Chapter 2

Synthesis of Coumarin derivatives using Phosphotungstic acid as catalyst.
Coumarin and its derivatives signify a major class of heterocycle and a number of preparations have been known since late 1800’s. Coumarin, the parent substance of the benzopyran-2-ones group, was first isolated from Tonka beans in 1820. Several coumarin derivatives have been found to be widely distributed in the plant kingdom. Particularly the plants belonging to the natural orders of Orchidaceae, Leguminosae, Rutaceae, Umbelliferae and Labiatae are rich sources of naturally occurring coumarins.\(^1\) Coumarin was initially considered to be a benzoic acid derivative, but its synthesis by W.H. Perkin\(^2\) from salicylaldehyde by means of his classical reaction established its relation to \(-o\)-hydroxycinnamic acid, which loses a molecule of water in forming the lactone ring.

However, different constitutional formulae have been suggested from time to time. Of the various formulae proposed by Perkin (1), Basecke (2), Strecker, Fittig and Tiemann (3), Salkowski (4) and Morgan and Micklethwait (5), compound (3) has been found to be in complete accord with the known reactions of coumarin derivatives and has been universally accepted as correct.\(^3\)

![Chemical structures](attachment:image.png)

A research paper entitled “A solvent-free synthesis of coumarins using Phosphotungstic acid as catalyst” is published in *Catalysis Letters*, 2009, 131(1-2), 321-327.
Thus, coumarin and its derivatives are from the point of view of their chemical constitution, a group of lactones derived from \(\alpha\)-hydroxycinnamic acids. Alternately stated, a coumarin ring system is formed by the fusion of benzene and 1,2-pyrone ring, i.e., coumarin is a class of heterocyclic compounds containing oxygen as a member of the heterocyclic ring. Therefore, coumarin and its derivatives have shown a number of versatile and biodynamic pharmacological activities along with fluorescent properties.

### The synthesis of coumarin derivatives.

Of the number of synthetic methods, there are few which have yielded important results, there are several others whose applications are less general. All these methods center round the possibility of building up the pyrone ring on a suitable benzene derivative.

**(i) Perkin reaction**

Perkin first synthesized coumarin from salicylaldehyde by heating it with acetic anhydride and anhydrous sodium acetate.\(^2\)

\[
\begin{align*}
\text{HO} & \quad \text{CHO} + (\text{CH}_3\text{CO})_2\text{O} \quad \text{CH}_3\text{COONa} \\
\text{HO} & \quad \text{CH}=\text{CHCOONa} \quad \rightarrow \\
\text{HO} & \quad \text{CH}=\text{CHCOONa} \quad \rightarrow \\
\text{HO} & \quad \text{CH}=\text{CHCOONa} \quad \rightarrow \\
\end{align*}
\]

This reaction occurs with the formation of an intermediate \(\alpha\)-hydroxycinnamic acid derivative \((6)\) which passes spontaneously into the lactone \((7)\) when liberated from its sodium salt. This method was
successfully used by Tiemann and Herzfeld\textsuperscript{4}, Taage\textsuperscript{5} and later on by numerous workers in the field. E. Spath\textsuperscript{1} has utilized this reaction to synthesize several naturally occurring coumarins. It has however its limitations: the appropriate initial \(\sigma\)-hydroxyaldehydes are rather difficult to obtain from many substituted phenols; the method gives coumarins unsubstituted in the pyrone ring; the yields obtained are also low. Yanagisawa and Kondo claim to have improved the yields by using iodine as catalyst in the reaction\textsuperscript{6}.

(ii) Pechmann reaction

Pechmann found that a coumarin derivative is formed when a mixture of phenol and malic acid is heated in the presence of concentrated sulfuric acid\textsuperscript{7}.

\[
\begin{array}{cccc}
\text{HO} & \text{OH} & \text{COOH} & \text{H}_2\text{SO}_4 \\
\text{CH}_2\text{CH(OH)COOH} & \rightarrow & \text{HO} & \text{O} \\
& & \text{CH} & \text{CH} \\
& & \text{C} & \text{O} \\
& & \text{O} & \text{O} \\
& & \text{O} & \text{O} \\
\end{array}
\]

This method has limited applicability. Many substituted phenols do not undergo this reaction; only coumarins unsubstituted in the pyrone ring are obtained.

(iii) Pechmann-Duisberg reaction

Pechmann and Duisberg found that phenols condense with \(\beta\)-ketonic esters in the presence of sulfuric acid giving coumarin derivatives\textsuperscript{8}. This reaction has found extensive applications in the synthesis of various coumarin derivatives.
(iv) Knoevenagel reaction

Knoevenagel developed a method for the synthesis of coumarin derivatives from \( \alpha \)-hydroxyaldehydes by condensation with ethyl malonate, ethyl acetoacetate, ethyl cyanoacetate, etc., in the presence of piperidine, pyridine and other organic bases.\(^9\)

\[
\begin{align*}
\text{HO} & \quad \text{OH} \\
\text{CHO} & \quad \text{COOC}_2\text{H}_5
\end{align*}
\]

\[
\text{Piperidine, pyridine Base}
\]

\[
\text{HO} \quad \text{O} \\
\text{CH}_3
\]

\[
\text{R} = \text{COOC}_2\text{H}_5, \text{COCH}_3
\]

(v) Other reaction methods

This reaction has been successfully used by various workers, notably by Shah and Shah\(^{10}\), to prove the ortho position of the formyl group to the hydroxyl group in their studies on \( \gamma \)-substitution in the resorcinol nucleus. They have synthesized a large number of coumarin derivatives by this method by the condensation of formylated 4-acylresorcinols and other di- and tri-hydroxyacetophenones with malonic ester, acetoacetic ester and cyanoacetic ester. This method has been found to be better than the Perkin-Robinson method\(^{11}\) of pyrylium salt formation on account of the smoothness with which it works.

\( \alpha \)-Hydroxyaldehydes and phenyl acetonitrile condense in the presence of sodium ethoxide or alcoholic potash, giving 3-phenylcoumarins.\(^{12}\)
Pandya and his coworkers have investigated the Knoevenagel reaction with various aldehydes in the presence of pyridine alone and have found that a trace of pyridine is efficacious in bringing about the condensation with nearly theoretical yields.\(^\text{13}\) Thus pyridine in traces is quite comparable to Knoevenagel's famous reagent piperidine in traces. In a series of papers, Pandya and his coworkers have investigated many other bases, which have been found to possess a similar efficiency in promoting these reactions. They have also made a study of constitutional factors by using differently substituted aldehydes.\(^\text{14}\) Pandya and Sodhi have obtained 3-aminocoumarin in excellent yield by condensing salicylaldehyde with glycine in the presence of a trace of pyridine.\(^\text{15}\) Ghosal found that the reaction between an \(\sigma\)-hydroxybenzaldehyde and cyanoacetophenone in the presence of hydrogen chloride gives a benzoylecoumarin instead of the expected pyrylium derivative.\(^\text{16}\)

Sonn found that resorcinol condenses with cyanoacetic ester under the conditions of the Hoesch reaction,\(^\text{18}\) the ketimine hydrochloride obtained on hydrolysis gives ultimately 4,7-dihydroxycoumarin.\(^\text{17}\)
Weiss and Merksammer found that resacetophenone on condensation with ethyl ethoxymethyleneacetoacetate by heating with alcoholic sodium ethoxide gave 7-hydroxy-3,6-diacetylcoumarin.\(^\text{19}\) Weiss and Kratz extended the method and found that ethyl ethoxymethylene malonate similarly condensed to give coumarin-3-carboxylates from resorcinol derivatives, the carbethoxyl group having hydrolyzed to the carboxyl group.\(^\text{20}\)

Baker et al., found that a formylphenylacetonitrile and its derivatives condense with resorcinol and other phenols in the presence of phosphorus oxychloride or dry hydrogen chloride as condensing agent, leading to the production of 3-phenylcoumarins in poor yields and not the isomeric 3-phenylchromones (isoflavones).\(^\text{21}\)
Chakravarti and Majumdar have developed a method by which
3,4-dialkyl-substituted coumarins not available by the usual methods may be
synthesized: o-hydroxyaryl alkyl ketones, under the conditions of the
Reformatsky reaction, are ultimately converted into coumarin derivatives.²²

A rapid development in the chemistry of coumarins is due mainly to
the synthetic method universally known as the Pechmann reaction, which
consists in reacting phenols with β-ketonic esters in the presence of sulfuric
acid. Various workers have studied the Pechmann reaction using different
reaction conditions and various catalysts. A brief literature survey is as
follows-

Pickett et al., have synthesized dihydrocoumarins in 40 to 60% yields
in one step by heating acrylic esters with an excess of phenol in the presence
of base catalysts.²³
Gunnewegh et al., have synthesized coumarin derivatives from \textit{m}-substituted phenols and \(\alpha,\beta\)-unsaturated carboxylic acids catalyzed by solid-acid catalysts, such as zeolite H-Beta or Amberlyst-15, in toluene as solvent was studied. The conversion involves esterification followed by alkylation (ring closure). Ring closure of the ester is promoted both by an appropriate substituent on the aromatic ring and by Michael activation of the \(\beta\)-carbon of the ester. These influences were studied by variation of the reactants. 7-hydroxy-3,4-dihydrocoumarin is formed in high yield when resorcinol and propenoic acid were used as reactants.

Zeitler et al., have synthesized dihydrocoumarin derivatives from \(\alpha\)-hydroxycinnamaldehyde in the presence of triazolin-5-ylidene carbenes under oxidative conditions, their unsaturated counterparts in moderate to high yield.

Gabriele et al., have reported a novel approach for the synthesis of coumarin derivatives starting from readily available 2-(1-hydroxyprop-2-yynyl)phenols, based on unprecedented palladium-catalyzed dicarbonylation.
process. Reactions were carried out in the presence of catalytic amounts of PdI₂ in conjunction with an excess of KI in MeOH as a solvent at room temperature and under 90 atm of CO to give 3-[(methoxycarbonyl)-methyl]coumarins in good to high isolated yields (62-87 %).²⁶

Surya Prakash Rao et al., have developed a facile, convenient, efficient, and high yielding synthesis of a combinatorial library of 3-aroylcoumarins by the condensation of easily available α-aroylketene dithioacetals (AKDTAs) and 2-hydroxybenzaldehydes (salicylaldehydes)/2-hydroxy-1-naphthaldehyde in the presence of catalytic amount of piperidine in THF reflux.²⁷

Fillion et al., have synthesized a series of 4-substituted 3,4-dihydrocoumarins using Yb(OTf)₃ as a catalyzed from phenols and 5-alkylidene Meldrum’s acids in high isolated yields.²⁸
Kelin Li et al., have developed a electrophilic palladium-catalyzed cycloisomerization of brominated aryl propiolates produces brominated coumarins. The brominated coumarins can be diversified by reduction of the Pd (II) catalyst to Pd (0) followed by Suzuki, Sonogashira, Heck or Hartwig-Buchwald coupling. Thus, a single loading of precatalyst can be used to conduct sequential reactions, allowing the synthesis of functionalized coumarins.\(^\text{29}\)

Dittmer et al., have synthesized coumarins, 4-hydroxycoumarins, and 4-hydroxyquinolin-2(1H)-ones can be conveniently prepared by treatment of \(\alpha\)-halocarboxylic acid esters of salicylaldehyde, \(o\)-hydroxyacetophenone, methyl salicylate and methyl \(N\)-methyl- or \(N\)-phenylantranilates with sodium or lithium telluride. Phenylketene formation competes with cyclization of the \(R\)-chlorophenylacetate ester of methyl salicylate as demonstrated by a trapping experiment with benzylamine. Elemental tellurium may be recovered and reused.\(^\text{30}\)
Kadnikov et al., have developed the palladium-catalyzed annulation of internal alkynes by o-iodophenols in the presence of CO results in exclusive formation of coumarins. No isomeric chromones have been observed. The best reaction conditions utilize the 2-iodophenol, 5 equiv of alkyne, 1 atm of CO, 5 mol % Pd(OAc)$_2$, 2 equiv of pyridine and 1 equiv of $n$-Bu$_4$NCl in DMF at 120 °C. The use of a sterically unhindered pyridine base is essential to achieve high yields. A wide variety of 3,4-disubstituted coumarins containing alkyl, aryl, silyl, alkoxy, acyl and ester groups have been prepared in moderate to good yields.\(^{31}\)
Still, numerous catalysts are being used for the synthesis of coumarin derivatives as given in Table-1.

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Catalyst</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Sulfated Ce₅Zr₁₋₀₂ solid</td>
<td>32</td>
</tr>
<tr>
<td>2.</td>
<td>1-butyl-3-methylimidazolium hexafluorophosphate ([bmim]PF₆) and 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF₄) ionic liquids</td>
<td>33</td>
</tr>
<tr>
<td>3.</td>
<td>Small pore size zeolite E₄a</td>
<td>34</td>
</tr>
<tr>
<td>4.</td>
<td>PtCl₃/AgOTf, K₂PtCl₄/AgOTf and K₂PtCl₄/AgOAc.</td>
<td>35</td>
</tr>
<tr>
<td>5.</td>
<td>Bismuth (III) nitrate pent hydrate Bi(NO₃)₃.5H₂O</td>
<td>36</td>
</tr>
<tr>
<td>6.</td>
<td>Titanium (IV) chloride (TiCl₄)</td>
<td>37</td>
</tr>
<tr>
<td>7.</td>
<td>Wells-Dawson heteropolyacid (H₆P₂W₁₈O₆₂.2₄H₂O)</td>
<td>38</td>
</tr>
<tr>
<td>8.</td>
<td>Indium (III) chloride (InCl₃)</td>
<td>39</td>
</tr>
<tr>
<td>9.</td>
<td>HClO₄·SiO₂</td>
<td>40</td>
</tr>
<tr>
<td>10.</td>
<td>Heteropolyacids (HPAs) H₁₄[NaP₅W₃₀O₁₁₀], H₄[PMo₁₁VO₄₀], H₅[PMo₁₀V₂O₄₀] and H₆[P₃W₁₈O₆₂].</td>
<td>41</td>
</tr>
<tr>
<td>11.</td>
<td>Nano-crystalline sulfated-zirconia solid acid</td>
<td>42</td>
</tr>
<tr>
<td>12.</td>
<td>K.Al(SO₄)₂.12H₂O (alum)</td>
<td>43</td>
</tr>
<tr>
<td>13.</td>
<td>SnCl₂.2H₂O (10 mol %)</td>
<td>44</td>
</tr>
<tr>
<td>14.</td>
<td>Zirconium (IV) chloride (ZrCl₄)</td>
<td>45</td>
</tr>
<tr>
<td>15.</td>
<td>W/ZrO₂</td>
<td>46</td>
</tr>
<tr>
<td>16.</td>
<td>Gallium triiodide (Gal₃)</td>
<td>47</td>
</tr>
<tr>
<td>17.</td>
<td>Iodine (I₂)</td>
<td>48, 52</td>
</tr>
<tr>
<td>18.</td>
<td>Boron trifluoride dehydrate (BF₃.H₂O)</td>
<td>49</td>
</tr>
</tbody>
</table>
Phosphotungstic acid Catalyst

<table>
<thead>
<tr>
<th>No.</th>
<th>Substance</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>19.</td>
<td>NaH₂SO₄·H₂O (10 mol %)</td>
<td>50</td>
</tr>
<tr>
<td>20.</td>
<td>Samarium (III) nitrate hexahydrate [Sm(NO₃)₃·6H₂O]</td>
<td>51</td>
</tr>
<tr>
<td>21.</td>
<td>1-Butyl-3-methylimidazolium chloroauminate, [bmim]Cl·2AlCl₃ ionic liquid</td>
<td>53</td>
</tr>
<tr>
<td>22.</td>
<td>chlorosulfonic acid (ClSO₃COOH)</td>
<td>54</td>
</tr>
<tr>
<td>23.</td>
<td>Oxalic acid</td>
<td>55</td>
</tr>
<tr>
<td>24.</td>
<td>H₃PMO₁₂O₄₀ and H₃PW₁₂O₄₀ Keggin heteropolyacids</td>
<td>56</td>
</tr>
<tr>
<td>25.</td>
<td>Dipyridine copper chloride (CuPy₂Cl₂)</td>
<td>57</td>
</tr>
<tr>
<td>26.</td>
<td>Stannic (IV) chloride (SnCl₄·5H₂O)</td>
<td>58</td>
</tr>
<tr>
<td>27.</td>
<td>Vanadium (III) chloride (VCl₃)</td>
<td>59</td>
</tr>
<tr>
<td>28.</td>
<td>N, N, N-trimethyl-N-propanesulfonic acid ammonium hydrogen sulfate [TMPSA][HSO₄]</td>
<td>60</td>
</tr>
<tr>
<td>29.</td>
<td>Alumina supported MoO₃</td>
<td>61</td>
</tr>
<tr>
<td>30.</td>
<td>Silica sulfuric acid</td>
<td>62</td>
</tr>
<tr>
<td>31.</td>
<td>Zirconyl chloride octahydrate</td>
<td>63</td>
</tr>
<tr>
<td>32.</td>
<td>Non-chloroauminate acidic ionic liquids</td>
<td>64</td>
</tr>
<tr>
<td>33.</td>
<td>NaH₂SO₄·SiO₂ and silica chloride</td>
<td>65</td>
</tr>
</tbody>
</table>

Phosphotungstic acid (PTA) is a heteropolyacid with the chemical formula H₃PW₁₂O₄₀. It is normally present as a hydrate. EPTA is the name for ethanolic phosphotungstic acid, its alcohol solution used in biology. It has the appearance of small, colorless-greyish or slightly yellow-green crystals, with melting point 89 °C (24 H₂O hydrate). It is odourless and soluble in water (200 g/100 ml). It is non toxic especially, but a mild acidic
irritant. The compound is known by a variety of different names and acronyms including:

- Phosphotungstic acid (PTA), (PWA)
- Tungstophosphoric acid (TPA)
- 12-phosphotungstic acid
- 12-tungstophosphoric acid
- dodecatungstophosphoric acid

In the above the "12" or "dodeca" reflects the fact that the anion contains 12 tungsten atoms. Some early workers who did not know the structure, e.g. Wu \(^6\) called it phospho-24-tungstic acid as they formulated it as \(3\text{H}_2\text{O}.\text{P}_2\text{O}_5.24\text{WO}_3.59\text{H}_2\text{O}, \left(\text{P}_2\text{W}_{24}\text{O}_{80}\text{H}_6\right).29\text{H}_2\text{O}\), which correctly identifies the atomic ratios of P, W and O. This formula was still quoted in papers as late as 1970.\(^6\)

Heteropolyacids are green catalysts that function in a variety of reaction fields and are efficient bifunctional catalysts, safety, quantity of waste and separability.\(^6\) Among the Keggin-type heteropolyacids are more active and possess stronger Bronsted acidity than the usual mineral acids such as \(\text{H}_2\text{SO}_4\), \(\text{HCl}\), \(\text{HNO}_3\)\(^6\) and conventional solid acids such as \(\text{SiO}_2\)-\(\text{Al}_2\text{O}_3\), \(\text{H}_3\text{PO}_4\text{-SiO}_2\), zeolites including \(\text{HX}, \text{HY}, \text{H-ZSM-5}, \text{Amberlyst-15}\) and \(\text{Nafion-H}\).\(^7\) Among heteropoly acids, phosphotungstic acids are the most widely used catalysts\(^7\) owing to their high acid strength, thermal stabilities and low reducibilities. Some of the applications of phosphotungstic acid in organic synthesis are as follows:
Mallik et al., have synthesized a series of eco-friendly solid acid catalyst by supporting phosphotungstic acid onto hydrous zirconia by an incipient wetness impregnation method in order to contribute towards clean technology. Their catalytic activities were evaluated for oxybromination reaction of phenol by varying different reaction parameters. The electrophilic substitution of bromine generated in situ from KBr as a bromine source and hydrogen peroxide as an oxidant. The 15 wt.% of phosphotungstic acid supported on hydrous zirconia shows highest surface area acid sites and gives about 93% conversion with 81% \textit{para}-selectivity.\textsuperscript{73}

\[
\begin{align*}
\text{Phenol} & \quad \text{ZPTA, AcOH} \\
& \quad \text{KBr, 30\% H}_2\text{O}_2 \\
\rightarrow & \quad \text{Parabromophenol} + \text{ orthobromophenol}
\end{align*}
\]

Devassy \textit{et al.}, have carried out the alkylation of resorcinol with \textit{tert}-butanol using zirconia supported phosphotungstic acid (PTA) as catalyst in liquid phase conditions. Among the different PTA loaded catalysts, the 15\% PTA/ZrO\textsubscript{2} calcined at 750 °C was found to be the most active and yielding \textit{4-tert}-butyl resorcinol and 4,6-\textit{di-tert}-butyl resorcinol as major products under optimized reaction conditions.\textsuperscript{74}
Rajagopal et al., have carried out the regioselective monobromination of aromatic substrates with $N$-bromosuccinimide in excellent isolated yields (84-98%) using phosphotungstic acid supported on zirconia as a novel heterogeneous catalyst. Remarkably, the new catalyst system described brought about the side-chain bromination of aromatics to afford bromomethyl arenes in excellent yields (86-98%) without the need for a radical initiator. Recovery and recyclability of the catalyst have been well established.\textsuperscript{75}

\[
\text{Ar-} \text{H} + \text{Br} \rightarrow \text{Ar-} \text{Br}
\]

The synthesis of 3,4-dihydropyrimidin-2(1H)-ones was carried out by one pot condensation of aryl aldehydes, urea derivatives and $\beta$-diketones using sulfated zirconia or phosphotungstic acid as catalysts.\textsuperscript{76}

\[
\text{Sulfated Zirconia / PWA}
\]

Where $X = O/S$

Phosphotungstic acid was also used as an environmentally benign solid acid catalyst for synthesis of aryl-1,4,dibenzo[$\alpha$,$\beta$]xanthenes by condensation of $\beta$-napthol and arylaldehydes. It was observed that 100 mg of phosphotungstic acid is quite efficient for the condensation of $\beta$-napthol and aryl aldehydes to produce the corresponding xanthenes under solvent free condition and microwave irradiation.\textsuperscript{76}
Phosphotungstic acid (PTA) was found to be a promising solid acid catalyst as an alternative to the conventional stoichiometric reagents for the rearrangement of benzyl phenyl ether giving 2-benzyl phenol as a major product and 4-benzyl phenol and dibenzylated phenols as side products.\(^7\) Catalyst was recovered from the reaction mixture and reused again without loss of activity.

Tungstophosphoric acid catalyzed rapid and good yielding reactions of \(\alpha,\beta\)-unsaturated aldehydes with arenethiols to give the corresponding 4-thioaryl-1,2,3,4-tetrahydro-1-benzothiopyrans (thiochromans) under solvent-free and room temperature conditions.\(^8\)

Sivaprasad et al., have developed a simple and efficient method for the synthesis of quinaldines and lepidines by one-pot reaction of anilines with crotonaldehyde or methyl vinyl ketone using phosphotungstic acid, a Keggins-type heteropolyacid, under both thermal and microwave irradiation conditions.\(^9\)
Rocha et al., have developed direct transformations of \( \alpha \)-pinene oxide to either campholenic aldehyde, trans-carveol, trans-sobrerol or pinol using phosphotungstic acid as catalyst. The use of very low catalyst loading (0.005-1 mol\%) and the possibility of catalyst recovery and recycling without neutralization are significant advantages of this simple, environmentally benign and low cost method.\(^{80}\)

Wang et al., have developed mild nucleophilic substitution reactions of benzhydrylic, benzylic, allylic and simple aliphatic alcohols with sulfonamides, benzamide and 4-nitroaniline in the presence of 12-phosphotungstic acid as an efficient, eco-friendly, cheap and air and moisture-tolerant catalyst for the construction of C-N bonds. The amine derivatives were obtained in good yields (up to 98\%). The reusable nature of 12-phosphotungstic acid makes this protocol more attractive.\(^{81}\)
Giri et al., have synthesized benzimidazoles in very good yield from \(o\)-phenylenediamine and aromatic aldehydes in the presence of monoammonium salt of 12-tungstophosphoric acid \([(NH_4)_2PW_{12}O_{40}]\), an efficient heterogeneous catalyst. This catalyst has the advantages of simple workup procedure, water insolubility and good activity with high yield for the synthesis of benzimidazole derivatives.\(^8^2\)

\[
\begin{align*}
\text{R} &= \text{-Ph; } \text{R}_1 = \text{-H, - CH}_3, \text{CF}_3 \\
\text{R}_2 &= \text{-H, - CH}_3; \text{R}_3 = \text{-H, NO}_2
\end{align*}
\]

Suresh Babu et al., have developed a regioselective cleavage of epoxides with aromatic amines in the presence of tungstophosphoric acid as a catalyst. The reaction proceeded rapidly and afforded the corresponding \(\beta\)-amino alcohols in moderate to high yields.\(^9^3\)
The application of clean catalytic technologies, especially those with the use of heterogeneous catalysts, is becoming increasingly important for the development of environmentally benign chemical processes. The drive towards clean technology has encouraged the application of solvent-free conditions. A move away from the use of solvents in organic synthesis has led in some cases to improved results and more benign synthetic procedures. Our approach reduces the use of organic solvents, which are potentially toxic, hazardous and uses simple and mild conditions with inherently lower costs.

In the present study, our ongoing work devoted towards the development of environment friendly, rapid synthesis of heterocyclic molecules of biological interest, we explored the possibility of synthesizing coumarin derivatives (Scheme-1) from Pechman condensation, which involves reaction between phenols and β-ketoesters, in the presence phosphotungstic acid as a catalyst under solvent-free conditions to facilitate the rapid synthesis of drugs from commercially available building blocks. All the reactions involved are highly efficient to give the desired compounds in high yield and high purity. And also, this adopted procedure is simple, rapid and eco-friendly due to easy experimental procedures. The versatility of this methodology can be extended to develop a stream-lined approach to other drugs like heterocycles in solvent-free conditions. All these are reported compounds but the catalyst and methodology used is newer.
Scheme-1.

In summary, we have developed an efficient, facile and environmentally acceptable synthetic methodology for the synthesis of coumarin derivatives using phosphotungstic acid as a catalyst under solvent-less condition. The attractive features of this procedure are the mild reaction conditions, high conversions, ease of separation and recyclability of the catalyst, inexpensive and environmentally friendly catalyst, excellent yields, all of which make it a useful and attractive strategy for the preparation of various coumarin derivatives simply by changing different substrates. The versatility of this methodology is suitable for library synthesis in drug discovery efforts.

The melting points of the products were determined by open capillaries on a Buchi apparatus and are uncorrected. The IR spectra were recorded on a Nicolet Impact-410 FT-IR Spectrophotometer using KBr pellets. The $^1$H and $^{13}$C NMR spectras were recorded on a 300MHz Bruker-Avanace NMR instrument in CDCl$_3$ and the chemical shifts were expressed in parts per million (ppm) with tetramethylsilane (TMS) as an internal standard. Mass spectrometer with ionization energy maintained at 70eV using on Shimadzu mass spectrometer. The elemental analysis was carried
Phosphotungstic acid Catalyst

out by using Heraus CHN rapid analyzer. All the compounds gave C, H and N analysis within ± 0.4% of the theoretical values. The homogeneity of the compounds was described by TLC on aluminum silica gel 60 F\textsubscript{254} (Merck) detected by U.V light (254 nm) and iodine vapours.

The mixture of phenols (1mmol), the β-keto ester (1mmol) and phosphotungstic acid (2 mol%) was refluxed at 90 °C with stirring for the indicated time (Table-4), and reaction monitored by TLC. After completion of reaction, the mixture got solidified within an hour. The resulting solidified mixture was diluted with ethyl acetate (1 ml) and the catalyst was separated. The filtrate obtained was washed with water (two times) and the solvent evaporated under reduced pressure yielded the crude product, which was purified by recrystallization. All synthesized coumarin derivatives were characterized using analytical techniques like IR, \textsuperscript{1}H NMR, \textsuperscript{13}C NMR and mass spectroscopy. Also the melting points were measured for all synthesized coumarin derivatives and were compared with the corresponding reported melting points.

2.8.1 Optimization of temperature

First, the optimization of the reaction, the effect of solvent, temperature and catalyst were carried by selecting phenol and ethyl acetoacetate as a model. After stirring for 2-3 hrs, reaction did not proceed...
as monitored by TLC at room temperature in solvent-free conditions. Subsequently, the mixture was heated to reflux at different temperatures ranging from 60 to 120 °C, with an increment of 10 °C each time. The yield of product 1a was increased and the reaction was raised from 60 °C to 90 °C (Table-1, entries 1-4). However, no significant increase in the yield of product (1a) was observed as the reaction temperature was raised from 100 °C to 120 °C (Table-1, entries 5-7). Therefore, 90 °C was chosen as the reaction temperature for all further reactions.

**Table-1**

Temperature optimization for the synthesis of (1a) under solvent free condition using PTA as catalyst.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Temperature (°C)</th>
<th>aTime (min)</th>
<th>bYield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>60</td>
<td>90</td>
<td>82</td>
</tr>
<tr>
<td>2</td>
<td>70</td>
<td>75</td>
<td>86</td>
</tr>
<tr>
<td>3</td>
<td>80</td>
<td>50</td>
<td>86</td>
</tr>
<tr>
<td>4</td>
<td>90</td>
<td>30</td>
<td>95</td>
</tr>
<tr>
<td>5</td>
<td>100</td>
<td>30</td>
<td>88</td>
</tr>
<tr>
<td>6</td>
<td>110</td>
<td>20</td>
<td>84</td>
</tr>
<tr>
<td>7</td>
<td>120</td>
<td>20</td>
<td>84</td>
</tr>
</tbody>
</table>

a - Reaction time is monitored by TLC at time interval of 10 min.
b - Reaction condition: Phenol (1mmol), ethylacetocacetate (1mmol) and catalyst 2 mol% at different temperatures under solvent free conditions.
2.8.2 Optimization of catalyst concentration

To evaluate the effect of catalyst concentration, Pechmann condensation of phenol and ethyl acetoacetate in equimolar ratio (1:1) was carried out in presence of different amounts of catalyst (1, 2, 5, 10 mol %) at 90 °C under solvent free conditions and the isolated yields of the product are shown in Table-2. From this we concluded that 2 mol% of PTA to be optimum amount of the catalyst for this reaction. Use of higher amounts of catalyst (5 & 10 mol%) neither improves the yield nor reaction time further.

Table-2

Effect of catalyst concentration for the synthesis of 4-methyl coumarin\(^a\) (a)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst concentration (% mol)</th>
<th>Time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>60</td>
<td>88</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>30</td>
<td>95</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>30</td>
<td>92</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>30</td>
<td>95</td>
</tr>
</tbody>
</table>

\( ^a\) Reaction condition: Phenol (1mmol) and ethylacetoacetate (1mmol) at 90 °C by varying the amount of catalyst under solvent-free conditions.

2.8.3 Optimization of solvents

After optimizing the temperature and amount of catalyst, the reaction is carried out in solvents like toluene, THF, acetonitrile 1,4-dioxane and also without solvent. It is observed that, reaction in solvents takes more time and
also the yield are low compared to the solvent-free condition (Table-3). Considering the importance of green chemistry, the solvent-free reaction conditions are the advantageous aspect of the present method, since it avoids the use of environmental hazardous and toxic solvents. The efficiency of PTA catalyst was demonstrated by synthesizing the range of coumarins using series of monohydric and polyhydric phenols and ethyl acetoacetate (Table-4). The catalyst was found to be equally effective for phenols bearing either electron-donating or electron-withdrawing substituents.

Table-3

PTA catalyzed one-pot synthesis of 4-methyl coumarin\(^a\) (a) with/without solvent

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Catalyst (mol %)</th>
<th>Time (min)</th>
<th>(^b)Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Toluene</td>
<td>2</td>
<td>120</td>
<td>76</td>
</tr>
<tr>
<td>2</td>
<td>THF</td>
<td>2</td>
<td>120</td>
<td>87</td>
</tr>
<tr>
<td>3</td>
<td>Dioxane</td>
<td>2</td>
<td>90</td>
<td>69</td>
</tr>
<tr>
<td>4</td>
<td>Acetonitrile</td>
<td>2</td>
<td>135</td>
<td>77</td>
</tr>
<tr>
<td>5</td>
<td>None</td>
<td>2</td>
<td>45</td>
<td>95</td>
</tr>
</tbody>
</table>

\(\text{a- Reaction condition: Phenol (1mmol) and ethylacetoacetate (1mmol)}\)

solvent (5ml) or no solvent at 90 °C.

\(\text{b- Isolated yields.}\)
Table 4

Synthesis of coumarins using Phosphotungstic acid as a catalyst

<table>
<thead>
<tr>
<th>Entry</th>
<th>Phenol</th>
<th>Product</th>
<th>Reaction Time (in mins)</th>
<th>Yield (%)</th>
<th>Melting point (°C)</th>
<th>Literature Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td></td>
<td><img src="image" alt="Product" /></td>
<td>45</td>
<td>95</td>
<td>84-85</td>
<td>[84]</td>
</tr>
<tr>
<td>1b</td>
<td><img src="image" alt="Phenol" /></td>
<td><img src="image" alt="Product" /></td>
<td>30</td>
<td>90</td>
<td>131-132</td>
<td>131-133 [84]</td>
</tr>
<tr>
<td>1c</td>
<td><img src="image" alt="Phenol" /></td>
<td><img src="image" alt="Product" /></td>
<td>30</td>
<td>94</td>
<td>157-159</td>
<td>156-158 [84]</td>
</tr>
<tr>
<td>1d</td>
<td><img src="image" alt="Phenol" /></td>
<td><img src="image" alt="Product" /></td>
<td>30</td>
<td>94</td>
<td>186-187</td>
<td>185-186 [84]</td>
</tr>
<tr>
<td>1e</td>
<td><img src="image" alt="Phenol" /></td>
<td><img src="image" alt="Product" /></td>
<td>45</td>
<td>91</td>
<td>164-165</td>
<td>166-167 [85]</td>
</tr>
<tr>
<td>1f</td>
<td><img src="image" alt="Phenol" /></td>
<td><img src="image" alt="Product" /></td>
<td>90</td>
<td>60</td>
<td>156-158</td>
<td>154-155 [85]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>1g</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td><img src="sa.png" alt="Structure" /></td>
<td><img src="sa.png" alt="Structure" /></td>
<td>30</td>
<td>88</td>
<td>283-284</td>
<td>284-285</td>
<td></td>
</tr>
<tr>
<td><img src="sa.png" alt="Structure" /></td>
<td><img src="sa.png" alt="Structure" /></td>
<td>30</td>
<td>84</td>
<td>243-245</td>
<td>244-245</td>
<td></td>
</tr>
<tr>
<td><img src="sa.png" alt="Structure" /></td>
<td><img src="sa.png" alt="Structure" /></td>
<td>30</td>
<td>92</td>
<td>255-256</td>
<td>258-259</td>
<td></td>
</tr>
<tr>
<td><img src="sa.png" alt="Structure" /></td>
<td><img src="sa.png" alt="Structure" /></td>
<td>45</td>
<td>85</td>
<td>225-226</td>
<td>227-228</td>
<td></td>
</tr>
<tr>
<td><img src="sa.png" alt="Structure" /></td>
<td><img src="sa.png" alt="Structure" /></td>
<td>30</td>
<td>89</td>
<td>217-218</td>
<td>268-269</td>
<td></td>
</tr>
<tr>
<td><img src="sa.png" alt="Structure" /></td>
<td><img src="sa.png" alt="Structure" /></td>
<td>45</td>
<td>82</td>
<td>185-186</td>
<td>184-186</td>
<td></td>
</tr>
</tbody>
</table>

a- Reaction condition: phenols (1mmol) and β-keto ester (1mmol)  
phosphotungstic acid (2 mol %) at 90 °C under solvent free conditions.  
b- All products were characterized by comparison of their mp, IR, NMR,  
MS and elemental analysis with those of authentic samples.  
c- For every 15 mins monitored by TLC.  
d- Isolated yields.  
e- Melting points are uncorrected.
2.8.4 Comparison with other catalysts

Furthermore, in order to show the excellent catalytic activity of the catalyst, we carried out the synthesis 7-hydroxy-4-methyl coumarin (entry 1d in Table-4) catalyzed by other several catalysts under the same reaction conditions (Table-4). It shows that the yield of the desired product in the presence of PTA is higher than that in the presence of other catalysts. From these results we concluded that, the present method was superior to reported methods regarding yields and reaction time. Also, the work-up of present method was easy and it includes pouring of reaction mixture onto ice-water to precipitate the solid, which could be collected by filtration to give the corresponding coumarin products with better yield.

Table-4

Comparison of catalytic activity of PTA with several catalysts for synthesis of 7-hydroxy-4-methyl coumarin\(^4\) (1d)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Reaction time (min)</th>
<th>(^b)Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>SnCl(_2) .2H(_2)O</td>
<td>150</td>
<td>55</td>
</tr>
<tr>
<td>2</td>
<td>KA(_1)(SO(_4))(_2) . 12H(_2)O</td>
<td>120</td>
<td>86</td>
</tr>
<tr>
<td>3</td>
<td>p-Toluene sulfonic acid</td>
<td>90</td>
<td>78</td>
</tr>
<tr>
<td>4</td>
<td>Stannic(IV) chloride</td>
<td>45</td>
<td>86</td>
</tr>
<tr>
<td>5</td>
<td>Iodine</td>
<td>240</td>
<td>75</td>
</tr>
<tr>
<td>6</td>
<td>Phosphotungstic acid</td>
<td>30</td>
<td>94</td>
</tr>
<tr>
<td>7</td>
<td>vanadium(III)chloride (VCl(_3))</td>
<td>45</td>
<td>90</td>
</tr>
<tr>
<td>8</td>
<td>TiCl(_4)</td>
<td>50</td>
<td>90</td>
</tr>
</tbody>
</table>

\(^a\) Reaction condition: Phenol (1mmol), \(\beta\)-keto ester (1mmol) and corresponding catalysts (2% mmol) at 90 °C under solvent free conditions.

\(^b\) Isolated yields.
2.8.5 Regeneration of catalyst

To examine the reusability, the catalyst recovered by filtration from the reaction mixture phenol and ethylacetacetoacetate after dilution with ethyl acetate was reused as such for subsequent experiments (up to four cycles) under similar reaction conditions. The observed fact that yields of the product remained comparable in these experiments (Table-5), established the recyclability and reusability of the catalyst without significant loss of activity.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (mol %)</th>
<th>Reaction time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>----</td>
<td>180</td>
<td>--</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>45</td>
<td>95c</td>
</tr>
<tr>
<td>3</td>
<td>Cycle 1</td>
<td>45</td>
<td>95</td>
</tr>
<tr>
<td>4</td>
<td>Cycle 2</td>
<td>45</td>
<td>94</td>
</tr>
<tr>
<td>5</td>
<td>Cycle 3</td>
<td>45</td>
<td>94</td>
</tr>
</tbody>
</table>

Cycle 1, 2, 3 indicate the reusability of the catalyst regenerated from experiment.

a- Isolated yields.
b- Blank experiment without using catalyst.
c- Reaction conditions as in Table-4.

The structures of synthesized coumarin (1a-11) were supported by IR, $^1$H NMR, $^{13}$C NMR and Mass spectrometry.
The IR spectrum of all the compounds (Ia-Ii) had the characteristic C=O stretching band at 1693-1715 cm\(^{-1}\) in coumarin derivatives. The C=C stretching band at 1420-1493 cm\(^{-1}\) was observed in all the compounds respectively. The -CH stretching band is observed at 2973-2920 cm\(^{-1}\), respectively.

The \(^1\)H NMR spectra of all the compounds (Ia-Ii) exhibited structure revealing proton signals at \(\delta\) 7.22-7.7 ppm (multiplet, aromatic protons), \(\delta\) 6.28-6.53 ppm (C\(_3\)-H) protons and \(\delta\) 1.78-2.5 ppm (C\(_4\) methyl protons), respectively.

The \(^{13}\)C NMR spectra of all the compounds (Ia-Ii) showed sharp singlet signals at \(\delta\) 156-165 ppm for carbonyl carbon, at \(\delta\) 105-152 ppm for aromatic carbon atoms, at \(\delta\) 16-36 ppm saturated carbon atoms with CDCl\(_3\) solvent signals. The mass spectra of the same compounds showed peak corresponding to their molecular ion.

The IR, \(^1\)H NMR, \(^{13}\)C NMR and Mass spectra of some compounds are enclosed as Spectrum No. 1 - 8.

4-Methyl coumarin (Ia)

Yield 95%; Colorless crystalline solid; m.p. 84-85 °C; IR (KBr, \(\nu\) cm\(^{-1}\)): 2926 (-CH stretching), 1705 (-C=O stretching), 1489 (-C=C- stretching; \(^1\)H NMR (300MHz, CDCl\(_3\), \(\delta\) ppm): 1.78 (s, 3H, -CH\(_3\)), 6.31 (s, 1H, -C=CH, C\(_3\)-H), 7.19-7.54 (m, 4H, ArH); \(^{13}\)C NMR (75 MHz, CDCl\(_3\), \(\delta\) ppm): 17.65, 106.34, 118.94, 122.72, 124.10, 126.73, 129.4, 146.64, 154.43, 160.12. MS: \(m/z\) 160.00.

Anal. calcd. for C\(_{10}\)H\(_8\)O\(_2\): C, 74.99; H, 5.03; Found: C, 75.04, H, 5.01%.
4,7-dimethyl coumarin (1b)

Yield 90%; Colorless crystalline solid; m.p. 130-132 °C; IR (KBr, μ cm⁻¹): 2922 (-CH stretching), 1716 (-C=O stretching), 1571 (-C=C- stretching; ¹H NMR (300MHz, CDCl₃, δ ppm): 2.44 (s, 6H, -CH₃), 6.28 (s, 1H, -C=CH, C₃-H), 7.22-7.39 (m, 3H, ArH); ¹³C NMR (75 MHz, CDCl₃, δ ppm): 19.00, 21.34, 117.16, 120.05, 124.81, 133.06, 134.20, 152.02, 152.66, 161.39. MS: m/z 174.00. Anal. calcd. for C₁₁H₁₀O₂: C, 75.84; H, 5.79; Found: C, 75.87, H, 5.74%.

4-methyl-7-methoxy coumarin (1c)

Yield 94%; Colorless crystalline solid; m.p. 157-159 °C; IR (KBr, μ cm⁻¹): 2933 (-CH stretching), 1712 (-C=O stretching), 1565 (-C=C- stretching; ¹H NMR (300MHz, CDCl₃, δ ppm): 1.76 (s, 3H, -CH₃), 3.26 (s, 3H, -OCH₃), 6.34 (s, 1H, -C=CH, C₃-H), 7.22-7.39 (m, 3H, ArH); ¹³C NMR (75 MHz, CDCl₃, δ ppm): 20.03, 48.96, 105.81, 109.23, 112.5, 118.92, 123.07, 129.05, 150.07, 154.34, 158.65. MS: m/z 190.00. Anal. calcd. for C₁₁H₁₀O₃: C, 69.40; H, 5.25; Found: C, 69.43, H, 5.23%.

7-hydroxy-4-methyl coumarin (1d)

Yield 94%; Colorless crystalline solid; m.p. 184-186 °C; IR (KBr, μ cm⁻¹): 3432 (-OH stretching), 3432 (OH stretching), 2924 (-CH stretching), 1708 (-C=O stretching),
1569 (C=C-stretching); $^1$H NMR (300MHz, CDCl$_3$, $\delta$ ppm): 2.35 (s, 3H, -CH$_3$), 4.02 (s, 1H, -OH), 6.14 (s, 1H, -C=CH, C$_3$-H), 6.86-7.27 (m, 3H, ArH); $^{13}$C NMR (75 MHz, CDCl$_3$, $\delta$ ppm): 19.74, 105.32, 107.54, 109.65, 114.36, 123.33, 124.01, 140.21,141.65, 166.32. MS: m/z 176.00. Anal. calcd. for C$_{10}$H$_8$O$_3$: C, 68.12; H, 4.58; Found: C, 68.16, H, 4.59 %.

6-hydroxy-4-methyl coumarin (Ie)

Yield 91%; Colorless crystalline solid; m.p. 164 - 165 °C; IR (KBr, $\nu$ cm$^{-1}$): 3454 (-OH stretching), 2937 (-CH stretching), 1716 (-C=O stretching), 1545 (-C=C-stretching); $^1$H NMR (300MHz, CDCl$_3$, $\delta$ ppm): 1.87 (s, 3H, -CH$_3$), 4.54 (s, 1H, -OH), 6.28 (s, 1H, -C=CH, C$_3$-H), 7.16-7.36 (m, 3H, ArH); $^{13}$C NMR (75 MHz, CDCl$_3$, $\delta$ ppm): 21.15, 107.03, 113.04, 116.06, 120.03, 127.12, 145.43,149.08, 154.12,163.32. MS: m/z 176.00. Anal. calcd. for C$_{10}$H$_8$O$_3$: C, 68.12; H, 4.58; Found: C, 68.14, H, 4.57 %.

7,8 benzo-4-methyl coumarin (If)

Yield 60%; Colorless crystalline solid; m.p. 156-158 °C; IR (KBr, $\nu$ cm$^{-1}$): 2987 (-CH stretching), 1724 (-C=O stretching), 1565 (-C=C-stretching); $^1$H NMR (300MHz, CDCl$_3$, $\delta$ ppm): 1.96 (s, 3H, -CH$_3$), 6.34 (s, 1H, C=CH, C$_3$-H), 7.10-7.66 (m, 6H, ArH); $^{13}$C NMR (75 MHz, CDCl$_3$, $\delta$ ppm): 20.87, 108.12, 118.95, 121.08, 122.00, 123.13, 126.04, 130.05, 147.87, 157.43, 160.10. MS: m/z 210.00. Anal. calcd. for C$_{10}$H$_{10}$O$_2$: C, 79.97; H, 4.76; Found: C, 80.01, H, 4.75 %.
5,7-Dihydroxy 4-methyl coumarin (lg)

Yield 88%; Colorless crystalline solid; m.p. 283-284 °C; IR (KBr, ν cm⁻¹): 3513 (-OH stretching), 3469 (-OH stretching), 2945 (-CH stretching), 1709 (-C=O stretching), 1534 (-C=C- stretching);

¹H NMR (300MHz, CDCl₃, δ ppm): 2.04 (s, 3H, -CH₃), 4.65 (s, 1H, -OH), 6.16 (s, 1H, C=CH, C₃-H ), 6.98-7.12 (m, 2H, ArH), 8.45 (s, 1H, -OH);

¹³C NMR (75 MHz, CDCl₃, δ ppm): 17.34, 97.07, 101.15, 106.22, 109.54, 147.43, 151.34, 155.02, 157.04, 165.56. MS: m/z 192.00. Anal. calcd. for C₁₀H₈O₄: C, 62.50; H, 4.20; Found: C, 62.53, H, 4.23 %.

6,7-Dihydroxy 4-methyl coumarin (lh)

Yield 84%; Colorless crystalline solid; m.p. 243-245 °C; IR (KBr, ν cm⁻¹): 3534 (-OH stretching), 3479 (-OH stretching), 2917 (-CH stretching), 1716 (-C=O stretching), 1515 (-C=C- stretching); ¹H NMR (300MHz, CDCl₃, δ ppm): 1.67 (s, 3H, -CH₃), 5.45 (s, 1H, -OH), 6.32 (s, 1H, -C=CH, C₃-H ), 7.05-7.26 (m, 2H, ArH), 9.04 (s, 1H, -OH); ¹³C NMR (75 MHz, CDCl₃, δ ppm): 19.24, 96.23, 104.05, 107.04, 113.94, 145.06, 150.88, 155.05, 158.09, 164.06. MS: m/z 192.00. Anal. calcd. for C₁₀H₈O₄: C, 62.50; H, 4.20; Found: C, 62.51, H, 4.19 %.

5-hydroxy- 4,7-dimethyl coumarin (li)

Yield 92%; Colorless crystalline solid; m.p. 255-256 °C; IR (KBr, ν cm⁻¹): 3514(-OH stretching), 2943 (-CH stretching), 1703 (-C=O stretching),
1507 (-C=C- stretching); $^1$H NMR (300MHz, CDCl$_3$, δ ppm): 1.87 (s, 3H, -CH$_3$), 2.25 (s, 3H, -CH$_3$), 3.98 (s, 1H, -OH), 6.03 (s, 1H, C=CH, C$_3$-H), 7.12-7.23 (m, 2H, ArH); $^{13}$C NMR (75 MHz, CDCl$_3$, δ ppm): 17.89, 22.32, 106.31, 110.09, 111.90, 122.12, 136.73, 149.00, 152.02, 155.12, 160.09. MS: m/z 190.00. Anal. calcd. for C$_{10}$H$_8$O$_3$: C, 69.46; H, 5.30; Found: C, 69.50, H, 5.32 %.

4,6,7-trimethyl coumarin (1j)

Yield 85%; Colorless crystalline solid; m.p. 225-226 °C; IR (KBr, υ cm$^{-1}$): 2932 (-CH stretching), 1717 (-C=O stretching), 1556 (-C=C- stretching); $^1$H NMR (300MHz, CDCl$_3$, δ ppm): 1.69 (s, 3H, -CH$_3$), 2.39 (s, 6H, -CH$_3$), 6.34 (s, 1H, C=CH, C$_3$-H), 6.89-7.33 (m, 2H, ArH); $^{13}$C NMR (75 MHz, CDCl$_3$, δ ppm): 15.78, 21.33, 108.03, 120.22, 122.17, 126.59, 133.32, 139.32, 145.32, 157.13, 161.02. MS: m/z 188.00. Anal. calcd. for C$_{12}$H$_{13}$O$_2$: C, 76.57; H, 6.43; Found: C, 76.60, H, 6.45 %.

7-hydroxy 4,8-dimethyl coumarin (1k)

Yield 89%; Colorless crystalline solid; m.p. 217-218 °C; IR (KBr, υ cm$^{-1}$): 3512 (-OH stretching), 2947 (-CH stretching), 1709 (-C=O stretching), 1531 (-C=C- stretching); $^1$H NMR (300MHz, CDCl$_3$, δ ppm): 1.88 (s, 3H, -CH$_3$), 2.07 (s, 3H, -CH$_3$), 5.17 (s, 1H, -OH), 6.17 (s, 1H, C=CH, C$_3$-H), 6.92-7.12 (m, 2H, ArH); $^{13}$C NMR (75 MHz, CDCl$_3$, δ ppm): 11.06, 17.04, 101.05, 109.87, 116.32, 123.31, 125.05, 154.92, 155.92, 163.23. MS: m/z 190.00. Anal. calcd. for C$_{11}$H$_{10}$O$_3$: C, 69.46; H, 5.30; Found: C, 69.49, H, 5.32 %.
8-Nitro 4-methyl coumarin (II)

Yield 82%; Colorless crystalline solid; m.p. 185-186 °C; IR (KBr, v cm⁻¹): 2915 (-CH stretching), 1711 (-C=O stretching), 1506 (-C=C- stretching);

¹H NMR (300MHz, CDCl₃, δ ppm): 1.72 (s, 3H, -CH₃), 6.23 (s, 1H, -C=CH, C₃-H ), 7.42-8.04 (m, 3H, ArH); ¹³C NMR (75 MHz, CDCl₃, δ ppm): 17.65, 107.03, 120.88, 124.33 126.00, 124.33, 126.00, 132.76, 142.32, 145.04, 154.09, 162.04. MS: m/z 190.00. Anal. calcd. for C₁₀H₇NO₄: C, 58.54; H, 3.44; N, 6.83; Found: C, 69.49, H, 5.32 %.
Spectrum 1: IR Spectrum of compound (1b)

Spectrum 2: ^1^H NMR (300MHz) Spectrum of compound (1b) in CDCl$_3$. 

Phosphotungstic acid Catalyst
Spectrum 3: $^{13}$C NMR (75MHz) Spectrum of compound (1b)

Spectrum 4: Mass Spectra of compound (1b)
Spectrum 5: IR Spectrum of compound (1d)

Spectrum 6: $^1$H NMR (300MHz) Spectrum of compound (1d) in CDCl$_3$. 
Phosphotungstic acid Catalyst

Spectrum 7: $^{13}$C NMR (75MHz) Spectrum of compound (1d)

Spectrum 8: Mass spectra of compound (1d)
Phosphotungstic acid Catalyst

1. E Spath, 
   *Ber.*, 1937, 70A, 53.

2. H. J. Perkin, 

3. H. Schiff, 
   *Ber.*, 1872, 6, 665.

4. F. Tiemann and H. Herzfield, 
   *Ber.*, 1877, 10, 283.

5. C. Taage, 
   *Ber.*, 1887, 20, 2109.

6. H. Yanagisawa and H. Kondo, 
   *J. Pharm. Soc., (Japan)* 1921, 472, 498.

7. H. Pechmann, 
   *Ber.*, 1884, 17, 929.

8. H. Pechmann and C. Duisberg, 
   *Ber.*, 1883, 16, 2119.

9. E. Knoevenagel, 
   *Ber.*, 1898, 31, 2585 & 2596. 
   *Ber.*, 1904, 37, 4461.

10. H.A. Shah and R.C. Shah, 

11. H. Pechmann and R. Robinson, 

12. T. Kiewiet and H. Stephens, 

13. P.N. Kurien, K.C. Pandya and V.R. Surange, 

14. A.A. Khan, P.N. Kurien and K.C. Pandya, 
15. K.C. Pandya and T.S. Sodhi, 

16. S.C. Ghosal, 

17. A. Sonn, 
   *Ber.*, 1917, 50, 1292.

18. K. Hoesch, 
   *Ber.*, 1915, 48, 1122.

19. R. Weiss and E. Merksammer, 
   *Monatsh.*, 1928, 60, 115.

20. R. Weiss and A. Kratz, 
   *Monatsh.*, 1929, 61, 386.

21. I.C. Badhwar, W. Baker, B.K. Menon and K. Venkatraman, 

22. D. Chakravarti and B. Majumdar, 

23. J.E. Pickett and P.C. Van Dort, 

24. E.A. Gunnewegh, A.J. Hoefnagel and H.V. Bekkum, 

25. K. Zeitler and C.A. Rose, 

26. B. Gabriele, R. Mancuso, G. Salerno and P. Plastina, 

27. H.S. Prakash Rao and S. Sivakumar, 

   and T.C. Sitler, 
29. K. Li, Y. Zeng, B. Neuenswander and J.A. Tunge, 

30. D.C. Dittmer, Q. Li and D.V. Avilov, 

31. D.V. Kadnikov and R.C. Larock, 

32. B.M. Reddy, M.K. Patil and P. Lakshmanan, 

33. M.K. Potdar, M.S. Rasalkar, S.S. Mohile and M.M. Salunkhe, 

34. A. Hegedus and Z. Hell, 

35. J. Oyamada and T. Kitamura, 

36. V.M. Alexander, R.P. Bhat and S.D. Samant, 

37. H. Valizadeha and A. Shokravi, 

38. G.P. Romanelli, D. Bennardi, D.M. Ruiz, G. Baronetti, 
   H.J. Thomas and J. C. Autino, 

39. D. Subhas Bose, A.P. Rudradas and M. Hari Babu, 

40. M. Maheswara, V. Siddaiah, G.L.V. Damu, Y.K. Rao and C.V. Rao, 

41. M.M. Heravi, S. Sadjadi, H.A. Oskooie, R.H. Shoor and F.F. Bamoharram, 

42. B. Tyagi, M. K. Mishra and R. V. Jasra, 
43. J. Azizian, A.A. Mohammadi, Ilyar Bidar and P. Mirzaei, 

44. K.K. Upadhyay, R.K. Mishra and A. Kumar, 

45. G. Smitha and C. Sanjeeva Reddy, 

46. B.M. Reddy, V.R. Reddy and D. Giridhar, 

47. P. Sun and Z. Hu, 

48. J. Wu, T. Diao, W. Sun and Y. Li, 

49. E.V. Stoyanov and J. Mezger, 

50. J.H. Yang, C.B. Ji and Y.M. Zhao, 

51. S.S. Bahekar and D.B. Shinde, 

52. D. Prajapati and M. Gohain, 

53. M.K. Potdar, S.S. Mohile and M.M. Salunkhe, 

54. S.A. Kotharkar, S.S. Bahekar and D.B. Shinde, 

55. N.D. Kokare, J.N. Sangshetti and D.B. Shinde, 

56. R. Torviso, D. Mansilla, A. Belizán, E. Alesso, G. Moltrasio, 
P. Vázquez, L. Pizzio, M. Blanco and C. Cáceres, 


84. H. Valizadeh and A. Shockravi, 

85. V. Singh, J. Singh, K.P. Kaur and G.L. Kad, 

86. M.K. Potdar, S.S. Mohile and M.M. Salunkhe, 

87. S.A. Gibbs and S.K. De, 
_Synthesis_, 2005, 1231.