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THE CLAISEN REARRANGEMENT PROMOTED BY TITANIUM TETRACHLORIDE

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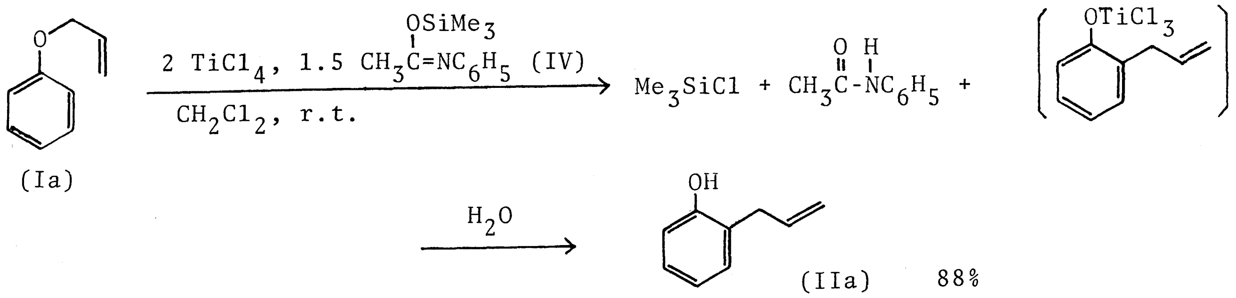
In coexistence with $TiCl_4$ and N-trimethylsilylacetanilide, allyl aryl ethers involving 2-butenyl phenyl ether and 3-methyl-2-butenyl phenyl ether were rearranged under mild conditions to afford allyl phenols in good yields.

The Claisen rearrangement is generally effected by prolonged heating (180°C-200°C) of the allyl phenyl ethers in solvents such as dimethylaniline.$^{1)}$ Further, it is also known that Lewis acids such as BF_3-$2CH_3COOH^{2)}$, $BCl_3{}^{3)}$ and $Et_2AlCl^{4)}$ cause the acid catalysed Claisen rearrangement under mild conditions. However, for the rearrangement of a wide variety of allyl phenyl ethers, these acid catalysts are not generally employed. For example, Et_2AlCl was not effective when used for the rearrangement of allyl aryl ethers bearing electron-donating groups on the aromatic ring, and the use of BCl_3 is limited to those cases when the allyl group was not highly substituted.

In the present communication we wish to report the usefulness of $TiCl_4$ in the Claisen rearrangement. When allyl phenyl ether(Ia) was treated with an equimolar amount of $TiCl_4$ in CH_2Cl_2 at -78°C, 2-(2-chloropropyl)phenol(III) was obtained as a major product, along with a small amount of 2-allylphenol(IIa). This result indicates that hydrogen chloride formed adds simultaneously to the double bond of 2-allylphenol(IIa), the rearranged product, to yield the chloride (III).

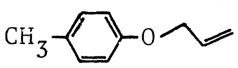
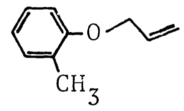
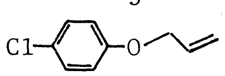
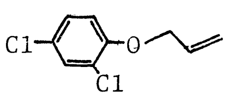
In order to prevent the formation of the chloride (III), the rearrangement was examined in the presence of a hydrogen chloride scavenger such as amines, cyclohexene oxide and silyl compounds to trap hydrogen chloride. After a number of investigations, it was found that when the reaction was carried out in the coexistence with N-trimethylsilylacetanilide (IV)$^{5)}$ at room temperature, 2-allylphenol (IIa) was exclusively obtained in 88% yield.



The experimental procedure is as follows: A CH_2Cl_2 (0.75 ml) solution of $TiCl_4$ (3.0 mmol) was added at room temperature under an argon atmosphere to a stirred solution of 1.5 mmol of Ia and 2.2 mmol of IV in 20 ml of CH_2Cl_2. After being stirred for 3 hr, the reaction mixture was hydrolyzed with 20 ml of water and extracted with ether. The extract was dried over anhydrous Na_2SO_4, and condensed under reduced pressure. The product (IIa)[6] was isolated in 88% yield after separation by thin layer chromatography.

Further, a detailed study on the reaction of various allyl aryl ethers (Ib-e) with $TiCl_4$ and IV was undertaken, and the results are summarized in Table.

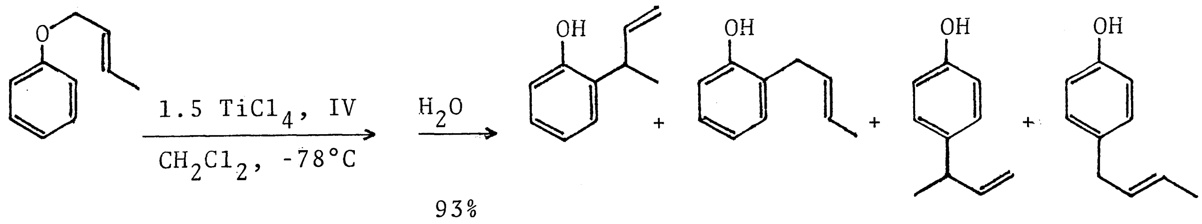
Table The Rearrangement of Substituted Allyl Aryl Ethers

Ether		Molar ratio (I) : (IV) : $TiCl_4$	Reaction time	Yield of Phenol (II), % ortho	para
Ib		1 : 1 : 1	1 hr	95[6]	—
Ic		1 : 1 : 1	overnight	50[6]	29[7]
Id		1 : 1 : 2	overnight	83[8]	—
Ie		1 : 1 : 2	24 hr	36[9]	—

The results show that allyl tolyl ethers (Ib, c) rearranged smoothly in the presence of an equimolar amount of IV and $TiCl_4$. On the other hand, an excess amount of

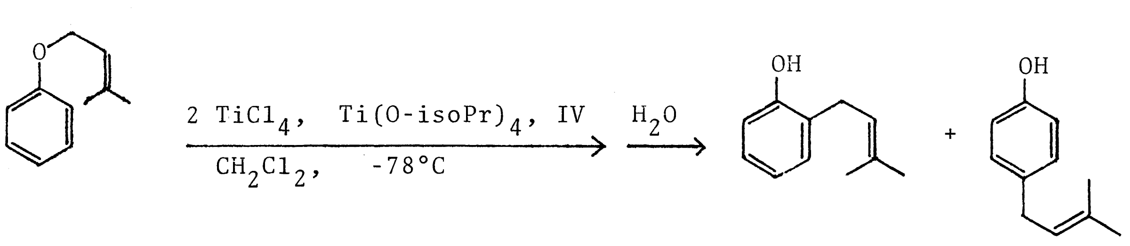
$TiCl_4$ was required for the rearrangement of allyl 2-chloro and 2,4-dichlorophenyl ethers (Id,e). In these cases, 2-allyl-4-chlorophenol and 2-allyl-4,6-dichlorophenol were produced in 83 and 36% yields, respectively, along with 2-chlorophenol and 2,4-dichlorophenol isolated in 10 and 30% yields.

In addition, the rearrangement of substituted allyl phenyl ethers, such as 2-butenyl phenyl ether (V) and 3-methyl-2-butenyl phenyl ether (X) were examined. Into a mixture of 3.8 mmol of V and IV in 30 ml of CH_2Cl_2, a CH_2Cl_2 (4 ml) solution of 5.7 mmol of $TiCl_4$ was added with stirring at -78°C, and after 10 min, the mixture was quenched with water. By thin layer chromatography the products were separated into two fractions. The less polar fraction is ortho rearranged products[10] (VI and VII in the ratio of 2.5 to 1.0) in isolated yield of 74%. The more polar fraction is para rearranged products[10] (VIII and IX in the ratio of 1.0 to 4.8) in isolated yield of 19%.



(V) (VI) (VII) (VIII) (IX)

In contrast to the above results none of the rearranged product was isolated but a large amount of phenol was obtained when 3-methyl-2-butenyl phenyl ether (X) was treated with $TiCl_4$ and IV. On the other hand, it was found that when the mixture of 2 equimolar amounts of $TiCl_4$ and an equimolar amount of $Ti(O\text{-}isoPr)_4$ in 10 ml of CH_2Cl_2 was added to the mixture of an equimolar amounts of X and IV at -78°C, the rearrangement proceeded rapidly within 10 minutes and 2-(3-methyl-2-butenyl)phenol (XI)[11] and 4-(3-methyl-2-butenyl)phenol (XII)[12] were isolated in 25% and 27% yields, respectively.



(X) (XI) 25% (XII) 27%

These results indicate that when $TiCl_4$ is employed in the rearrangement of allyl aryl ethers (I), it is as effective as BCl_3 which has been hitherto considered to be the most suitable acid catalyst. Further, it is also noted that the rearrangement of 2-butenyl phenyl ether (V) proceeds in higher yield (93%) than in the case of BCl_3 (55%)$^{3)}$, and even 3-methyl-2-butenyl phenyl ether (X) is converted into the rearranged phenols (XI, XII) by the combined used of $TiCl_4$ with $Ti(O\text{-}isoPr)_4$.

In conclusion, it is noted that, the present method using $TiCl_4$ possesses a preparative advantage over the hitherto known acid catalyst BCl_3.

References

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4) F. M. Sonnenberg, J. Org. Chem., 35, 3166 (1970).

5) This reagent was prepared by the reaction of trimethylsilyl chloride with lithioacetanilide in THF at 0°C, and purified by distillation (bp 60°C/1 mmHg).

6) The nmr spectra of these compounds were identical with those cited in C. J. Pauchert and J. R. Campbell "The Aldrich Library of NMR Spectra", Vol. IV, (1974).

7) nmr; (CCl_4) δ 2.19 (s, 3H), 3.27 (d, 2H), 5.42 (broad, 1H, OH), 4.82-6.29 (3H, $-CH=CH_2$), 6.46-7.09 (m, 3H).

8) nmr; (CCl_4) δ 3.27 (d, 2H), 5.47 (s, 1H, OH), 4.84-6.27 (3H, $-CH=CH_2$), 6.44-7.14 (m, 3H).

9) nmr; (CCl_4) δ 3.44 (d, 2H), 4.97-6.41 (3H, $-CH=CH_2$), 5.69 (s, 1H, OH), 7.11 (d, 1H), 7.28 (d, 1H).

10) These products were separated by preparative gas chromatography and the structures were determined according to the nmr spectra (CCl_4); VI: δ 1.36 (d, 3H), 3.40-3.93 (m, 1H), 4.90-5.30 (m, 3H, $=CH_2$ and OH), 5.78-6.33 (1H, $-CH=$), 6.55-7.20 (m, 4H). VII: δ 1.71 (m, 3H), 3.31 (m, 2H), 4.61 (s, 1H), 5.58 (m, 2H), 6.56-7.23 (m, 4H). VIII: δ 1.32 (d, 3H), 4.75-5.20 ($=CH_2$), 6.64 (d, 2H), 7.05 (d, 2H). IX: δ 1.70 (m, 3H), 3.06-3.38 (m, 2H), 4.33 (broad s, 1H, OH), 5.48 (m, 2H), 6.62 (d, 2H), 6.95 (d, 2H).

11) nmr; (CCl_4) δ 1.73 (s, 6H), 3.30 (d, 2H), 5.12-5.50 (m, 1H), 5.50 (s, 1H, OH), 6.50-7.20 (m, 4H).

12) nmr; (CCl_4) δ 1.70 (s, 6H), 2.20 (d, 2H), 5.27 (broad t, 1H), 6.10 (broad, 1H), 6.65 (d, 2H), 6.95 (d, 2H).

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