARRANGEMENT PRODUCTS OF DISSYMMETRICAL ETHERS

Product No.	Acetate	Yield %	B.p. °C/mm M.p. °C	Formula	Analysis % Calc. C	Analysis % Calc. H	Analysis % Found C	Analysis % Found H
XXV	XXX	72	164/0·5	$C_{19}H_{19}O_3Cl$	68·98	5·78	69·24	5·82
XXVI	XXXI	80	200/1·0	$C_{20}H_{22}O_4$	73·60	6·79	73·84	6·97
XXVIII	XXXII	75	85°	$C_{19}H_{19}O_3Cl$	68·98	5·78	68·63	5·83

Aluminium chloride cleavage of the rearrangement products

The rearrangement product (0·01 mole) was dissolved in dry benzene (25 ml) and refluxed with anhyd $AlCl_3$ (0·02 mole) for 2 hr. The red soln was decomposed with ice and 1:1 HCl and then extracted with ether. The ether extract was washed with 20% NaOHaq and the alkaline extract acidified with dil HCl. It was then extracted with ether, the ether extract washed with water and dried ($MgSO_4$). Evaporation of the ether soln and distillation of the phenolic product *in vacuo* afforded the phenols. Their identity and relative ratios were determined by VPC analysis.

Base-catalysed cleavage of the rearrangement products

The rearrangement product (0·01 mole) was dissolved in MeOH (50 ml) containing KOH (0·05 mole) and the soln was concentrated. It was then heated in an oil bath at 110–120° (inside temp) for 4 hr. The alkaline mixture was diluted with water, extracted with benzene and the benzene soln extracted with 20% NaOHaq. The combined alkaline extracts were acidified with dil HCl and extracted with ether. The ether extract was washed free of acid, dried ($MgSO_4$) and evaporated. The crude phenolic products were analysed by VPC.

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