RESEARCH ARTICLE

POLYMER-ENABLED PATHWAYS FOR SUSTAINABLE OXIDATION OF AROMATIC SECONDARY ALCOHOLS

Chandrakant V. Magar

Department of Chemistry,

Sant Tukaram college of Arts, and Science College, Parbhani, M.S. 431401, India

*Corresponding author E-mail: cvmagar@gmail.com

DOI: https://doi.org/10.5281/zenodo.17442576

Abstract:

Solid polymer-supported oxidizing reagents have emerged as a significant class of heterogeneous oxidants, bridging the gap between homogeneous reactivity and heterogeneous recyclability. This review highlights the mechanistic and kinetic aspects of PSOR-mediated oxidation reactions. Key emphasis is placed on diffusion–reaction interplay, rate-controlling regimes, and representative mechanistic models such as Langmuir–Hinshelwood and Eley–Rideal. Polymer-supported reagents are reagents reagents[1–3] covalently or ionically anchored to insoluble polymer matrices such as polystyrene, polyacrylamide, or polyethylene glycol. When oxidizing functionalities are immobilized on these supports, they form solid polymer-supported oxidizing reagents. Chemical kinetics has been intensely shaped by ground-breaking contributions from researchers such as Ludwig Ferdinand Wilhelmy, Wilhelm Ostwald, C. F. Wenzel, Louis Jacques Thénard, Pierre Eugène Marcelin Berthelot, Léon Pean de Saint-Gilles, Peter Waage, and Harcourt, who laid the foundations for contemporary understanding of reaction rates and mechanisms [4–5]. This review significantly examines the oxidizing agents employed in oxidation kinetics, with a focus on pharmaceutical compounds. Using solid polymer-supported reagents, we investigate the reaction rates of aromatic-substituted alcohols and elucidate the underlying oxidation mechanisms. This approach advances the understanding of chemical kinetics, providing valuable insights into the oxidation behavior of drug molecules.

Keywords: Solid-Polymeric Reagent; Solid-Supported Reagent, Oxidation, Alcohols.

1. Introduction:

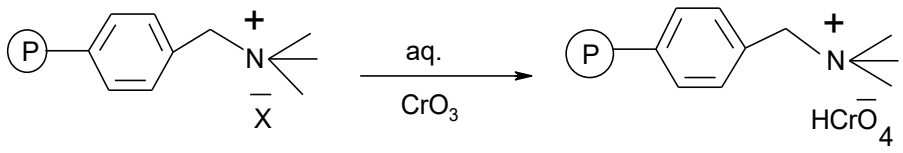
The use of polymer-supported species in chemical synthesis and separation continues to expand across industries[6]. In pharmaceuticals, polymer-supported reagents are routinely employed for the efficient synthesis of diverse small-molecule libraries [7], serving as solid-supported reagents or scavengers that enhance reaction efficiency, selectivity, and purification. Prior to Merrifield's

pioneering work in 1963, chemical synthesis was performed exclusively in solution. In 1962, he introduced a functionalized styrene-divinylbenzene copolymer for tetrapeptide synthesis, employing carbobenzoxy (Cbz)-protected amino acids. Sequential deprotection with HBr/HOAc and coupling allowed peptide chain elongation, with the final product cleaved from the polymer by saponification [8].

The synthetic process relied on straightforward, repetitive manipulations: sequential addition and removal of solvents and reagents to the polymer-bound substrate. Merrifield recognized that this simplicity made the method highly amenable to automation, leading to the development of apparatus capable of fully automated synthesis [9–18]. The efficiency and reproducibility of solid-phase synthesis (SPS), in stark contrast to the labor-intensive solution-phase methods, even for simple tetrapeptides, marked a transformative advancement in synthetic chemistry.

2. Preparation Of Supported Oxidizing Agent:

Ambersep 900 (chromate form, 10 g) was stirred with a saturated aqueous periodate solution (5 mL in 25 mL water) at room temperature for 25 min. Chromate ions were displaced within 60 min, yielding the periodate-loaded resin. The resin was sequentially washed with water, acetone, and THF, then vacuum-dried at 323 K for 6-7 hr. The dried resin was stored and used for kinetic studies.



[X = Cl] Polymer supported oxidizing agent

3. Resin Capacity Determination:

The capacity of chromate-form Ambersep 900 was determined iodometrically, yielding 2.10 and 2.12 eq/L, and used consistently in kinetic studies. Elemental nitrogen analysis indicated loadings of 1.55 and 1.90 eq/L.

4. Kinetic Study:

The reaction mixture was prepared by combining alcohol, the supported oxidant, and solvent. Reactions were conducted at 320 ± 1 K under constant magnetic stirring. At defined intervals, aliquots were withdrawn using a micropipette, quenched in 5 mL of 1,4-dioxane, and analyzed spectrophotometrically using an Schmadzu 1800 UV–Vis spectrophotometer. Double runs confirsmed rate constants reproducible within ±1 %.

5. Results and Discussion:

Table 1: Study rate of reaction for change in concentration of alcohol

Alcohols	45 mg	50 mg	55 mg	60 mg
	$k \times 10^{-4}$ min^{-1}			
1-Phenylethanol	1.30	1.61	1.82	2.07
4-Methoxyphenylethanol	1.48	1.64	1.85	2.10
4-Methylphenylethonal	1.42	1.70	2.02	2.20
4-Fluorophenylethanol	1.52	2.78	2.20	2.25

Table 2: Study rate of reaction for change in concentration of polymeric reagent

Alcohols	40 mg	50 mg	60 mg	70 mg
	$k \times 10^{-4}$ min^{-1}			
1-Phenylethanol	1.42	1.40	2.60	2.70
4-Methoxyphenylethanol	1.54	1.60	2.70	2.75
4-Methylphenylethonal	1.66	1.75	2.80	2.80
4-Fluorophenylethanol	2.02	1.86	2.90	2.85

It is evident from the information from above table that,

1. The graphically calculated 'k' values at different time intervals remain nearly constant.
2. The absorbance versus time plots consistently exhibits linear trends passing through the origin.
3. The average 'k' value, when considering all kinetic runs with varying polymeric reagent weights for each type of alcohol, also remains constant.

Table 3: Study of rate of solvent change on reaction Rate

Alcohols	Dielectric Constant	C_6H_{12}	CCl_4	1,4 -Dioxane	$CHCl_3$
		$k \times 10^{-4}$ min^{-1}			
1-Phenylethanol	2.05	1.30	1.30	2.00	1.85
4-Methoxyphenylethanol	2.20	1.45	1.40	1.85	1.75
4-Methylphenylethonal	2.25	1.55	1.50	2.45	1.60
4-Fluorophenylethanol	4.85	1.65	1.60	2.60	1.55

The Influence of Change in Temperature on Reaction Rate

The activation energy (Ea) analysis reveals a different trend: the activation energy for para-substituted 1-Phenyl ethanol follows a specific order, indicating.

1-Phenylethanol >4-Methylphenylethanol >4-Methoxyphenylethanol > 4-Florophenylethanol

Table 4: The Influence of temperature Change on reaction rate

Alcohols	40°C	45°C	50°C	55°C
	$k \times 10^{-4}$ min^{-1}			
1-Phenylethanol	1.70	1.80	2.30	2.40
4-Methoxyphenylethanol	1.75	1.85	2.40	2.45
4-Methylphenylethonal	1.80	1.90	2.52	2.50
4-Fluorophenylethanol	1.85	1.95	2.64	2.60

Table 5: Temperature Coefficient of P-substituted alcohols

Sr. No.	Alcohols	Temperature coefficient
1	1-Phenylethanol	1.56
2	4-Methoxyphenylethanol	1.67
3	4-Methylphenylethonal	1.71
4	4-Fluorophenylethanol	1.82

The reasonable values of activation enthalpy ($\Delta H^{\#}$) and activation entropy ($\Delta S^{\#}$) observed in this study provide valuable insights into the nature of electron transfer processes involved. These values fall within a range that is typically positive for reactions involving electron transfers

Table 6: Study of Energy of activation of P-Substituted alcohols

Sr. No.	Alcohols	E_a Kcal mol^{-1}
1	1-Phenylethanol	12.33
2	4-Methoxyphenylethanol	12.53
3	4-Methylphenylethonal	12.69
4	4-Fluorophenylethanol	11.78

Frequency Factor:

The combination of a low frequency factor (A) and negative activation entropy further reinforces our earlier assessment of the reaction. The consistency in the free energy of activation ($\Delta G^{\#}$) across all oxidation reactions is a noteworthy observation. This consistency strongly indicates that a similar mechanism likely governs all of these reactions. The near-identical $\Delta G^{\#}$ values imply that, despite potential variations in reactants or reaction conditions, the overall energy barrier that must be overcome to reach the transition state remains remarkably constant. This suggests a common set of chemical pathways and interactions, regardless of the specific reactants involved.

Table 7: Frequency factor for P-Substituted alcohols

Sr. No.	Alcohols	Frequency Factor × 10^{-5} min^{1}
1	1-Phenylethanol	3.93
2	4-Methoxyphenylethanol	4.25
3	4-Methylphenylethonal	5.30
4	4-Fluorophenylethanol	6.20

Table 8: Enthalpy of activation of P-substituted alcohols

Sr. No.	Alcohols	$\Delta H^{\#}$ Kcal mol^{-1}
1	1-Phenylethanol	5.667
2	4-Methoxyphenylethanol	4.734
3	4-Methylphenylethonal	3.567
4	4-Fluorophenylethanol	7.479

The negative values of the activation entropy ($\Delta S^{\#}$) in each case serve as compelling evidence supporting the assertion that the rate-determining step entails the association of molecules, accompanied by a restriction in their freedom of motion. This implies that the transition state exhibits a higher degree of orderliness compared to the initial reactant molecules.

Table 9: Entropy of activation for P-Substituted alcohols

Sr. No.	Alcohols	$\Delta S^{\#}$ e.u
1	1-Phenylethanol	-54.92
2	4-Methoxyphenylethanol	-52.95
3	4-Methylphenylethonal	-46.30
4	4-Fluorophenylethanol	-54.70

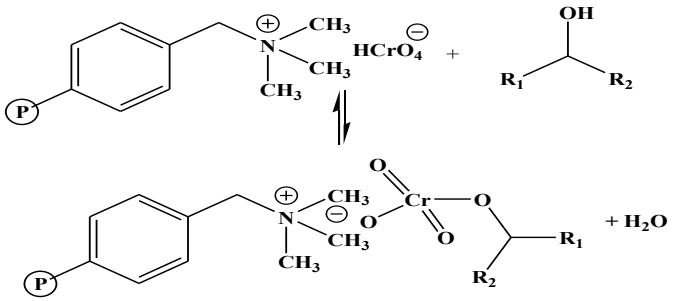
Table 9: Free energy of activation of P-Substituted alcohols

Sr. No.	Alcohols	$\Delta G^{\#}$ Kcal.mol^{-1}
1	1-Phenylethanol	24.20
2	4-Methoxyphenylethanol	24.23
3	4-Methylphenylethonal	24.30
4	4-Fluorophenylethanol	24.40

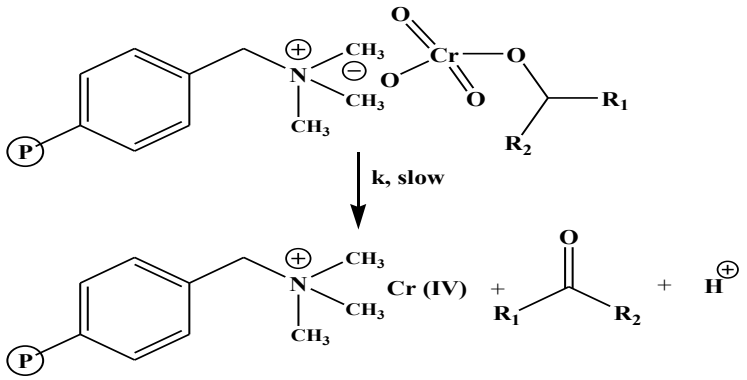
Based on the experimental results, which show zero-order kinetics for the oxidation of substituted 1-phenylethanol, a plausible reaction mechanism can be proposed.

Scheme of Mechanism

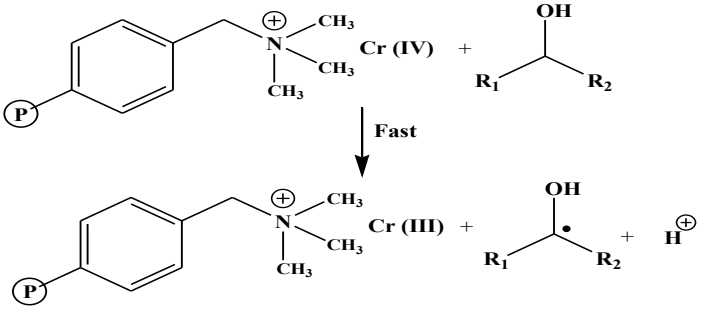
1] The initial step in the mechanism involves the development of an ester



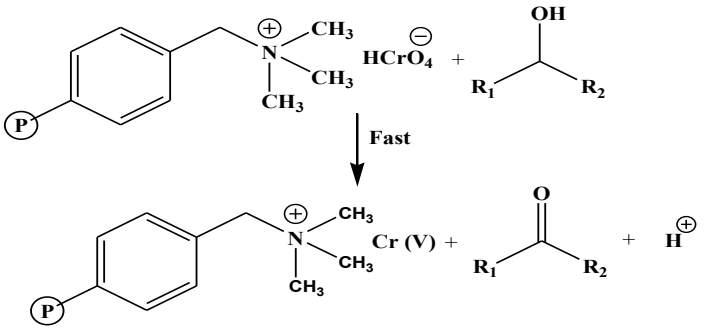
2] In the succeeding step, the formed ester will experience decomposition, yielding a ketone. This progression leads to the formation of the intermediate chromium (IV) in the second, which is also the slower, step.



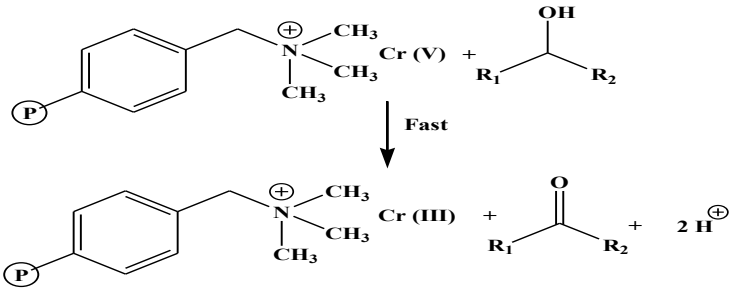
3] The intermediate Chromium (IV) undergoes a reaction with another alcohol, resulting in the development of free radical. This free radical formation was substantiated by observing the polymerization of acrylonitrile within the reaction mixture as well as by ESR spectrum.



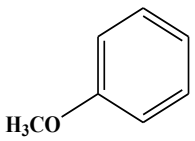
4] The free radical will counter with a second oxidant position in the polymeric reagent in a fast step leading to the creation of chromium (V).



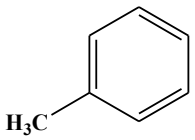
5] Transition chromium (V) in the last step reacts with alcohol to produce ketone. The test for formation of chromium (IV) and chromium (V) by their characteristic induced oxidation of iodine and manganese (II) were not successful, probably due to heterogeneity of the reaction mixture.



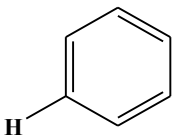
Where R_2 = -CH_3 and R_1 =



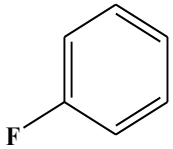
4-Methoxyacetophenone



4-Methylacetophenone



Acetophenone



4-Fluoroacetophenone

Based on the above scheme, the initial solid-phase ester formation is expected to follow a second-order rate law. Assuming this step reaches equilibrium rapidly, it does not significantly affect the overall rate, resulting in a zero-order dependence on the rate constant k.

k for the slower subsequent step, in which the corresponding ketone is formed.

References:

1. Sherrington, D. C., & Hodge, P. (1988). *Syntheses and separations using functional polymers*. John Wiley & Sons.
2. Ley, S. V., Baxendale, I. R., Bream, R. N., Jackson, P. S., Leach, A. G., Longbottom, D. A., Nesi, M., Scott, J. S., Storer, R. I., & Taylor, S. J. (2000). *Journal of the Chemical Society, Perkin Transactions 1*, (23), 3815.
3. Buchmeiser, M. R. (Ed.). (2003). *Polymeric materials in organic synthesis and catalysis*. Wiley-VCH.
4. Drewry, D. H., Coe, D. M., & Poon, S. (1999). *Medicinal Research Reviews, 19*(2), 97.
5. Kirschning, A., Monenschein, H., & Wittenberg, R. (2001). *Angewandte Chemie International Edition, 40*(4), 650.
6. Ley, S. V., Baxendale, I. R., Brusotti, G., Caldarelli, M., Massi, A., & Nesi, M. (2002). *Il Farmaco, 57*(4), 321.
7. Chesney, A. (1999). *Green Chemistry*, 1, 209.
8. Cano, M., & Balasubramanian, S. (2003). *Drugs of the Future, 28*, 659.
9. Kirschning, A., Monenschein, H., & Wittenberg, R. (2000). *Chemistry – A European Journal, 6*(21), 4445.
10. Reader, J. C. (2004). *Current Topics in Medicinal Chemistry, 4*(7), 671.
11. Marshall, G. R. (2003). *Journal of Peptide Science, 9*(9), 534.
12. Merrifield, R. B. (1963). *Journal of the American Chemical Society, 85*(14), 2149.
13. Merrifield, R. B., & Stewart, J. M. (1965). *Nature, 207*, 522.
14. Merrifield, R. B. (1965). *Science, 150*(3696), 178.
15. Sonawane, V. Y., & Hilage, N. P. (2008). *Journal of the Indian Council of Chemistry, 25*(2), 122.
16. Sonawane, V. Y., & Hilage, N. P. (2009). *Oriental Journal of Chemistry, 25*(2).
17. Sonawane, V. Y. (2018). *IOSR Journal of Applied Chemistry, 11*, 36–39.
18. Sonawane, V. Y. (2020). *Journal of Emerging Technologies and Innovative Research, 7*(4), 162–164.
19. Magar, C. V. (2021). *International Journal of Research in Engineering and Science, 9*(9), 67–70.