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Borderline Mechanisms Involving Ion-molecule Pairs for the Nucleophilic Substitution Reactions of Benzhydrol and Its Derivatives. Facile Formation and Cleavage of Diphenylmethyl Ethers for the Protection of Hydroxyl Groups.

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Abstract: *Nucleophilic substitution reactions of benzhydrol and its derivatives, in refluxing benzene in the presence of para-toluenesulfonic acid, took different routes depending on whether para-toluenesulfonic acid was used in excess or in catalytic amounts. In the first case the reactions took place via benzhydryl carbocations and in the second case they proceeded via intimate ion-molecule pairs. On the basis of this study, facile methods for introduction and removal of* $CHPh_2$ *as a protective group of alcohols are presented.* © 1998 Elsevier Science Ltd. All rights reserved.

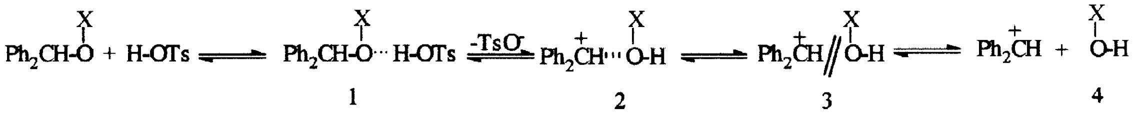
Recently we studied several nucleophilic substitution reactions of benzhydrol and some of its derivatives in benzene or toluene catalyzed by para-toluenesulfonic acid.[1] Now we have investigated these reactions in benzene further and have found that their outcome depend on whether para-toluenesulfonic acid was used in excess or in catalytic amounts as shown below:

1a. $Ph_2CHOH \xrightarrow{\text{TsOH cat.}} Ph_2CHOCHPH_2$
b. $Ph_2CHOH \xrightarrow{\text{TsOH exc.}} Ph_3CH + Ph_2CH_2 + PhCOPh$
2a. $Ph_2CHOCHPh_2 \xrightarrow{\text{TsOH cat.}}$ no reaction
b. $Ph_2CHOCHPh_2 \xrightarrow{\text{TsOH exc.}} Ph_3CH + Ph_2CH_2 + PhCOPh$
3a. $PhCO_2CHPh_2 \xrightarrow{\text{TsOH cat.}}$ no reaction
b. $PhCO_2CHPh_2 \xrightarrow{\text{TsOH exc.}} Ph_3CH + Ph_2CH_2 + PhCOPh + PhCO_2H$
4a. $Ph_2CHO(CH_2)_7CH_3 \xrightarrow{\text{TsOH cat.}}$ no reaction
b. $Ph_2CHO(CH_2)_7CH_3 \xrightarrow{\text{TsOH exc.}} Ph_3CH + Ph_2CH_2 + PhCOPh + CH_3(CH_2)_7OH + Ph(CH_2)_7CH_3$

In all cases the substrate and para-toluenesulfonic acid were dissolved in benzene and the solution was refluxed under a Dean-Stark trap for about six hours after which aqueous $NaHCO_3$ was added to the reaction mixture to remove TsOH.

Mechanistically we view the reactions as occurring via intimate ion-molecule pairs **2**, via solvent-separated ion-molecule pairs **3** or via benzhydryl carbocations as shown in scheme 1.

Scheme 1



$$Ph_2CH\text{-}\overset{X}{\overset{|}{O}} + H\text{-}OTs \rightleftharpoons Ph_2CH\text{-}\overset{X}{\overset{|}{O}}\cdots H\text{-}OTs \xrightleftharpoons{-TsO^-} Ph_2\overset{+}{CH}\cdots\overset{X}{\overset{|}{O}}\text{-}H \rightleftharpoons Ph_2\overset{+}{CH}//\overset{X}{\overset{|}{O}}\text{-}H \rightleftharpoons Ph_2\overset{+}{CH} + \overset{X}{\overset{|}{O}}\text{-}H$$

1 2 3 4

1a, 2a, 3a, 4a X = H 1b, 2b, 3b, 4b X = $CHPh_2$ 1c, 2c, 3c, 4c X = COPh 1d, 2d, 3d, 4d X = $(CH_2)_7CH_3$

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In the presence of a catalytic amount of para-toluenesulfonic acid, since the medium had a low ionizing power, the reaction progressed only until the formation of 2 which was the possible electrophile.[1] In the presence of an excess of para-toluenesulfonic acid, since the medium acquired a higher ionizing power the reaction progressed until the formation of the benzhydryl carbocation which was the possible electrophile. In this case benzene trapped the free benzhydryl carbocation forming triphenylmethane.[2] While the free benzhydryl carbocation had the required electrophilicity to react with benzene[2], 2 had not. The formation of diphenylmethane and benzophenone in reactions 1b, 2b, 3b and 4b can be explained as shown in scheme 2 for reaction 4b.

Scheme 2

$$Ph_2\overset{+}{C}H + Ph_2CH\text{-}O\text{-}(CH_2)_7CH_3 \rightleftharpoons Ph_2CH_2 + Ph_2C{=}\overset{+}{O}\text{-}(CH_2)_7CH_3 \xrightarrow[TsO^-]{H_2O} Ph_2C{=}O + CH_3(CH_2)_6CH_2OH + TsOH$$

$CHPh_2$ is a protective group for alcohols.[3] On the basis of our previous work,[1] we propose easy methods for the introduction and removal of the $CHPh_2$ group. For introduction equimolar amounts of alcohol and benzhydrol were refluxed in benzene in the presence of a catalytic amount of para-toluenesulfonic acid under a Dean-Stark trap until no more water formed. Usual work up gave excellent yields of the benzhydryl ethers.[4] For $CH_3(CH_2)_7OCHPh_2$ we obtained 92% yield.

For removal of the $CHPh_2$ protective group, the benzhydryl ether dissolved in benzene was first refluxed in the presence of excess benzoic acid and a catalytic amount of TsOH under a Dean-Stark trap until no more water formed:

$$Ph_2CHOR + 2\,PhCO_2H \xrightarrow[C_6H_6]{TsOH\ cat} \underset{5}{PhCO_2CHPh_2} + \underset{6}{PhCO_2R} + H_2O$$

After removal of the acids, most of the benzene was taken off in vacuo. Then the ester mixture was separated by column chromatography. Alkaline hydrolysis of 6 allowed recovery of the free alcohol in high yield. For example $Ph_2CHO(CH_2)_7CH_3$ gave 89% yield of 1-octanol.

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