An unexpected reaction of camphor with sodium metal

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Reaction of camphor with sodium metal at elevated temperature in refluxing THF or toluene, furnishes an unexpected product. The product has been identified by spectral analysis and its structure confirmed by single crystal X-ray diffraction study. A preliminary mechanistic explanation has been suggested to explain this reaction.

Keywords: Camphor, sodium metal, unexpected reaction

The molecule of camphor has fascinating structural features due to its rigid bicyclic framework. Camphor is abundantly available in chirally pure form of D-isomer in nature. Presence of a ketone group, α-methylene group and bicyclic structure collectively offer opportunities for introducing different functional groups and induce chemical transformations on this molecule. Camphor has been utilized as starting material for the preparation of a range of useful compounds such as some natural products, chiral auxiliaries, chiral molecules used in asymmetric synthesis, preparation of NMR shift reagents, etc. This also serves as raw material for obtaining other synthetically valuable compounds such as isoborneol, isobornyl amine, camphorquinone, camphoric acid, camphorsulfonic acid, camphorsultam, etc.

Results and Discussion

Reaction of camphor or derivatives of camphor have occasionally resulted in the formation of unexpected products. In some cases a skeletal reorganization was observed with the formation of cyclopentanoid structures or in some cases cyclohexanoids were formed. As part of an ongoing project of preparation and utilization of novel chiral molecules obtained from camphor, we were interested to explore its enolate chemistry. Several attempts to prepare and trap the enolate of camphor in the presence of Lewis acid or strong bases are known. The stabilized enolates or enamines are then converted to useful α-functionalized camphor derivatives. The goal of the present study was to prepare enolate of camphor and perform its addition to certain aldehydes (Scheme I).

During this investigation the reaction of camphor with sodium metal was explored. In the absence of a proton donor, an unusual result was observed, which is presented here. Reaction of camphor with sodium in dry THF or in dry toluene at reflux conditions resulted in the formation of a new compound. This compound was obtained as a white crystalline solid by column chromatography over silica gel and its structure was established by spectroscopic analysis and confirmed to be by single crystal analysis (Scheme II).

The 1H NMR spectra of clearly indicated presence of one olefinic proton as a doublet (J = 10.4 Hz) and six different singlets of methyl groups. While infrared spectra clearly established presence of two different carbonyl groups, one absorption band may be for α,β-unsaturated ketone (1706 cm⁻¹), the other of an acid carbonyl (1729 cm⁻¹) and the C=C system (1660 cm⁻¹). The mass spectra and 13C NMR also supported this structure. Mass spectra indicated M⁺ (m/z 318), loss of CO (m/z 290) and CO₂ (m/z 272) confirming the presence of acid group. The 13C NMR and various DEPT experiments clearly confirmed four methylenes (δ 32.7, 30.1, 27.0, 26.9), two methine carbons (δ 47.8 and 47.5) and four quaternary carbons (δ 57.9, 55.8, 47.9 and 46.1). This also confirmed two carbonyl groups, ketone (δ 207.3) and the acid carbonyl (δ 182.5), besides olefinic ones, α-carbon (δ 144.0) and β-carbon (δ 130.6). We were also able to confirm the structure of 3 by single crystal X-ray analysis. The ORTEP diagram of the structure is presented in Figure 1. The molecules of 3 are held together with intermolecular hydrogen bonding between the acid and the bicyclic ketone (Figure 2).
The reaction of camphor with dissolving metal in liquid ammonia was extensively studied by Huffman and others in the late 1980s when they isolated different reduced products and pinacol derivatives. The authors have mentioned the formation of \( \alpha \)-radical of camphor.

\[
\text{D-Camphor I}
\]

\[
\text{base} \quad \text{ArCHO} \quad \text{Ar} \quad \text{2}
\]

**Scheme I** — Proposed reaction of camphor

\[
\text{Na}^+ \quad \text{THF/PhCH}_3 \quad \text{reflux} \quad \text{3 (23 \% Y)} \quad + \text{borneol and isoborneol (35 \%)}
\]

**Scheme II** — Observed reaction of camphor

4 (Ref 25b) which might be the first step in the formation of product 3 (Scheme III). The dimerization of this radical is also reported and supports the possibility of the formation of bicamphor 5 in the present case. This may be followed by the formation of another tertiary \( \alpha \)-radical 6 from the dimer. The radical 6 may induce a homolytic \( \alpha \)-cleavage of the other bicyclic system, forming a stable \( \alpha,\beta \)-unsaturated carbonyl system 7 having an acyl radical, which may abstract hydrogen from solvent to give aldehyde 8 which may form the acid 3 during the aerial work-up. The stereochemical orientations of the observed products are in accordance with this plausible mechanism (Scheme I). Starting with D-camphor 1 furnished the chiral product 3 with specific rotation of +80.8° (c = 1, CHCl₃).

It is significant to note that neutral or acidic work-up does not affect the observed yield of the product 3. The title compound was isolated in moderate yield.

**Figure 1** — ORTEP diagram of 3

**Figure 2** — Crystal packing and hydrogen bonding in 3
(23%) along with a mixture of borneol and isoborneol (35%, ratio of 7:3). The unreacted camphor and some unidentified material, which may include pinacol coupling product\textsuperscript{26d}, accounted for the rest of the material.

There may be an another possible pathway to explain this observation\textsuperscript{28}. The radical \textsuperscript{4} or the Na-enolate of camphor \textsuperscript{9}, may react with traces of oxygen resulting in the formation of peroxo species \textsuperscript{10}, which may generate aldehyde-acid \textsuperscript{11}. This may undergo an aldol reaction with \textsuperscript{1} or \textsuperscript{9} to afford the final product \textsuperscript{3} (Scheme IV). A small amount of aldehyde-acid\textsuperscript{29} \textsuperscript{12} was detected in GC-MS analysis of the reaction mixture.

In another experiment, the reaction was conducted in degassed toluene to eliminate the traces of oxygen. In the absence of oxygen the products \textsuperscript{3} and \textsuperscript{12} were not detected by GC-MS analysis or by \textsuperscript{1}H NMR of the crude reaction mixture, however borneol and isoborneol could be detected. At the same time, reaction conducted under the atmosphere of nitrogen mixed with oxygen (~10%), furnished the final product \textsuperscript{3} (in lower yield of 7%), along with camphoric acid \textsuperscript{13}, its formation could be due to the oxidation of \textsuperscript{11} or \textsuperscript{12}. The title reaction did not proceed at ambient temperature, either in THF or in toluene. These observations tend to favor the second mechanism proposed in Scheme IV.

The formation of borneol, isoborneol along with the dimer of camphor \textsuperscript{5}, was established by GC-MS analysis (peak at m/z 302) indicating towards the intermediate radical species. Our efforts to prepare Na-enolate \textsuperscript{9} by reaction of camphor with NaH were not successful; apparently a stronger base such as n-BuLi is required for the enolate formation\textsuperscript{25b}.

In an attempt to further examine the scope of this unusual reaction, a cyclic ketone, cyclohexanone \textsuperscript{14}, was treated under similar conditions. In this case, the expected products of self condensation \textsuperscript{15} and \textsuperscript{16} were
3-(3-(stirring under N₂) sodium metal (0.23 g, 9.85 mmol) was added with 1286, 1254, 1101, 1063, 951 cm⁻¹. Specific optical rotation was measured on Jasco P-2000 polarimeter. Uncorrected. Spectra were recorded on a Perkin-Elmer FTIR RXI spectrometer as KBr pellets. Melting point was measured on Thermo-Fischer DSQ II GCMS instrument, IR spectra were recorded as KBr pellets. Mass spectra were recorded on a single crystal X-ray diffraction facility of the Faculty of Science. The authors wish to thank the Council of Scientific and Industrial Research (CSIR), New Delhi for the award of fellowship to ANK. The authors are grateful to DST-PURSE for the single crystal X-ray diffraction facility of the Faculty of Science. The authors wish to thank Prof. Vishwakarma Singh of IIT, Bombay for helpful discussions.

Conclusions
In conclusion we have reported the formation of an unusual product during the reaction of camphor with sodium metal, involving a dimer and its skeletal rearrangement. The product is adequately characterized by spectroscopic techniques and supported by X-ray crystal analysis.

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References
Details of crystallographic analysis of 3 have been deposited with the Cambridge Crystallographic Data Centre (CCDC 980095). Copies of the data can be obtained from http://www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CD21EZ, UK (fax: +44-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).


The second possible pathway to explain the formation of the product 3 was suggested by one of the referees, for which we express our gratitude.

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