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Wolff Rearrangement of α-Diazoketones Using in Situ Generated Silver Nanoclusters as Electron Mediators

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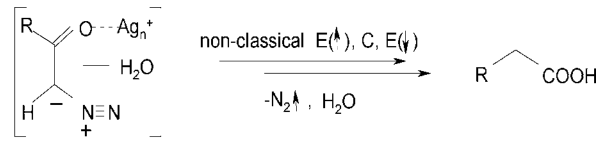
ABSTRACT



Ag_n = Silver nanocluster, R= $CH_3(CH_2)_{10}$ -, Ph-CH_2-,

Ph-, 2-I-Ph-, 4-MeO-Ph-, 3-Diazocamphor

We report Wolff rearrangement of α-diazoketones by in situ generated silver nanoclusters (Ag_n, 2–4 nm) from silver(I) oxide (Ag_2O) involving a nonclassical electron-transfer process. Our results show that Ag_n^+/Ag_n^0 redox couple allows the initial removal of an electron from α-diazoketone and its back-donation after chemical reaction(s). Controlled potential coulometry (CPC) of various α-diazoketones results in the realization of Wolff-rearranged carboxylic acids in excellent yields.

The Wolff rearrangement of α-diazocarbonyl compounds has been of tremendous synthetic utility for over 100 years.[1,2] The rearrangement involves a stereospecific 1,2-carbon shift leading to the formation of ketene via a short-lived α-keto-carbene intermediate[3,4] following the expulsion of a nitrogen molecule. This α-elimination of dinitrogen can be initiated under the influence of thermal energy, ultraviolet light, transition-metal catalyst, or microwave radiation.[5] Use of catalysts such as silver(I) salts is one of the central routes to accomplish the rearrangement, and our group has recently shown that silver nanoclusters (Ag_n) are the true catalytic species against the generally presumed involvement of silver(I) ions.[6] Although many explicit suggestions, like the reduction of activation energy and the stabilization of reaction intermediates, have been made, the mechanistic role of the transition-metal catalyst remains enigmatic.[7]

Attempts[8,9] to trigger the α-elimination of nitrogen from α-diazocarbonyl compounds either by the removal or the

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addition of an electron using conventional electrodes, like platinum, glassy carbon, lead to the realization of products arising from carbene cation radical (CCR) or carbene anion radical[10,11] (CAR) intermediates, respectively. However, the formation of products arising from α-ketocarbene intermediates is significantly missing. Similarly, efforts[12] to induce the rearrangement by removing an electron from α-diazoacetophenone using triarylamine radical cation have failed, probably due to the nonoccurrence of back-donation of electron to the intermediate product. Significantly, a redox electrocatalyst offers a unique possibility to simultaneously remove one electron and to back-donate following the α-elimination of dinitrogen from the diazo compounds or vice versa. In the present study, we show that in situ generated Ag_n from Ag_2O acts as electron mediator during the Wolff rearrangement.

We monitored the change in open circuit potential[13] (OCP) between Ag_2O coated working electrode and Ag/AgCl reference electrode as a function of temperature (Figure 1) following the addition of 1-diazo-2-tridecanone, **1a** (see Table 1). Initially, the OCP decreases from 0.31 V (300 K) to 0.299 V (306 K) and then begins to rise along with copious evolution of nitrogen from the working electrode with a shift of about 34 mV in the anodic direction (Figure 1, curve B). The initial shift of OCP in cathodic direction during the induction period (before the onset of nitrogen evolution) indicates the reduction of Ag_2O. UV−vis[14] analysis shows the presence of a surface plasmon absorption band at ca. 400 nm, a distinct characteristic of Ag_n (Supporting Information, SI-1.2). Transmission electron microscopy (TEM) also confirms the presence of nearly monodispersed Ag nanoclusters (2−4 nm; Supporting Information, SI-1.1). This in situ formation of Ag_n triggers the decomposition of α-diazoketone, **1a**, and hence, the OCP moves rapidly to more positive values. The anodic direction of the OCP change and the nature of the electrocatalyst together indicate the oxidation of α-diazoketone, **1a**, as one of the important steps during the sequential generation of ketene (Scheme 1). In contrast, experiments performed in the absence of diazo compound show no such noteworthy change in OCP (Figure 1, curve A).

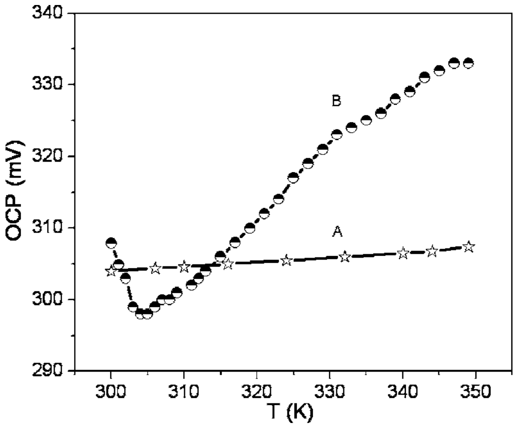

Figure 1. Plot of open circuit potential (OCP) as a function of temperature for the cell made up of silver(I) oxide coated on platinum wire as the working electrode and Ag/AgCl as the reference electrode in aqueous acetonitrile (H_2O/CH_3CN; 1:10 v/v) solution (A) and following the addition of the 1-diazo-2-tridecanone, **1a** (B).

Table 1. Cyclic Voltammetric Features[a] of the Ag_n^0/Ag_n^+ Redox Couple in the Absence and Presence of α-Diazoketones, **1a**−**f**, at 0.01 V s^{-1}

α-diazoketone **1**, R	Ep_a (V)	Ep_c (V)	ΔEp (V)	$E_{1/2}$ (V)	yield[b] (from CPC) (%)
i	0.34	0.20	0.14	0.27	-
ii: **1a**, $CH_3(CH_2)_{10}-$	0.40	0.23	0.17	0.31	94
iii: **1b**, Ph-CH_2-	0.40	0.18	0.22	0.29	95
iv: **1c**, Ph−	0.47	0.17	0.30	0.32	92
v: **1d**, 2-I-Ph−	0.41	0.18	0.23	0.29	96
vi: **1e**, 4-MeO-Ph−	0.59	0.11	0.48	0.35	87
vii: **1f**, 3-diazocamphor	0.43	0.19	0.24	0.31	*c*

[a] Votammograms were recorded by coating silver (I) oxide over a platinum disk (2 mm) electrode, followed by three cycles (−0.05 to +0.8 V) in aqueous acetonitrile solution using *n*-Bu_4NClO_4 (0.1 M) as supporting electrolyte, to obtain a stable electrochemical response for in situ generated Ag_n before introducing α-diazoketones, **1a**−**f**, with respect to Ag/AgCl electrode. [b] Chemical yields of the isolated carboxylic acids, **8a**−**e** (Supporting Information, SI-7), were determined following the controlled potential coulometry (CPC) of α-diazoketones, **1a**−**f**, using a divided cell assembly containing Ag_n as anode and graphite as cathode. [c] CPC of **1f** leads to the exclusive formation of tricyclic ketone (Scheme S1, Supporting Information, SI-8.1).

The electrochemical behavior of Ag_2O in the absence of α-diazoketone also reveals the in situ formation of Ag_n

$$Ag_2O + H_2O + 2e^- \rightarrow 2Ag^0 + 2OH^-$$
$$(E^\circ = 0.342 \text{ V vs NHE}) \qquad (1)$$

Voltammetric analysis of these in situ generated Ag_n clusters in aqueous acetonitrile reveals the presence of a distinct redox couple with unique electron-transfer properties as represented by curve A in Figure 2.

The redox couple is centered at ca. 0.27 V with anodic and cathodic peaks at ca. 0.34 and 0.2 V, respectively. Furthermore, the ratio of areas of anodic to cathodic peaks is fairly close to unity (1.13), while individual peak potential shows marginal variation as a function of the scan rate.[15] More significantly, the larger magnitude of separation

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[11] (a) Note: Mass spectroscopy detects the formation of carbene cation radicals from α-diazocarbonyl compounds in the gas phase. Furthermore, mass spectroscopic detection of charged Fischer-type copper and silver α-heterocarbenoid intermediates during the metal-mediated Wolff-rearrangement of diazomalonate has been reported recently (see the Supporting Information, SI-6.2). (b) Julian, R. R.; May, J. A.; Stoltz, B. M.; Beauchamp, J. L. *J. Am. Chem. Soc.* **2003**, *125*, 4478.

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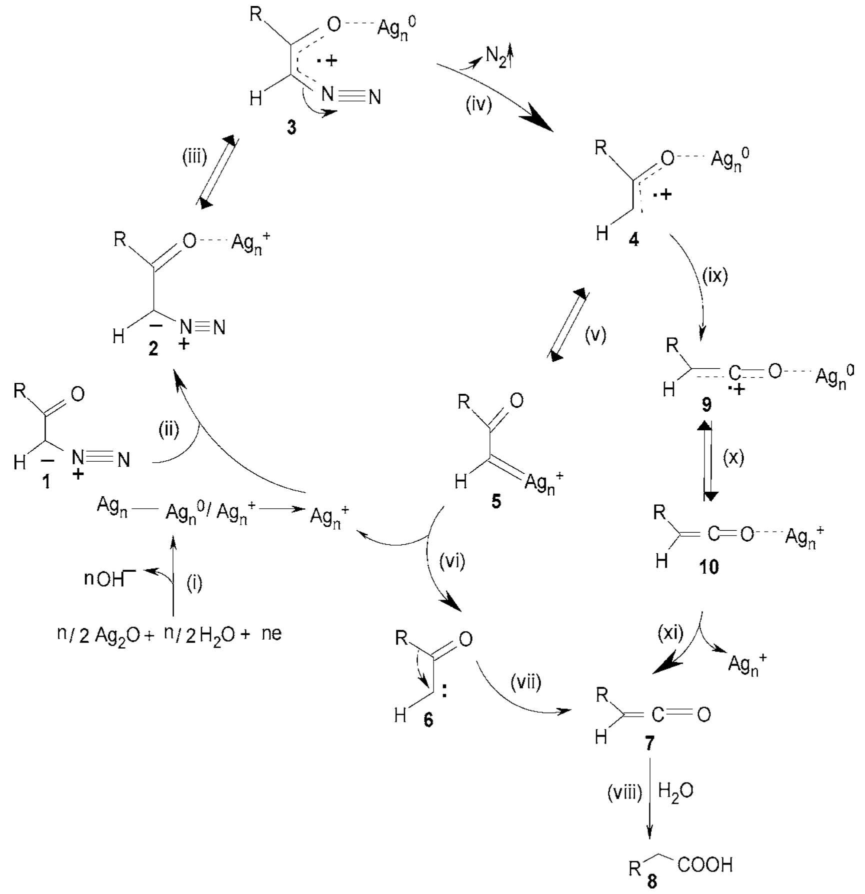
Scheme 1. Schematic Representation of the Electrocatalytic Role of in Situ Generated Silver Nanoclusters (Ag_n, Size 2−4 nm) during the Wolff Rearrangement of α-Diazoketones, **1a**−**e** (Table 1), Involving Two Nonclassical Electron-Transfer Pathways



between anodic and cathodic peaks (ΔEp ≈ 0.14 V) plays a decisive role for the occurrence of coupled chemical reaction (vide infra) due to the enhancement of time interval between two electron-transfer steps.[16,17] The origin of the redox couple could be attributed to the occurrence of an electron-transfer process represented by the following equation:

$$Ag_n^{\ +} + e^- \rightarrow Ag_n^{\ 0} \tag{2}$$

An estimation of the rate constant k^0 for this process based on the magnitude of ΔEp is ca. $4.14 \times 10^{-4}\ s^{-1}$.[18] Importantly, individual peak potential of in situ generated Ag_n does not vary with either the nature or the concentration of the supporting electrolyte, although they are strongly influenced by both solvent and substrate nature.

In comparison, the cyclic voltammogram of Ag_n in the presence of α-diazoketone, **1a**, shows drastic changes suggesting the occurrence of a remarkable coupled chemical reaction (CV-B in Figure 2). For example, forward scan of the first cycle ($\nu = 0.01\ V\ s^{-1}$) shows a more anodically shifted, steeply descending oxidation peak at around 0.4 V

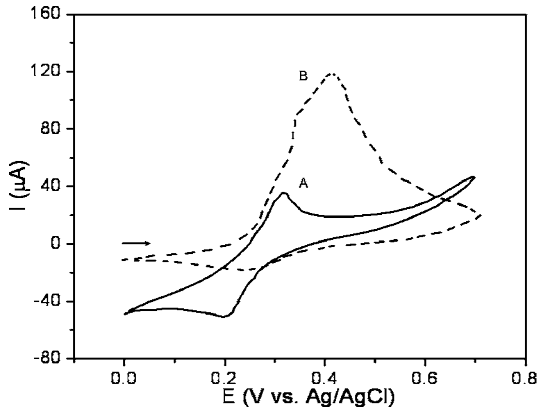


Figure 2. Superimposed cyclic voltammograms of in situ generated silver nanoclusters from silver(I) oxide in aqueous acetonitrile (H_2O/CH_3CN, 1:10 v/v) containing 0.1 M n-Bu_4NClO_4 as supporting electrolyte with reference to Ag/AgCl electrode at the scan rate of $0.01\ V\ s^{-1}$: (A) in the absence of α-diazoketone, (B) in the presence of α-diazoketone, **1a**.

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(15) Note: The capping agents stabilize and guide its electron-transfer behavior. For example, benzoic acid protected Ag clusters exhibit redox behavior over a wide range of scan rate (from 1.0×10^{-3} to $30.0\ Vs^{-1}$; ref 6b).

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with a higher peak current. The nature of this peak is reminiscent of an electron transfer followed by a chemical reaction. In comparison, the reverse scan depicts a substantially suppressed cathodic peak exhibiting a plateau around 0.2 V. More importantly, the forward scan of the second cycle shows an anodically shifted descending peak around 0.40 V with a prepeak around 0.35 V. The rise in peak current along with the retention of voltammetric pattern following the addition of more amount of **1a** indicates the involvement of the electrochemical reaction, while the position of new prepeak at 0.35 V in close proximity with the anodic peak of the original redox couple reveals the regeneration[19] of electrocatalytic species $\mathrm{Ag_n}^+$. However, a reverse scan of the second cycle is unable to show two cathodic peaks corresponding to respective anodic peaks due to the plateau-like nature of the cathodic response. Successive cycles show a similar voltammetric pattern with decreased peak current. The anodic peaks move in a more positive direction, while a cathodic plateau shifts more negatively with increasing scan rate. However, voltammograms beyond $\nu \gg 0.1$ $\mathrm{Vs^{-1}}$ are electrochemically silent. Qualitative comparison between the nature of anodic (peak) and cathodic (plateau) peaks indicates the occurrence of a kinetically faster oxidation process. This analysis is in agreement with the shift of OCP to more positive values following the onset of the Wolff rearrangement (vide supra). Significantly, the zero current curve-crossing phenomenon with thermodynamically more facile second electron transfer step than the first is absent, collectively suggesting the occurrence of a nonclassical electron-transfer process.[16,17]

The voltammograms of various α-diazoketones, **1b**−**f** (Table 1), evoke subtle yet informative features leading to the understanding of stereoelectronic effects associated with the nonclassical electron-trasfer process. For example, among aromatic diazoketones, the anodic peak potential ($\mathrm{Ep_a}$) increases from the iodo, **1d** (0.41 V) through **1c** (0.47 V) to **1e** (0.59 V), indicating the relative order of thermodynamic difficulty to oxidize the respective diazoketones. Furthermore, the magnitude of ΔEp as well as the difference of the half-wave potential ($E_{1/2}$) of $\mathrm{Ag}_n^{\,0}/\mathrm{Ag}_n^{\,+}$ redox couple in the presence and absence of respective α-diazoketeones also increase in a similar manner, leading to a decrease in the rate of the nonclassical electron-transfer process (Supporting Information, SI-3). These results are in good agreement with the previous reports.[20] Significantly, the CPC of 3-diazocamphor, **1f** (vide infra), results in the exclusive formation of the tricyclic ketone **11**, arising from an intramolecular insertion of α-ketocarbene intermediate into the C−H bond (Scheme S-1, Supporting Information).[5] This substantiates the characteristic evidence of involvement of a nonclassical E(↑), C, E(↓) pathway (vide infra).

Application of an anodic bias on Ag_n-coated platinum electrode (0.5 V vs Ag/AgCl) in aqueous acetonitrile solution of α-diazoketone, **1a**, containing pyridine as the nucleophilic probe gives rise to a UV−vis absorption band around $\lambda =$ 422 nm, indicating the formation of α-ketocarbene intermediate **6** and/or ketene **7** (Scheme 1). However, it is difficult to discriminate between these two intermediates due to their similar peak positions in the UV−vis absorption band arising from pyridine−α-ketocarbene ylide[3,4] and pyridine−ketene ylide.[21]

We propose two nonclassical electron-transfer pathways for the Wolff rearrangement (Scheme 1). The E(↑), C, E(↓) pathway[22] represented by steps iii, iv, and v, respectively, leading to the formation of α-ketocarbene **6** (involving structure **5**, which is more or less similar to the Fischer carbene intermediate) followed by the instantaneous generation of ketene **7**. Alternatively, the E(↑), C, C, E(↓) pathway represented by steps iii, iv, ix, and x, respectively, involves the rearrangement of carbene cation radical,[11] ultimately leading to ketene **7**.

Another remarkable evidence for these mechanistic features (Scheme 1) arises from CPC by the application of an appropriate oxidation potential at room temperature (303 K), which leads to the realization of Wolff rearranged carboxylic acids from α-diazoketones, **1a**−**e**, in excellent yield (Table 1). On the other hand, CPC of the α-diazoketone, **1a**, using Pt as anode (1.2 V vs Ag/AgCl) gives merely a mixture of neutral reaction products.

In conclusion, we have shown that the addition of Ag(I) oxide to the solution of α-diazoketone results in the in situ generation of silver nanoclusters which function as electron mediators in Wolff rearrangement. More importantly, this work provides an efficient preparative electrochemical route to realize Wolff-rearranged products in excellent yields at room temperature. The technique can be advantageously utilized in the homologation of naturally occurring α-amino acids to β-amino acids, some of the key building blocks of protenogenic β-peptides. We strongly believe that several reactions are similarly catalyzed by metal nanoclusters,[23] and further studies in this direction are in progress.

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Supporting Information Available: Detailed experimental procedures, TEM images, UV−vis spectra, additional CV, and characterization of various products. This material is available free of charge via the Internet at http://pubs.acs.org.

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[19] Note: By increasing the amount of $\mathrm{Ag_2O}$ coated on the working electrode, we observed a rise in peak current with the retention of voltammetric pattern indicating the regeneration of electrocatalytic species $\mathrm{Ag}_n^{\,+}$ (Supporting Information, SI-2.2).

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[22] (a) We strongly believe that relative stability of adsorbed conformation of α-ketocarbene over Ag_n will play a decisive role in selecting the reaction pathway. Two possible pathways for the rearrangement from intermediate **5** are decomplexation of Ag_n followed by the rearrangement of free α-ketocarbene **6** (Scheme 1) and rearrangement of α-ketocarbene followed by the decomplexatio of Ag_n (not shown in Scheme 1). (b) Bogdanova, A.; Popik, V. V. *J. Am. Chem. Soc.* **2004**, *126*, 11293.

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