706. *Molecular Rearrangement and Fission of Ethers by Alkaline Reagents.*

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Under the influence of an alkaline reagent, an ether having a mobile proton may undergo rearrangement (*a*) or fission (*b*):

$$\mathrm{CR_2R'{\cdot}OH} \xleftarrow{a} \mathrm{CHR_2{\cdot}OR'} \xrightarrow{b} \mathrm{COR_2} + \mathrm{R'H}$$

The incidence of these reactions has been examined for phenacyl, 9-fluorenyl, and α-cyanobenzyl ethers in butanolic sodium butoxide. But-2-enyl, 1-methylallyl, and active α-methylbenzyl ethers of fluoren-9-ol showed unexpected behaviour.

The rearrangement of ethers, $\mathrm{CHR_2{\cdot}OR'} \longrightarrow \mathrm{CR_2R'{\cdot}OH}$, under energetic alkaline conditions has been recorded by Schorigin [1] and investigated extensively by Wittig,[2] Hauser,[3] and Curtin [4] and their collaborators. This change is often accompanied or superseded by a process of fission according to the more detailed scheme:

$$\mathrm{CHR_2{\cdot}OR'} \xrightarrow[-\mathrm{H^+}]{} {}^{-}\mathrm{CR_2{\cdot}OR'} \begin{cases} \longrightarrow \mathrm{CR_2R'{\cdot}O^-} \xrightarrow{\mathrm{H^+}} \mathrm{CR_2R'{\cdot}OH} \\ \longrightarrow \mathrm{COR_2} + \mathrm{R^-} \xrightarrow[\mathrm{H^+}]{} \mathrm{COR_2} + \mathrm{R'H} \end{cases}$$

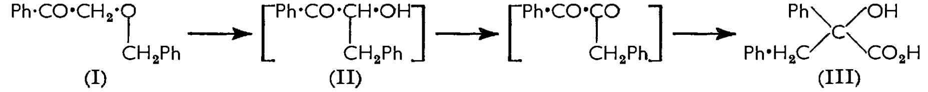
Cram, Kingsbury, and Langemann [5] have examined this process of fission in some detail.

The main driving force for the rearrangement is no doubt the transference of the formal charge from carbon to the more electronegative oxygen atom; rearrangement of tertiary amines, in which O in the scheme is replaced by NR″, takes place much less readily (following paper); rearrangement of quaternary ammonium compounds:

$$\mathrm{CHR_2{\cdot}\overset{+}{N}R''_2R'} \longrightarrow \mathrm{\overset{-}{C}R_2{\cdot}\overset{+}{N}R''_2R'} \longrightarrow \mathrm{CR_2R'{\cdot}NR''_2}$$

in which the formal charges disappear, is effected much more easily. Under the conditions used in this study (but not in Wittig's experiments), migration occurred only with groups of allyl or benzyl type. Rearrangement is evidently intrinsically less favoured than fission; the latter, though involving the separation of a carbanion, can proceed to the exclusion of rearrangement which in an ether would site the anionic charge on oxygen. Fission is favoured if R′ can tolerate an anionic charge: thus, in types of ethers in which other substituted benzyl groups migrate, 4-nitrobenzyl radicals are split off as *p*-nitrotoluene.

Phenacyl Ethers.—In most of the experiments now described, the alkaline reagent was n-butanolic sodium n-butoxide. This was first applied to benzyl phenacyl ether (I), the product being benzylphenylglycollic acid (III), presumably formed by dehydrogenation and benzilic transformation from the normal product of rearrangement (II):



(I) (II) (III)

When similarly treated, 4-nitrobenzyl phenacyl ether gave no hydroxy-acid, but some 30% of *p*-nitrotoluene.

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[1] Schorigin, *Ber.*, 1924, **57**, 1634; 1925, **58**, 2028; 1926, **59**, 2510.

[2] Wittig and Löhmann, *Annalen*, 1942, **550**, 260; Wittig and Happe, *ibid.*, 1947, **557**, 205; Wittig and Clausnitzer, *ibid.*, 1954, **588**, 145; Wittig and Stahnecker, *ibid.*, 1957, **605**, 69; Wittig, Döser, and Lorenz, *ibid.*, 1949, **562**, 192.

[3] Hauser and Kantor, *J. Amer. Chem. Soc.*, 1951, **73**, 1437.

[4] Curtin and Leskowitz, *J. Amer. Chem. Soc.*, 1951, **73**, 2630, 2633.

[5] Cram, Kingsbury, and Langemann, *J. Amer. Chem. Soc.*, 1959, **81**, 5785.

In the same way allyl phenacyl ether afforded an oily acid which by analogy should have been 2-hydroxy-2-phenylpent-4-enoic (and/or -3-enoic) acid. By reduction with hydriodic acid and red phosphorus the oily acid gave α-phenylvaleric acid:

$$\left.\begin{array}{l} CH_2{:}CH{\cdot}CH_2{\cdot}CPh(OH){\cdot}CO_2H \\ CH_3{\cdot}CH{:}CH{\cdot}CPh(OH){\cdot}CO_2H \end{array}\right\} \longrightarrow CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}CHPh{\cdot}CO_2H$$

Phenacyl phenyl ether was easily decomposed with liberation of phenol, and no rearrangement was observed under any conditions. With sodium butoxide, a major product was the secondary alcohol $HO{\cdot}CHPh{\cdot}CH_2{\cdot}OPh$, described by Guss.[6] Treatment of styrene chlorohydrin with sodium phenoxide gave the isomer $PhO{\cdot}CHPh{\cdot}CH_2{\cdot}OH$; if the first stage of this reaction were the production of phenylethylene oxide, Guss's work indicates that the final product would be predominantly the primary alcohol.

Acetonyl benzyl ether, submitted to the same treatment as the phenacyl ethers, darkened rapidly, and no homogeneous product could be isolated.

Fluorenyl Ethers.—9-Fluorenyl methyl and phenyl ether were unchanged by sodium butoxide, although Wittig and Happe [2] rearranged the former ether at a lower temperature by the use of ethereal phenyl-lithium. Under their conditions the intermediate carbanion should be less effectively stabilised by solvation and so more prone to rearrangement.

Benzyl 9-fluorenyl ether (IV), when warmed with butanolic sodium butoxide,[7] rearranged smoothly to 9-benzylfluoren-9-ol (V); the 4-bromobenzyl and 4-iodobenzyl ethers suffered the same change, but 9-fluorenyl 4-nitrobenzyl ether gave almost entirely fluorenone, with much *p*-nitrotoluene. Diphenylmethyl 4-nitrobenzyl ether behaved like the fluorenyl compound.

(IV) R = CH_2Ph
(VI) R = $CHMePh$
(VIII) R = $CH_2{\cdot}CH{:}CHMe$
(IX) R = $CHMe{\cdot}CH{:}CH_2$

(V) R = CH_2Ph
(VII) R = $CHMePh$
(X) R = $CH_2{\cdot}CH{:}CHMe$

Inactive 9-fluorenyl α-methylbenzyl ether (VI) was rearranged in the same way as the benzyl compound. The active ether, unexpectedly, gave the *inactive* alcohol (VII). This is in striking contrast with the rearrangement of a quaternary ammonium ion, $Ph{\cdot}CO{\cdot}CH_2{\cdot}\overset{+}{N}Me_2{\cdot}CHMePh$, in which the migration of the active α-methylbenzyl radical gives an active product, $Ph{\cdot}CO{\cdot}CH(NMe_2){\cdot}CHMePh$, of high optical purity.[8]

Both but-2-enyl 9-fluorenyl ether (VIII) and 9-fluorenyl 1-methylallyl ether (IX) gave in large yield 9-but-2′-enylfluoren-9-ol (X). It is not easy to accept a cyclic intramolecular mechanism for the rearrangement of ether (VIII) and a non-cyclic one for ether (IX). On the other hand, the isolation of the rearrangement products in good yield, in experiments with butanol as solvent, makes it improbable that the migrating group is ever kinetically free, whether as free radical or as ion, in which the distinction between but-2-enyl and 1-methylallyl would disappear. This is in contrast with the rearrangement of sulphinic esters, $Ar{\cdot}SO{\cdot}OR$, to sulphones, $Ar{\cdot}SO_2{\cdot}R$, in which the process is, at least mainly, intermolecular.[9] Cinnamyl 9-fluorenyl ether behaved like the butenyl compound, giving 9-cinnamylfluoren-9-ol.

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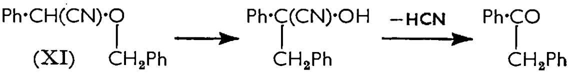
[6] Guss, *J. Amer. Chem. Soc.*, 1949, **71**, 3460; Guss and Williams, *J. Org. Chem.*, 1951, **16**, 1809.

[7] Marrian, Thesis, Glasgow, 1941.

[8] Campbell, Houston, and Kenyon, *J.*, 1947, 93.

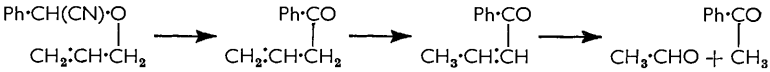
[9] Arcus, Balfe, and Kenyon, *J.*, 1938, 485; Cope, Morrison, and Field, *J. Amer. Chem. Soc.*, 1950, **72**, 59; Wragg, McFadyen, and Stevens, *J.*, 1958, 3603.

α-Cyanobenzyl Ethers.—α-Cyanobenzyl ethers contain a suitably placed mobile hydrogen atom, and the benzyl ether (XI) with hot sodium butoxide solution gave deoxybenzoin:



$$\text{(XI)}\ \begin{array}{c}Ph{\cdot}CH(CN){\cdot}O\\|\\CH_2Ph\end{array}\longrightarrow\begin{array}{c}Ph{\cdot}C(CN){\cdot}OH\\|\\CH_2Ph\end{array}\xrightarrow{-HCN}\begin{array}{c}Ph{\cdot}CO\\|\\CH_2Ph\end{array}$$

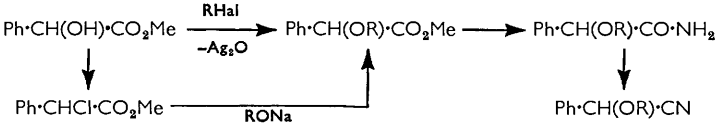
The methyl and phenyl ethers did not react in this way, giving no cyanide ion; the allyl ether gave cyanide ion with a little acetophenone, perhaps formed by way of allyl phenyl ketone and phenyl propenyl ketone:



$$\begin{array}{c}Ph{\cdot}CH(CN){\cdot}O\\|\\CH_2{:}CH{\cdot}CH_2\end{array}\longrightarrow\begin{array}{c}Ph{\cdot}CO\\|\\CH_2{:}CH{\cdot}CH_2\end{array}\longrightarrow\begin{array}{c}Ph{\cdot}CO\\|\\CH_3{\cdot}CH{:}CH\end{array}\longrightarrow\begin{array}{r}Ph{\cdot}CO\\|\\CH_3{\cdot}CHO + CH_3\end{array}$$

Preparation of Ethers.—Phenacyl and acetonyl ethers were mostly prepared by the sequence, $RHal + CH_2O + KCN \longrightarrow KHal + RO{\cdot}CH_2{\cdot}CN$; $RO{\cdot}CH_2{\cdot}CN + R'{\cdot}MgX \longrightarrow RO{\cdot}CH_2{\cdot}COR'$. Fluorenyl ethers, which also are not effectively obtained by Williamson synthesis, were produced, usually in moderate yield, by interaction of 9-bromofluorene and an alcohol in presence of a silver salt.[2,10] Acetonitrile is here a useful solvent, though an excess of alcohol is often necessary in any case. With allylic alcohols, the use of silver nitrate led to the formation of much 9-fluorenyl nitrate, and better yields of ether were obtained by using silver sulphate; silver perchlorate, applied to the case of bromofluorene and allyl alcohol, gave only a chlorinated product. This silver salt method was not successfully applied to phenacyl ethers; phenacyl bromide with silver nitrate in acetonitrile gave phenacyl nitrate even in presence of water, while silver sulphate did not react.

α-Cyanobenzyl ethers were produced from methyl mandelate by the alternative routes:



$$\begin{tikzcd}
Ph{\cdot}CH(OH){\cdot}CO_2Me \arrow[r, "RHal", "-Ag_2O"'] \arrow[d] & Ph{\cdot}CH(OR){\cdot}CO_2Me \arrow[r] & Ph{\cdot}CH(OR){\cdot}CO{\cdot}NH_2 \arrow[d] \\
Ph{\cdot}CHCl{\cdot}CO_2Me \arrow[ur, "RONa"'] & & Ph{\cdot}CH(OR){\cdot}CN
\end{tikzcd}$$

EXPERIMENTAL

Analytical and other data on ethers are assembled in Table 1.

Ether A.—Benzyloxyacetonitrile[11] (7 ml.) was added to the Grignard reagent from bromobenzene (10·5 ml.), magnesium (2·45 g.), and ether (50 ml.). After 12 hr. ice and dilute sulphuric acid were added. The product, isolated as usual, had b. p. 206°/16 mm.; a lower fraction was biphenyl. *Benzyl phenacyl ether 2,4-dinitrophenylhydrazone* formed fine orange needles (from chloroform–methanol), m. p. 182—184° (Found: C, 61·7; H, 4·6. $C_{21}H_{18}O_5N_4$ requires C, 62·0; H, 4·4%).

Ether B.—Diazoacetophenone (6 g.) and 4-nitrobenzyl alcohol (25 g.) in benzene (800 ml.) were stirred during addition of boron trifluoride–ether complex[12] (1 g.); a vigorous reaction ensued, with development of a deep red colour. After 1 hr. the solution was boiled with charcoal, filtered, and evaporated, and unchanged alcohol was extracted with boiling water. The residue was the ether B.

Ether C.—Powdered sodium cyanide (8·2 g.) was added to 38% aqueous formaldehyde (15 ml.) in methanol (15 ml.) with cooling. Allyl bromide (20·2 g.) in methanol (20 ml.) was added and the mixture heated. After the gentle reaction had subsided, the whole was refluxed for 5 min., cooled, diluted with water (50 ml.), and extracted with ether–ligroin (1 : 1). The extract gave *allyloxyacetonitrile* (10—12 g.), b. p. 149—157° (Found: N, 13·5. C_5H_7ON requires N, 14·4%). By the method used for ether A, the nitrile gave a crude product, contaminated with biphenyl which could not be removed. This material gave 67% of *allyl phenacyl ether*

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[10] Kliegl, Wünsch, and Weigele, *Ber.*, 1926, **59**, 631.

[11] Quarterman and Stevens, *J.*, 1955, 3293.

[12] Cf. Newman and Beale, *J. Amer. Chem. Soc.*, 1950, **72**, 5161.

TABLE 1. *Ethers prepared.*

	Solvent	M. p.	Found (%)		Formula	Reqd. (%)	
			C	H		C	H
Phenacyl ethers							
A Benzyl	MeOH–H_2O	62—64°	79·1	6·4	$C_{15}H_{14}O_2$	79·6	6·2
B 4-Nitrobenzyl [a]	MeOH; EtOH	98—99	66·4	4·6	$C_{15}H_{13}O_4N$	66·4	4·7
C Allyl	B. p. 130—143°/14 mm.						
D Phenacyl	MeOH; Lig [b]	117—118	75·5	5·1	$C_{16}H_{14}O_3$	75·5	5·5
9-*Fluorenyl ethers*							
E Phenyl [2]	MeOH	79—80 [c]	88·2	5·2	$C_{19}H_{14}O$	88·3	5·4
F Benzyl [2]		68—69	87·8	6·3	$C_{20}H_{16}O$	87·9	6·2
G 4-Bromobenzyl	MeOH	100—101	68·4	4·2	$C_{20}H_{15}OBr$	68·4	4·3
H 4-Iodobenzyl	MeOH	116	60·4	3·9	$C_{20}H_{15}OI$	60·3	3·8
I 4-Nitrobenzyl [d]	$COMe_2$–MeOH	125—126	75·9	4·7	$C_{20}H_{15}O_3N$	75·7	4·7
J (+)-α-Methylbenzyl [e]	EtOH	94—95 [g]	88·1	6·2	$C_{21}H_{18}O$	88·1	6·3
K (−)- [f] ,,	EtOH	94—95 [g]	88·3	6·3			
L (±)- ,,	MeOH	68—69 [g]	88·4	6·2			
M *p*-Nitrophenethyl [h]	MeOH	97—98·5	75·9	5·3	$C_{21}H_{17}O_3N$	76·1	5·2
N Allyl [2]							
O But-2-enyl	MeOH (−50°)	39—40	86·7	6·8	$C_{17}H_{16}O$	86·4	6·8
P 1-Methylallyl	B. p. 160°/0·2 mm.						
Q Cinnamyl	MeOH	103	88·1	5·7	$C_{22}H_{18}O$	88·5	6·0
Various							
R Diphenylmethyl 4-nitrobenzyl	MeOH	64—65	75·2	5·4	$C_{20}H_{17}O_3N$	75·2	5·3
S α-Cyanobenzyl methyl [20]	B. p. 128°/27 mm.						
T α-Cyanobenzyl phenyl	Lig	63°	(N, 6·8)		$C_{14}H_{11}ON$	(N, 6·7)	
U Benzyl α-cyanobenzyl	B. p. 192—194°/13 mm.		(N, 6·5)		$C_{15}H_{13}ON$	(N, 6·3)	
V Allyl α-cyanobenzyl	B. p. 132—134°/16 mm.		(N, 8·2)		$C_{11}H_{11}ON$	(N, 8·1)	

[a] Found: N, 5·3. Required, 5·3%. [b] Ligroin, b. p. 60—80°. [c] B. p. 78—80°/0·5 mm. [d] Found: N, 4·6. Required, 4·4%. [e] $[\alpha]_D^{22}$ +169·6° in EtOH. [f] $[\alpha]_D^{22}$ −164·6° in EtOH. [g] B. p. 100—140°/0·4 mm. [h] Found: N, 3·8. Required, 4·2%.

2,4-*dinitrophenylhydrazone*, orange-red needles (from ethanol), m. p. 137° (Found: C, 57·0; H, 4·5. $C_{17}H_{16}O_5N_4$ requires C, 57·3; H, 4·4%).

Ether D.—Phenacyl bromide (2 g.) was refluxed in toluene (30 ml.) with silver oxide (3 g.) for 12 hr. The residue from evaporation of the filtered solution was crystallised from methanol and from ligroin.

Phenacyl Nitrate.—Phenacyl bromide (5 g.) in benzene (10 ml.) was mixed with silver nitrate (5 g.) in dry acetonitrile (5 ml.) and reaction completed by warming. The filtered liquid was diluted with ether, washed with water, and evaporated, giving an oil which was crystallised from methanol (cooled in acetone–carbon dioxide) and then from ligroin. The *nitrate* formed plates, m. p. 53·5—54° (Found: C, 53·2; H, 4·2; N, 7·7. $C_8H_7O_4N$ requires C, 53·0; H, 3·9; N, 7·7%). *Phenacyl nitrate* 2,4-*dinitrophenylhydrazone* could not be purified by crystallisation; well-washed material had m. p. 176—177° (Found: C, 46·8; H, 3·2. $C_{14}H_{11}O_7N_5$ requires C, 46·6; H, 3·0%).

Ether E.[2]—This was not produced by the silver salt method. Potassium phenoxide [13] (3 g.) and 9-bromofluorene (5·6 g.) were refluxed for 5 hr. in xylene (20 ml.). The orange mixture was washed with water and distilled.

Ether F.—9-Bromofluorene (1 g.) in warm benzene was added to silver nitrate (1 g.) in benzyl alcohol (5 ml.), causing immediate precipitation of silver bromide. Methanol was added, and the liquid filtered, washed with water, and distilled in steam, leaving ether F.

Ether G.—*p*-Bromotoluene (40 g.) was brominated in carbon tetrachloride (200 ml.) containing dibenzoyl peroxide (2 g.); hydrolysis [14] then gave 4-bromobenzyl alcohol. The alcohol (13 g.) with silver nitrate (20 g.) in warm acetonitrile was added to 9-bromofluorene (9 g.) in benzene. The filtrate from precipitated silver bromide was washed with water and evaporated, and the residual crude ether boiled with successive quantities of water to remove unchanged alcohol.

Ether H.—This preparation was similar to that of G.

Ether I.—4-Nitrobenzyl chloride (83 g.) was boiled with sodium formate (54 g.) in formic

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[13] Jones and Cook, *J. Amer. Chem. Soc.*, 1916, **38**, 1537.

[14] Cf. Bodroux, *Bull. Soc. chim. France*, 1899, **21**, 289.

acid (60 ml.) and water (45 ml.) for 24 hr. Much of the water and formic acid were distilled off, and the lower oily layer separated from the cooled residue; the upper layer deposited a little alcohol when kept. The oil was boiled with water, most of it dissolving, leaving an oily residue; the solution deposited 4-nitrobenzyl alcohol. After recrystallisation from water the alcohol weighed 50 g. and had m. p. 92—93°. It was converted as above into the *fluorenyl ether.*

Ethers J, K, and L.—Active α-methylbenzyl alcohol[15] had $[\alpha]_D^{23}$ $+10{\cdot}6°$ and $-11{\cdot}09°$. An excess of each severally was used as solvent with bromofluorene and silver sulphate, and the mixtures were diluted with ethanol, filtered, and distilled.

Ether M.—9-Bromofluorene (1 g.) and *p*-nitrophenethyl alcohol (7 g.) in acetonitrile (10 ml.) reacted with silver sulphate; the ether was extracted by ligroin from an aqueous-methanolic solution of the filtered reaction mixture.

Ether N.—This[2] was obtained in improved yield by the use of silver sulphate. Silver perchlorate (2·1 g.) was added to 9-bromofluorene (2·4 g.) in allyl alcohol (2 ml.), and the filtered mixture was diluted with water and methanol and extracted with ligroin (b. p. 60—80°). The residue obtained on evaporation of the ligroin was crystallised repeatedly from methanol, giving an oxygen-free *substance*, m. p. 98°, which became pink when kept (Found: C, 61·5; H, 3·5; Cl, 34·5. $C_{16}H_{11}Cl_3$ requires C, 62·1; H, 3·5; Cl, 34·4%).

Ether O.—Silver sulphate was used, with excess of but-2-enyl alcohol as solvent (recovered by distillation). Water was added to the residue and the ether extracted with ligroin. This (b. p. 120—130°/0·5 mm.), when hydrogenated at room temperature over palladium–charcoal, gave fluorenol. The *dibromide*, prepared in carbon tetrachloride, crystallised from ethanol in needles, m. p. 83—84° (Found: C, 51·3; H, 3·9; Br, 40·0. $C_{17}H_{16}OBr_2$ requires C, 51·5; H, 4·0; Br, 40·4%).

Ether P.—Similarly prepared from 1-methylallyl alcohol,[16] this could not be crystallised even after chromatography over alumina. Its identity was confirmed by preparation of the *dibromide*, m. p. 146—148° (Found: C, 51·5; H, 4·1; Br, 40·0%), and by its behaviour on ozonolysis.[17] Ozonised oxygen (2%) was passed into the ether (0·2 g.) in ethyl bromide at −12°, the solvent removed in a vacuum below room temperature, and the ozonide dropped into a boiling mixture of water (20 ml.), zinc dust (0·3 g.), quinol (0·01 g.), and 1% silver nitrate solution (1 ml.). Water was added as the mixture was distilled and 50 ml. were collected. Formaldehyde was determined (37%) in the distillate by the chromotropic acid method,[18] and treatment with dimedone gave 31% of pure derivative, m. p. 186°. The crude dimedone derivative was unchanged after being refluxed with acetic acid, and still completely soluble in alkali, showing the absence of the acetaldehyde derivative. But-2-enyl fluorenyl ether gave similarly 3% of formaldehyde (chromotropic acid) and 60% of acetaldehyde (dimedone derivative, m. p. and mixed m. p. 137—139°). Allyl fluorenyl ether gave 39% of formaldehyde.

Ether Q.—Preparation as in case M, with silver nitrate or sulphate.

Ether R.—Preparation was as in case G, but with silver sulphate.

Ether S.—Phosphorus oxychloride (4 ml.) was added to α-methoxy-α-phenylacetamide[19] (4 g.) in pyridine (10 ml.), at $<100°$. The mixture was kept at this temperature for 15 min., then diluted with water, and the nitrile[20] (2·7 g.) was isolated.

Ether T.—Phenol (5·5 g.) was allowed to react with sodium dust (1·15 g.) in toluene (25 ml.), and methyl α-chloro-α-phenylacetate[21] (8 ml.) was added. After 1 hr. at 100°, the mixture was shaken with ether and sodium hydroxide solution, and the methyl phenoxyphenylacetate distilled (b. p. mainly 208—210°/23 mm.). Without further purification, it was heated with methanolic ammonia for 18 hr. at 68—70°, affording *phenoxyphenylacetamide*, m. p. 154° (from benzene–ligroin) (Found: C, 73·6; H, 5·8; N, 6·7. $C_{14}H_{13}O_2N$ requires C, 74·0; H, 5·8; N, 6·2%). As above, this afforded the ether T.

Ether U.—Methyl α-chloro-α-phenylacetate (9·6 g.) was added to a hot solution of sodium (1·4 g.) in benzyl alcohol (22 ml.), and the mixture heated on the steam-bath for 1·5 hr. The mixture was diluted with water and extracted with ether, the dried extract evaporated, and the residue heated with saturated methanolic ammonia for 22 hr. at 220°. After evaporation of the

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[15] Downer and Kenyon, *J.*, 1939, 1156.

[16] Delaby, *Compt. rend.*, 1922, **175**, 969.

[17] Cf. Church, Whitmore, and McGrew, *J. Amer. Chem. Soc.*, 1934, **56**, 178.

[18] MacFadyen, *J. Biol. Chem.*, 1945, **158**, 107.

[19] McKenzie, Martin, and Rule, *J.*, 1914, **105**, 1587.

[20] Hess and Dorner, *Ber.*, 1917, **50**, 392.

[21] Cf. Darzens, *Compt. rend.*, 1911, **152**, 1601.

TABLE 2. *Transformations of ethers.*

	Reagent	Temp.	Time	Products
Phenacyl ethers				
Benzyl	N-BuONa	120°	45 min.	$HO\cdot CPh(CH_2Ph)\cdot CO_2H$ [a] (25%)
,,	,,	,,	5 min.	,, + unchanged ester
4-Nitrobenzyl	0·5N-BuONa	100	2 hr.	*p*-Nitrotoluene (30%); BzOH (6%)
Allyl	N-BuONa	120	1 hr.	BzOH (little); $CH_2{:}CH\cdot CH_2\cdot CPh(OH)\cdot CO_2H$ [b] (little); much tar
Phenyl	,,	,,	20 min.	Much $PhO\cdot CH_2\cdot CHPh\cdot OH$;[c] BzOH; no $HO\cdot CPh_2\cdot CO_2H$
Fluorenyl ethers				
Methyl [10]	N-BuONa	120	1 hr.	Almost 100% recovery
Phenyl	,,	,,	1 hr.	,, ,,
Benzyl	,,	,,	2·5 hr.	9-Benzylfluoren-9-ol [n] (70%)
,,	$KNH_2–NH_3–Et_2O$	−30 to +10	1 hr.	Benzylfluorenol; fluorenone 2,4-dinitrophenylhydrazone (30%)
4-Bromobenzyl	N-BuONa	120	2·5 hr.	9-4′-Bromobenzylfluoren-9-ol [e] (61%); fluorenone dinitrophenylhydrazone
4-Iodobenzyl	,,	,,	2·5 hr.	9-4′-Iodobenzylfluoren-9-ol[f] (45%); fluorenone dinitrophenylhydrazone
4-Nitrobenzyl	0·4N-BuONa	75	3 hr.	*p*-Nitrotoluene (55%); fluorenone dinitrophenylhydrazone (95%)
(−)-α-Methylbenzyl	1·4N-BuONa	110	2 hr.	(±)-9-α-Methylbenzylfluoren-9-ol (80%) [g]
,,	$PhLi–Et_2O$	15	4 min.	,, ,, ,, [h] (60%)
(±)-α-Methylbenzyl	N-BuONa	120	2 hr.	,, ,, ,, [i]
4-Nitrophenethyl	0·7N-BuONa	70	10 min.	Insol. yellow solid;[j] fluorenone dinitrophenylhydrazone
Allyl	N-BuONa	120	2 hr.	9-Allylfluoren-9-ol [2, p]
But-2-enyl	,,	,,	2 hr.	9-But-2′-enylfluoren-9-ol
1-Methylallyl	,,	,,	2 hr.	,, ,,
Cinnamyl	,,	,,	20 min.	9-Cinnamylfluoren-9-ol [k] (70%)
,,	$PhLi–Et_2O$	15	1 min.	,, ,, ,, (90%)
Various				
Diphenylmethyl 4-nitrobenzyl	0·05N-BuONa	95	2 hr.	Benzophenone 2,4-dinitrophenylhydrazone (35%); *p*-nitrotoluene (12%)
α-Cyanobenzyl methyl	0·5N-BuONa	120	1 hr.	No CN^-
α-Cyanobenzyl phenyl	,,	,,	1 hr.	No CN^-
Allyl α-cyanobenzyl	,,	,,	3 min.	CN^- [l] (40%); little acetophenone 2,4-dinitrophenylhydrazone
Benzyl α-cyanobenzyl	,,	,,	10 min.	CN^- (43%); deoxybenzoin [m] (30%)
Acetonyl benzyl [11]	N-BuONa	,,	1 hr.	Much tar; little oily acid [d]

[a] Identical with a specimen prepared[q] from 1,3-diphenylpropylene oxide; oxidised by sodium dichromate in acetic acid to deoxybenzoin, identified as 2,4-dinitrophenylhydrazone. No non-acidic individual substance could be isolated, but presence of benzyl phenyl diketone was suspected. [b] The oily α-hydroxy-α-phenylpent-4-enoic acid, not volatile in steam, did not crystallise, and was boiled for 20 hr. with hydriodic acid and red phosphorus. Steam-distillation gave α-phenylvaleric acid,[r] m. p. and mixed m. p. 44—47° (from ligroin; identified as amide, m. p. 82—84°). [c] M. p. 61° (lit.,[7] 63—64°) (from ligroin) (Found: C, 78·7; H, 6·6. Calc. for $C_{14}H_{14}O_2$: C, 78·5; H, 6·6%). [d] Did not crystallise, even when seeded with benzylmethylglycollic acid.[s] When boiled with cadmium carbonate in methanol, this acid gave no crystallisable salt; under these conditions benzylmethylglycollic acid readily gave a *cadmium salt*, very hygroscopic needles from methanol containing a little acetic acid (Found: C, 50·7; H, 4·8. $C_{20}H_{22}O_4Cd$ requires C, 51·0; H, 4·7%). [e] New; m. p. 144—145° (from benzene–ligroin) (Found: C, 67·9; H, 4·7. $C_{20}H_{15}OBr$ requires C, 68·4; H, 4·3%). [f] New; m. p. 153—154° (from ligroin) (Found: C, 59·8; H, 3·9. $C_{20}H_{15}OI$ requires C, 60·3; H, 3·8%). [g] New; needles, m. p. 78—80°, from ligroin (Found: C, 88·0; H, 6·8. $C_{21}H_{18}O$ requires C, 88·1; H, 6·3%). [h] M. p. 79—82°. [i] M. p. 78·5—79°. Products *g*, *h*, *i* were inactive in alcohol and in chloroform; after several months each specimen had m. p. 105°; the substance is evidently dimorphous. [j] Could not be purified; m. p. 220° (Found: C, 75·6; H, 5·4; N, 5·3%). [k] New; m. p. 85—86·5° (from ligroin) (Found: C, 88·7; H, 6·0. $C_{22}H_{18}O$ requires C, 88·5; H, 6·1%). The alcohol (0·15 g.) in cold acetic acid, was treated with sulphuric acid (2 drops); a yellow colour developed, followed by a precipitate (0·11 g.), recognised as 9-cinnamylidenefluorene.[t] [l] By titration with silver nitrate. [m] Identified as 2,4-dinitrophenylhydrazone. The same rearrangement was effected by other reagents, including sodium acetate in boiling ethylene glycol; but under all effective conditions, deoxybenzoin is partially destroyed. [n] Ullmann and von Wurstemberger, *Ber.*, 1905, **38**, 4108. [p] Backer and Strating, *Rec. Trav. chim.*, 1941, **60**, 402. [q] Widman, *Ber.*, 1916, **49**, 477. [r] Pickard and Yates, *J.*, 1909, **95**, 1017; Baeyer and Co., G.P. 249,241, *Chem. Zentr.*, 1912, II, 396. [s] Michael and Gabriel, *Ber.*, 1879, **12**, 815. [t] Kuhn and Winterstein, *Helv. Chim. Acta*, 1928, **11**, 116.

methanol, α-*benzyloxy*-α-*phenylacetamide* (~15%) separated, which crystallised from methanol in needles, m. p. 134—135° (Found: N, 5·6. $C_{15}H_{15}O_2N$ requires N, 5·8%). It gave, as above, the ether U.

Ether V.—Silver oxide (29 g.) was added to methyl mandelate (20·5 g.) in allyl bromide (15 g.) with cooling, and the mixture was heated on the steam-bath for 4 hr. The silver salts were filtered off and washed with methanol, and the residue from evaporation of the filtrates was kept in methanolic ammonia for 16 hr. The methanol was distilled and the residue shaken with water, ligroin, and a little ether. The solid *allyloxyphenylacetamide* which separated crystallised from water in needles, m. p. 74° (Found: C, 69·0; H, 6·3. $C_{11}H_{13}O_2N$ requires C, 69·1; H, 6·8%). It was converted as above into ether V.

α-*Allyloxyacetamide*.—Silver oxide (34 g.) was added slowly to ethyl lactate (10 g.) and allyl bromide (17 ml.), and the initially vigorous reaction completed on the steam-bath (4 hr.). The filtered mixture was distilled, giving diallyl ether and a higher-boiling fraction which was shaken with 5% potassium hydroxide solution to remove ethyl lactate. Distillation then gave *ethyl* α-*allyloxypropionate* (2 g.), b. p. 50°/15 mm. (Found: C, 60·7; H, 8·95. $C_8H_{14}O_3$ requires C, 60·7; H, 8·9%). With methanolic ammonia in the cold it gave the *amide*, b. p. 107°/20 mm., m. p. 41° (from ligroin) (Found: C, 55·8; H, 8·4; N, 10·9. $C_6H_{11}O_2N$ requires C, 55·8; H, 8·6; N, 10·9%). The low yields discouraged further work in this series.

Transformations of the Ethers.—Identification of known solids implies in general the use of mixed m. p.s. Steps were usually taken to exclude air during the reactions. The products were separated into acidic and non-acidic, steam-volatile and non-volatile portions. Reaction conditions and products are assembled in Table 2. The products of rearrangement of fluorenyl ethers were often contaminated with fluorenol, best removed by refluxing ethanolic potassium ethoxide solution, with exposure to air, which effected oxidation to fluorenone.[22]

(*a*) To sodium (1·2 g.) in ethanol (30 ml.) were added phenol (6 g.) and styrene chlorohydrin [23] (5·2 g.), and the whole was refluxed for 5 hr. After dilution with water, 2-phenoxy-2-phenylethanol was extracted with ligroin and had m. p. 78—79° (lit.,[6] 80—81°) after recrystallisation (Found: C, 78·2; H, 6·7. Calc. for $C_{14}H_{14}O_2$: C, 78·5; H, 6·6%).

(*b*) But-2-enyl 9-fluorenyl ether gave a crude solid (80%), m. p. 85—100°; after being refluxed with ethanolic potassium ethoxide, this 9-*but*-2′-*enylfluoren*-9-*ol* had m. p. 106—108° (Found: C, 86·0; H, 6·6. $C_{17}H_{16}O$ requires C, 86·4; H, 6·8%). Hydrogenated over Raney nickel at room temperature in ethanol for 2·5 hr., the crude rearrangement product gave 65% of 9-n-butylfluoren-9-ol,[24] m. p. 124—126°; the pure 9-but-2′-enylfluoren-9-ol gave 65% of pure butylfluorenol, m. p. and mixed m. p. 129—130°. On ozonisation, as described for fluorenyl 1-methylallyl ether, the crude product of rearrangement gave 4·3% of formaldehyde (chromotropic acid method) and 34% of acetaldehyde (as dimedone derivative). In a comparative experiment, allylfluorenol gave 26% of formaldehyde (chromotropic acid) and 28% of formaldehyde dimedone derivative, with no evidence of acetaldehyde.

(*c*) 9-Fluorenyl 1-methylallyl ether gave crystalline but-2′-enylfluorenol (80%), which after purification had m. p. and mixed m. p. 109—110° (Found: C, 86·2; H, 6·8%). The pure product gave on hydrogenation 9-n-butylfluoren-9-ol in good yield; the crude material gave 80% of material, m. p. 121—124°, and thence after three crystallisations 50% of material, m. p. 125—126°. Ozonolysis of the crude rearrangement product gave 3% of formaldehyde (chromotropic acid) and 43% of acetaldehyde (as above).

(*d*) Attempts to prepare 9-s-butylfluoren-9-ol by Grignard reaction gave only fluorenol, and the rearrangement of 9-fluorenyl s-butyl ether could be effected neither by ethereal phenyllithium nor by potassium amide in liquid ammonia. The ether was prepared from 9-bromofluorene (6 g.) in butan-2-ol (100 ml.) and acetonitrile (5 ml.) with silver sulphate. It was purified by chromatography on alumina from ligroin (b. p. 40—60°), and crystallised from ligroin or methanol (cooling with acetone–carbon dioxide). 9-*Fluorenyl s-butyl ether* formed needles, m. p. 27—28° (Found: C, 85·0; H, 7·4. $C_{17}H_{18}O$ requires C, 85·7; H, 7·6%).

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[22] Cf. Cohen, *Rec. Trav. chim.*, 1919, **38**, 119.

[23] Detoeuf, *Bull. Soc. chim. France*, 1922, **31**, 176.

[24] Sprinzak, *J. Amer. Chem. Soc.*, 1952, **74**, 2116.