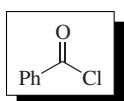


# Benzoyl Chloride<sup>1</sup>



[98-88-4]

 $C_7H_5ClO$ 

(MW 140.57)

InChI = 1/C7H5ClO/c8-7(9)6-4-2-1-3-5-6/h1-5H

InChIKey = PASDCCFISLVPSON-UHFFFAOYAL

(useful acylating agent; preparation of ketones from organometallic compounds;<sup>2,3</sup> preparation of 1,3-dicarbonyl compounds from enolates or enols;<sup>4,5</sup> Friedel–Crafts acylation and related reactions<sup>6</sup> with aromatic and heterocyclic compounds,<sup>7</sup> alkenes,<sup>8</sup> alkynes,<sup>9</sup> enoxysilanes,<sup>10</sup> and silicon compounds;<sup>11</sup> acylation of enol ethers, ketene acetals,<sup>12</sup> and enamines;<sup>13</sup> protection of alcohols as benzoates;<sup>14</sup> protection of amines as benzamides<sup>15</sup>)

**Physical Data:** bp 197.2 °C; mp –1 °C;  $d$  1.21 g cm<sup>-3</sup>.

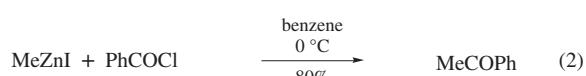
**Solubility:** slowly decomposed by water and alcohols; sol most organic solvents.

**Form Supplied in:** colorless liquid; penetrating odor; widely available.

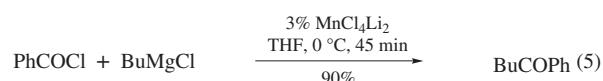
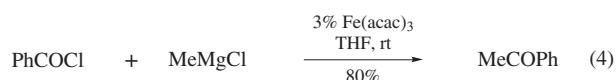
**Purification:** the good commercial grade of benzoyl chloride can be purified by distillation. The technical material must be purified as follows: a 50% solution of PhCOCl in ether or cyclohexane is washed with cold 5% aqueous sodium bicarbonate; after drying over  $CaCl_2$  the solvent is eliminated under vacuo and the PhCOCl is distilled.<sup>16</sup>

**Handling, Storage, and Precautions:** use in a fume hood; lachrymatory, irritating to skin, eyes and mucous membranes; toxic by inhalation and ingestion.

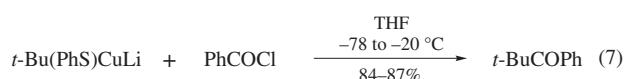
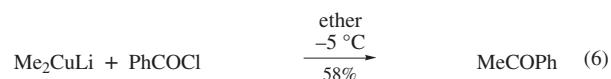
**Acylation of Organometallic Compounds.**<sup>2,3</sup> PhCOCl reacts with various organometallic reagents to give the corresponding phenyl ketones in variable yields. The first acylation reactions were performed with organocadmium and organozinc compounds (eqs 1 and 2).<sup>3a,b</sup> In THF, organozinc reagents give poor results; however, the yields are clearly improved in the presence of **Tetrakis(triphenylphosphine)palladium(0)** (eq 3).<sup>3c</sup>



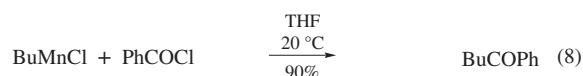
With the very reactive organomagnesium compounds, the acylation takes place in the presence of  $Fe(acac)_3$ <sup>3d</sup> or  $MnCl_2$ <sup>3e</sup> (eqs 4 and 5). It is worthy of note that the 1,2-addition, which is rapid under these reaction conditions (10–20 °C), is completely avoided.



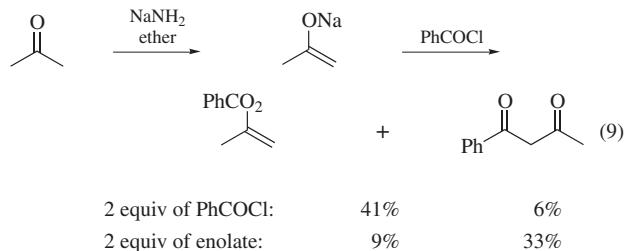
Organocupper (60% of PhCOMe from  $MeCu\cdot PBu_3$ )<sup>3f</sup> and cuprate reagents (eq 6),<sup>3g</sup> which are now widely used, give only moderate yields of phenyl ketones. Better yields are obtained at low temperature by using a large excess of organocuprate<sup>3h</sup> or heterocuprate (eq 7).<sup>3i</sup>



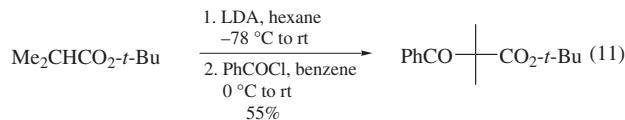
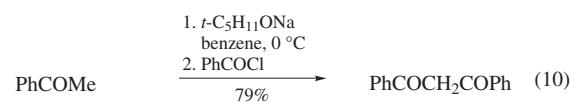
Organomanganese compounds afford excellent yields by the use of a stoichiometric amount of reagents under mild conditions (eq 8).<sup>3j</sup>

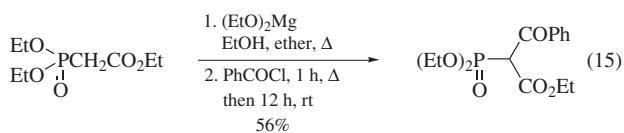
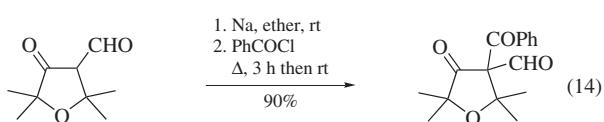
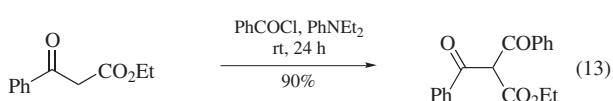
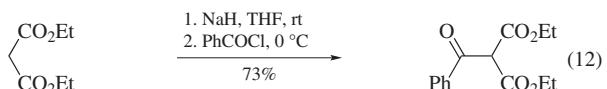


**Acylation of Enolates, Enols, and Related Reactions.**<sup>4,5</sup> According to the reaction conditions, PhCOCl reacts with ketone enolates to lead to enol benzoates (*O*-acylation, kinetic product) or  $\beta$ -diketones (*C*-acylation, thermodynamic product) (eq 9).<sup>5a</sup>

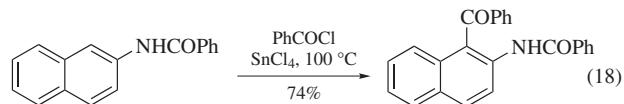
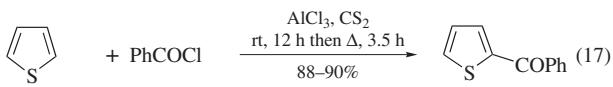
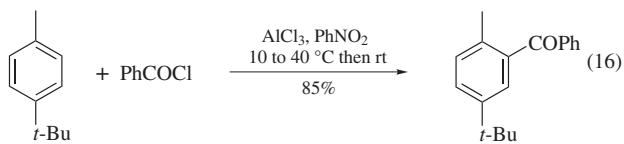


PhCOCl very often gives a mixture of the *O*- and *C*-acylated products. To prepare the enol ester (kinetic conditions) a more reactive acylating agent such as **Acetyl Chloride** is generally used. Moreover, carboxylic acid anhydrides are generally preferred to acyl halides. Accordingly, PhCOCl is preferred to prepare 1,3-dicarbonyl compounds. Ketones (eq 10),<sup>5b</sup> esters (eq 11),<sup>5c</sup> and more commonly  $\beta$ -keto esters or related CH acidic compounds (eqs 12–15)<sup>5d–g</sup> can be *C*-acylated via the preformed enolate (eq 11) or directly under basic conditions (eq 13).<sup>5e</sup>

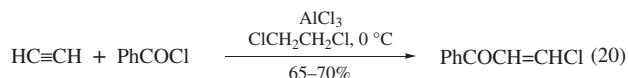
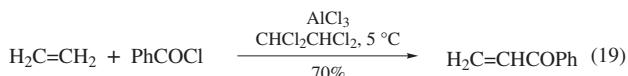




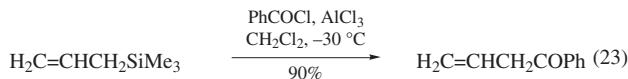
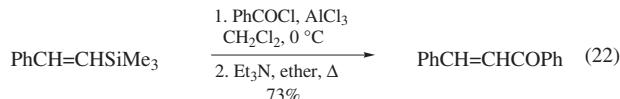
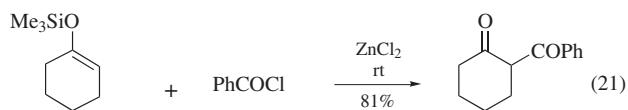
**Friedel-Crafts Acylation and Related Reactions.<sup>6,7</sup>** Aromatic compounds (eqs 16 and 17)<sup>7a,b</sup> are acylated by PhCOCl in the presence of a Lewis acid such as AlCl<sub>3</sub>, TiCl<sub>4</sub>, BF<sub>3</sub>, SnCl<sub>4</sub>, ZnCl<sub>2</sub>, or FeCl<sub>3</sub>, or of a strong acid such as polyphosphoric acid or CF<sub>3</sub>SO<sub>3</sub>H.<sup>6</sup> Metallic Al or Fe and iodine (in situ formation of a Lewis acid) can also act as a catalyst.<sup>6</sup> Various solvents that have been used to perform this reaction are CS<sub>2</sub>, CH<sub>2</sub>Cl<sub>2</sub>, 1,2-dichloroethane, nitrobenzene, and nitromethane.<sup>6</sup> PhCOCl is less reactive than aliphatic carboxylic acid chlorides (with benzene in nitromethane the relative reaction rates are PhCOCl:MeCOCl = 6:100).<sup>7a</sup> As for all electrophilic substitutions, the rate and the regioselectivity of the acylation closely depend on the nature and on the position of the substituents on the aromatic system<sup>6</sup> (eqs 16 and 18<sup>7c</sup>). The nature of the solvent can also exert a strong influence.<sup>6</sup>



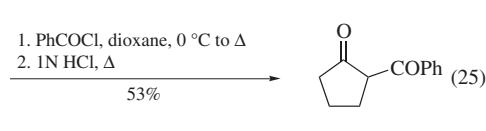
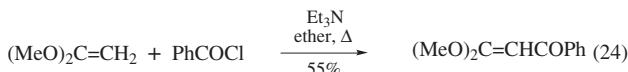
The electrophilic acylation of alkenes or alkynes is another example of Friedel-Crafts reactions and is carried out under similar conditions.<sup>6,8,9</sup> With PhCOCl, alkenes can lead to  $\beta$ -chloro alkyl ketones or, more frequently, to the corresponding  $\alpha,\beta$ -ethylenic ketones (eq 19)<sup>8b</sup> according to the reaction conditions.<sup>6,8a</sup> PhCOCl also adds to triple bonds to give a  $\beta$ -chloro vinyl ketone<sup>9</sup> (eq 20).<sup>9b</sup>



Under Friedel-Crafts conditions, PhCOCl reacts with various silicon compounds. Thus  $\beta$ -diketones are easily obtained from enoxysilanes<sup>10a,b</sup> (eq 21).<sup>10c</sup> Conversely, vinyl-, aryl-, and allylsilanes lead to the corresponding vinyl, aryl, and allyl ketones in good yields<sup>11a–e</sup> (eqs eq 22<sup>11d</sup> and eq 23<sup>11e</sup>). Vinylsilanes can lead to a mixture of  $\beta$ -chloro alkyl ketones and conjugated enones; a basic treatment is then necessary to obtain only the enone (eq 23).

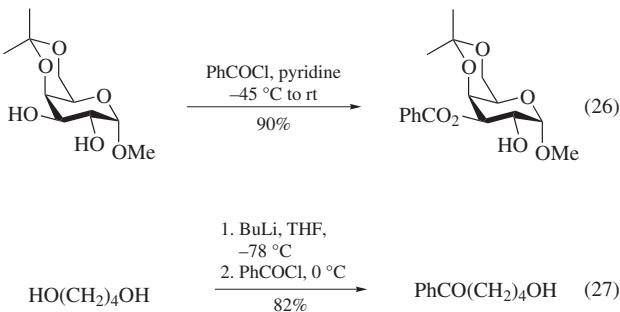


**Acylation of Enol Ethers, Ketene Acetals,<sup>12</sup> and Enamines.<sup>13</sup>** Enol ethers,<sup>12a</sup> ketene acetals (eq 24),<sup>12b</sup> and enamines (eq 25)<sup>13g</sup> react with PhCOCl to provide the corresponding  $\beta$ -acylated products (eq 24).<sup>12b</sup> The acylation of enamines has been extensively studied (eq 25),<sup>13a–f</sup> the resulting  $\beta$ -acyl enamine is generally hydrolyzed to give  $\beta$ -diketones (eq 25).

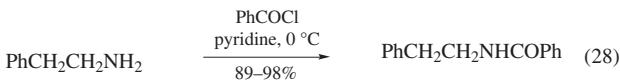


**Protection of Alcohols as Benzoates<sup>14</sup> and of Amines as Benzamides.<sup>15</sup>** PhCOCl easily reacts with alcohols to give the corresponding benzoates in excellent yields.<sup>14a</sup> The acylation is performed in the presence of an amine, very often pyridine or triethylamine. CH<sub>2</sub>Cl<sub>2</sub> or a large excess of amine is generally used as solvent (eq 26).<sup>14d</sup> The reaction has also been performed by phase transfer catalysis (PhCOCl, benzene, Bu<sub>4</sub>NCl, 40% NaOH).<sup>14e</sup> Alternatively, the alcohol can be converted to lithium alcoholate (with BuLi), which readily reacts with PhCOCl to give quantitatively the corresponding benzoate (eq 27).<sup>14f</sup> Tributyltin ether

prepared by treatment of the alcohol with **Bis(tributyltin) Oxide** has also been used as intermediate.<sup>14g</sup> Benzoates are very often prepared to protect alcohols<sup>14b,c</sup> because they are more stable than acetates and their tendency to migrate to adjacent hydroxyl groups is lower.<sup>14h,i</sup> In most cases the benzoylation of polyhydroxylated molecules is more selective than the acetylation.<sup>14h,i</sup> PhCOCl has also been used to monoprotect diols,<sup>14f</sup> and to acylate a primary alcohol in the presence of a secondary alcohol.<sup>14j</sup> Under similar conditions (pyridine), phenols are converted to aryl benzoates.<sup>14a,k</sup>



PhCOCl reacts also easily with primary or secondary amines in the presence of a base, aqueous alkali (Schotten–Bauman procedure), or tertiary amines (pyridine or Et<sub>3</sub>N), to afford the corresponding amides (eq 28).<sup>15b</sup> This reaction is used to protect amines.<sup>15c</sup>



**Miscellaneous Reactions.** PhCOCN (see **Acetyl Cyanide**), which is used as acylating agent (for instance, to protect alcohols)<sup>17a</sup> can be prepared by reacting PhCOCl with **Copper(I) Cyanide** (60–65%).<sup>17b,c</sup> Diazoalkanes are readily acylated by PhCOCl to give diazo ketones.<sup>18a,b</sup> These compounds are interesting as intermediates<sup>18c–e</sup> to prepare  $\alpha$ -halo ketones,  $\alpha$ -hydroxy ketones or arylacetic acids (Arndt–Eistert reaction).<sup>18e</sup> PhCOCl has also been used to prepare volatile acyl chlorides (C<sub>2</sub> to C<sub>6</sub>) from the corresponding carboxylic acids.<sup>19</sup> On the other hand, it reacts with sulfoxides to lead generally to the corresponding  $\alpha$ -chloro sulfides (Pummerer rearrangement).<sup>20</sup>

**Related Reagents.** Acetyl Chloride; Acetyl Cyanide; Benzoic Anhydride.

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