Pergamon

Tetrahedron Letters, Vol. 35, No. 33, pp. 6043-6046, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)01273-3

2,2-Dimethylcyclopropyl 4-Methylphenyl Ketone as a SET Probe

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Abstract. *2,2-Dimethylcyclopropyl 4-methylphenyl ketone in the presence of SmI_2 and DMPU is a good SET probe. The ortho positions of the aromatic ring provide a good source to trap the newly formed tertiary radical.*

The existence of single electron transfer (SET) reactions has been argued for over 20 years.[1] The common approach for experimental detection of SET involves the use of intramolecular rearrangements and phenyl cyclopropyl ketone has been used for this purpose. However, there are several conflicting reports in the literature about the fate of the cyclopropyl ring in ketyl radical anions. Exhaustive electrolysis of phenyl cyclopropyl ketone yields the corresponding pinacol without ring opening.[2] Dissolving metal reduction of phenyl cyclopropyl ketone reportedly yields benzylcyclopropane.[3] More recently, Tanko has conducted an extensive study of aryl cyclopropyl ketones to form aryl cyclopropyl ketyl anions using voltametric techniques. Their seminal work has shown that for simple aryl cyclopropyl ketyl anions, ring opening is reversible, $K_{eq}= 2x10^{-8}$, and greatly disfavored from loss of resonance stabilization. They conclude that these systems " are unsuitable probes for single electron transfer." [4]

Our initial studies[5] on the reduction of cyclopropyl phenyl ketone and 2,2-dimethylcyclopropyl phenyl ketone with sodium naphthalide were not definitive. While the former gave greater than 70% of n-propyl phenyl ketone, the yields of monomeric products from the latter were approximately 30%. Furthermore, the exclusive monomeric product was neopentyl phenyl ketone which is indicative of anionic ring opening as no isopentyl phenyl ketone, the expected product from radical opening, was observed.

Samarium II has evolved as a unique single electron reducing agent and its broad application has been reviewed[6]. The role of DMPU or HMPA used in conjuction with the SmI_2 system has also been discussed.[7] Our first attempts using 2,2-dimethylcyclopropyl phenyl ketone and Sm II/DMPU/THF gave a preponderance of high molecular weight compounds, dimers and trimers, presumably from radical attack of one substrate at the para position of another.[4a] These reaction products were significantly reduced by blocking this reaction pathway with a p-methyl group. When we used SmI_2 and DMPU to reduce 2,2-dimethylcyclopropyl 4-methylphenyl ketone **1**, we observed a product distribution indicative of a clear SET process as outlined in Scheme I and Table 1.

Scheme I

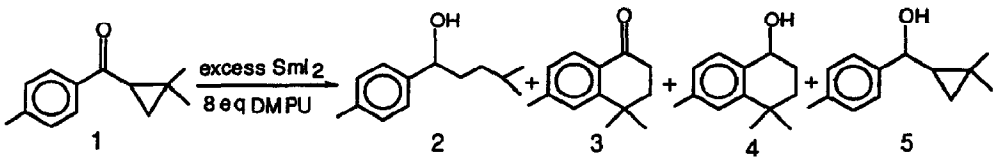


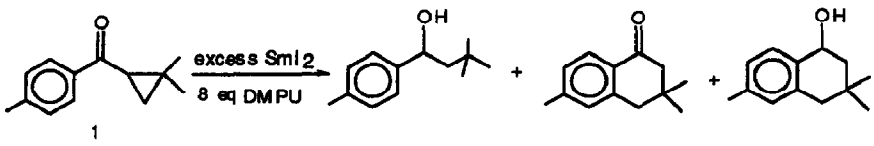
Table 1

run \ yield %	1	2	3	4	5
a	44	trace	21	6	8
b	7	20	30	16	9

a, b, with 3 eq t-BuOH, adding ketone to 5 eq SmI_2, a, adding time 13 min, waiting 5 min.
b, adding time 10 min, waiting 120 min.

If a two electron reduction was operative, we would expect comparable rearrangement products arising from ring opening to a primary carbanion as illustrated in Scheme II. However, none of these products, as unlikely as they may seem, were found under our conditions.

Scheme II



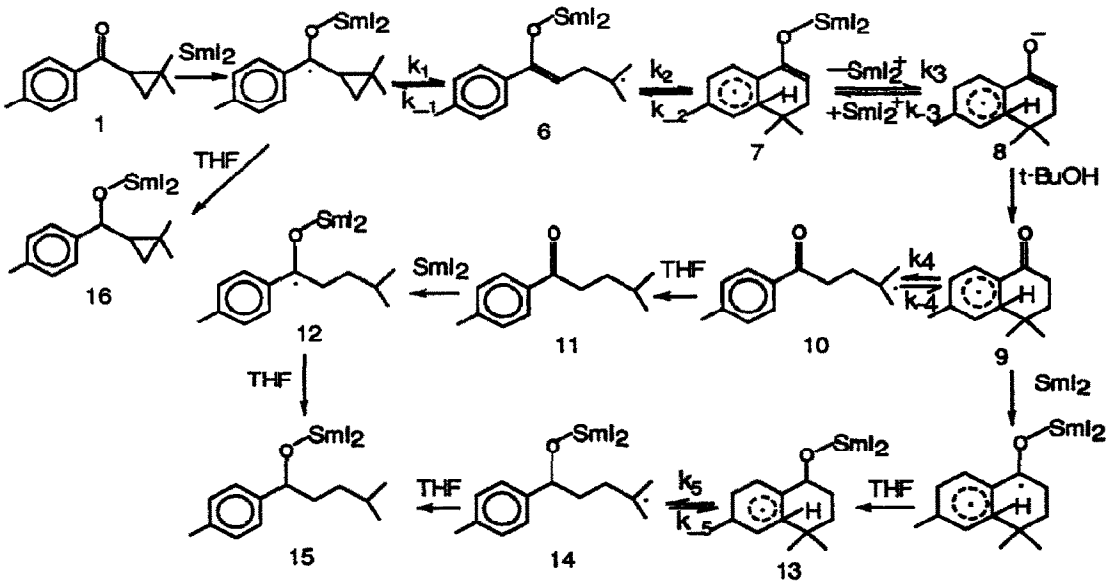
The product yields from reduction of ketone **1** were determined by GC using hexadecane as an internal standard. Compounds **3** and **4** were identified by spectral analysis (^1H, ^{13}C NMR and HRMS) although **4** was analyzed as the alkene dehydration product which occurred on the GC. Compounds **2** and **5** were independently synthesized. While the yields of **2, 3, 4,** and **5** are reproducible under identical reaction conditions, they vary depending on reaction times.

There are several interesting observations that arise from these studies. The first is that no disproportionation products are produced. This is true for both 2,2-dimethylcyclopropyl phenyl ketones (with

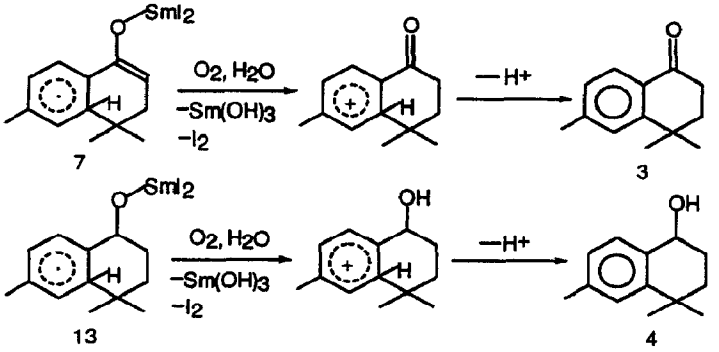
or without the para methyl group) as well as for cyclopropyl phenyl ketone which gives propyl phenyl ketone as the major product. Secondly, the electrophilic nature of the ring opened tertiary radical from **1** (**6** in Scheme III) is indicated by the formation of cyclized products **3** and **4** and by dimer formation from 2,2-dimethylcyclopropyl ketone. If cyclization is exclusively a " cage process ", then 2, 2-dimethylcyclopropyl phenyl ketone should behave similarly.

Although Scheme III and IV are highly speculative and require further study for substantiation, they account for the products formed. It is almost certain that tertiary radicals do not abstract hydrogen from aromatic adducts **7** and **13** and Scheme IV is shown as one way the oxidation could occur.[8,9] Regardless of the validity of the mechanistic proposal, 2,2-dimethylcyclopropyl 4-methylphenyl ketone reacts with SmI_2 by a single electron transfer.

Scheme III



Scheme IV



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(*Received in USA* 8 *February* 1994; *revised* 1 *June* 1994; *accepted* 28 *June* 1994)