Pergamon

Tetrahedron Letters, Vol. 37, No. 12, pp. 1965-1966, 1996

0040-4039/96 $15.00 + 0.00

S0040-4039(96)00181-5

Facile New Methods for Introduction and Removal of the Diphenylmethyl Group as a Protective Group of Carboxylic Acids

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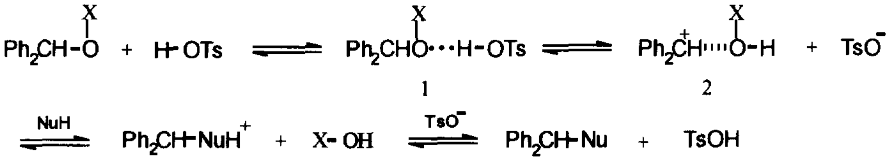
Keywords: Diphenylmethyl Ester, Carboxylic Acid Protective Group, Intimate Ion-molecule Pair Intermediate, $A_{AL}2$ Mechanism.

***Abstract**: Easy new methods for introducing and removing the diphenylmethyl group as a protective group of carboxylic acids are presented. For the formation of the diphenylmethyl esters from the carboxylic acids and benzhydrol, the unusual $A_{AL}2$ mechanism is followed.*

We have studied several nucleophylic substitution reactions of benzhydrol and some of its derivatives in non polar solvents (benzene or toluene) catalyzed by para-toluenesulfonic acid. The nature of these reactions and the products formed are described in the scheme.

Scheme



X = H, $CHPh_2$, COR
NuH = nucleophylic compound = Ph_2CHOH, RCO_2H, $PhCH_3$.
Ph_2CHNu = $Ph_2CHOCHPh_2$, $Ph_2CHOCOR$, ortho and para $Ph_2CHC_6H_4CH_3$.

Mechanistically we view the reactions as occurring via intimate ion-molecule pair intermediates **2** analogous to the ones proposed by Katritzky and coworkers.[1] The intermediacy of free benzhydryl carbocations in the reactions is precluded since when benzhydrol was treated with para-toluenesulfonic acid in benzene, with water removal, no triphenylmethane formed at all. Ohwada has reported that benzene traps free benzhydryl carbocations quantitatively forming triphenylmethane.[2] When $Ph_2CH^{18}OH$ was treated with $PhCO_2H$ and a catalytic amount of TsOH in refluxing benzene under a Dean-Stark trap until no more water formed, it was found that $PhCO_2CHPh_2$ and H_2O^{18} were the products. These facts are consistent with the mechanism of the scheme which in this case corresponds to the unusual $A_{AL}2$ mechanism.[3]

Benzhydryl ether and benzhydryl benzoate are inert to hydrolysis when refluxed with para-toluenesulfonic acid in an aqueous medium (water or water-dioxane). In contrast, benzhydryl ether was converted to benzhydryl benzoate when refluxed, with water removal, with a catalytic amount of para-toluenesulfonic acid in benzene in the presence of benzoic acid. Also benzhydryl benzoate was converted to benzoic acid and tolyldiphenylmethane when refluxed with para-toluenesulfonic acid in toluene. We reason that these reactions occur because para-toluenesulfonic acid is not ionized in benzene or toluene thereby allowing the formation of 1 which is the precursor of the intimate ion-molecule pair 2. In the conversion of 1 into 2 bonds are concertedly broken and formed.

The diphenylmethyl group is a commonly used protective group for carboxylic acids.[4] On the basis of our preceding study, we present new, easier methods for the introduction and removal of the diphenylmethyl group. For introduction, a slight excess of the carboxylic acid dissolved in benzene was refluxed with benzhydrol 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 good yields of the diphenylmethyl esters (table 1).

Table 1	*RCO_2H[5]*	*% Yield RCO_2CHPh_2[6]*
	R = Ph	78
	R = $PhCH_2$	83
	R = Ph_2CH	81

For removal of the $CHPh_2$ group, the ester dissolved in excess toluene was refluxed in the presence of an equivalent molar amount of TsOH for about 8 hours. Aqueous $NaHCO_3$ extraction followed by concentration, acidification and cooling gave good yields of the carboxylic acids (table 2).

Table 2	*RCO_2CHPh_2*	*% Yield RCO_2H*
	R = Ph	83
	R = $PhCH_2$	95
	R = Ph_2CH	78

References and Notes

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2. Ohwada, T.; Shudo, K.J. *J. Am. Chem. Soc.* **1988**, *110*, 1862 - 1870.
3. March, J. "*Advanced Organic Chemistry*". 4th edit., Wiley, New York, **1992** pp 378 - 382.
4. Greene, T.W. "*Protective Groups in Organic Synthesis*"; Wiley, New York, **1981** pp 173 - 74.
5. The carboxylic acids were obtained from Aldrich.
6. $PhCO_2CHPh_2$: M.p. 87 - 88 °C (Lit.[7] 87.5 - 88 °C), ^{1}H-NMR ($CDCl_3$) δ 7.1(s, 1H), 7.2 - 7.6(m, 13H), 8.1 - 8.2(m, 2H). $PhCH_2CO_2CHPh_2$: M.p 94 - 95°C, ^{1}H-NMR ($CDCl_3$) δ 3.7(s, 2H), 6.9(s, 1H) 7.2 - 7.4(m, 15H). $Ph_2CHCO_2CHPh_2$.: M.p 107 - 108 °C, ^{1}H-NMR ($CDCl_3$) δ 5.15(s, 1H), 6.9(s, 1H) 7.2 - 7.4(m, 20H).
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(*Received in USA* 4 *October* 1995; *revised* 9 *January* 1996; *accepted* 12 *January* 1996)