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A FACILE METHOD FOR REGIOSELECTIVE 1,2-CARBONYL TRANSPOSITION OF Δ^2-CYCLOHEXENONE SYSTEMS LEADING TO THE POSITIONALLY ISOMERIC Δ^2-CYCLOHEXENONES

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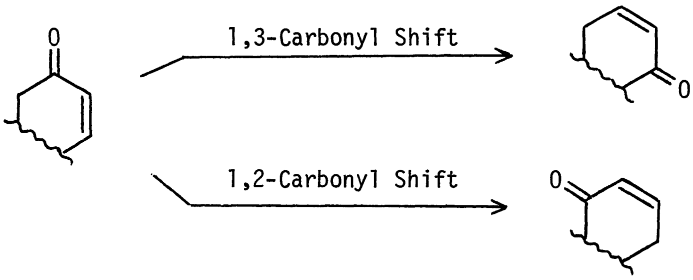
A new, facile procedure is described which allows the regioselective 1,2-carbonyl transposition of Δ^2-cyclohexenone systems leading to the positionally isomeric Δ^2-cyclohexenones. The scope and limitation of the method is presented.

The ability to transpose both the carbonyl group and the olefinic bond within a given conjugated enone framework (*i.e.*, enone transposition) enhances the synthetic importance of the enone synthons and thereby offers a wide degree of latitude in organic synthesis. Although a number of synthetic methods have become available for effecting 1,3-carbonyl transposition of α,β-enones leading to the isomeric α,β-enones (eq 1),[1,2] there have been only a limited number of methodologies for 1,2-carbonyl transposition of α,β-enones leading to the isomeric α,β-enones (eq 2).[3,4]



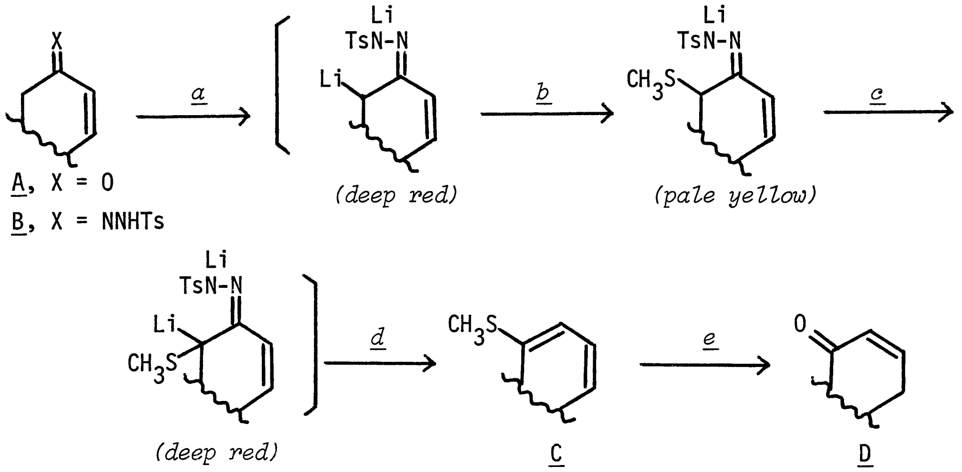
(1)

(2)

Herein we wish to report a new, facile procedure for the regioselective 1,2-carbonyl transposition of Δ^2-cyclohexenone systems leading to the positionally isomeric Δ^2-cyclohexenones which is represented by the conversion of A→D (Scheme 1). The complete transformation is therefore a three-step operation and the key step is the one-pot conversion of the enone tosylhydrazone (B) to the dienol thioether (C) which can be performed in the same manner as recently reported by our laboratory for the one-pot conversion of ketone tosylhydrazone to the enol thioether of transposed ketone.[6] Hydrolysis of the dienol thioether (C) affords the transposed α,β-enone (D) *via* migration of the olefinic bond.[3a] Typical procedures employed for the synthetic sequence are shown in Scheme 1.[7,8]

Table 1 shows the results in applying this synthetic sequence to monocyclic and fused-ring systems. The most notable feature of this approach compared with the existing ones[3] is the shorter length of the synthetic sequence which results from the fact that both the oxidation and reduction steps required for the carbonyl transposition can be accomplished in a one-pot manner. The versatility of our procedure is particularly well demonstrated by the transformations of

Scheme 1



a: BuLi (2.1 equiv), THF- $(CH_3)_2NCH_2CH_2N(CH_3)_2$ (v/v=2 : 1), -78°C, *b*: CH_3SSCH_3 (1.0 equiv), -78—0°C, *c*: BuLi (1.0 equiv), -78°C, *d*: room temp., 5—8 hr → H_2O, *e*: $HgCl_2$(3 equiv), aq. CH_3CN, 50-80°C

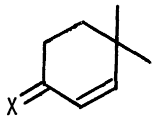
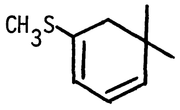
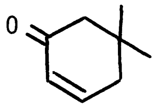
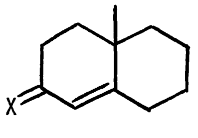
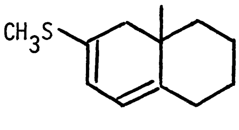
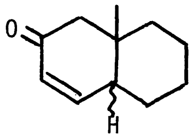
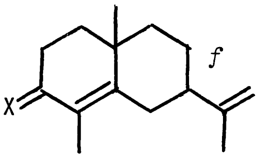
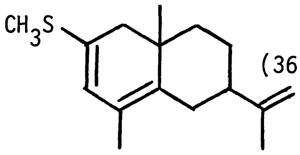
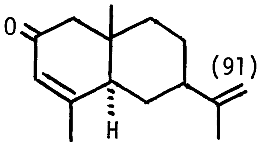
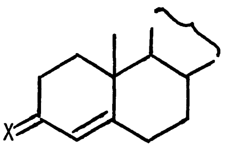
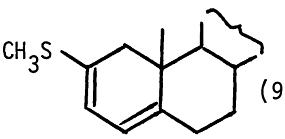
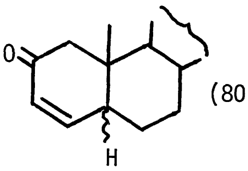
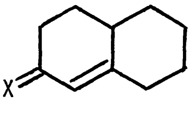
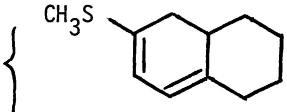
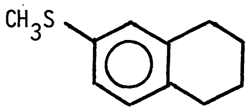
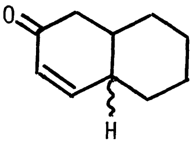
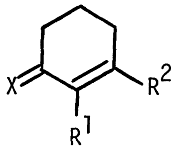
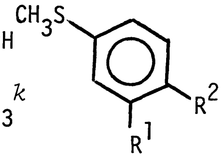
Δ^4-3-octalone systems readily obtainable *via* the Robinson annelation to the Δ^3-2-octalone derivatives which are generally much less accessible (entries 2 — 4, Table 1).

At this point, we should mention the stereochemical outcome in applying this enone transposition to the fused-ring systems. As shown in Table 1, we found that hydrolysis of the dienol thioethers derived from Δ^4-3-octalone systems afforded the *trans*-fused isomer as the sole product (entry 3) or resulted in the formation of a mixture of the *cis*- and *trans*-fused isomers (entries 2 and 4). Hence it appears that the stereochemical outcome depends upon the structure of the bicyclic dienol thioethers and is difficult to predict.

Finally, let us discuss the scope and limitation of this enone transposition. As shown in entries 5 - 7 (Table 1), we found that application of the procedure for the one-pot conversion of B→C described above to the Δ^2-cyclohexenone systems in which any ring-methylenes are not *geminally* substituted gave rise to considerable amounts of the aromatized products. These thioanisole derivatives are formed presumably *via* rapid aromatization (dehydrogenation) of the once formed dienol thioethers by exposure to air during the work-ups. Consequently, the present procedure is not applicable to Δ^2-cyclohexenone systems of which the dienol thioethers are prone to undergo aromatization by atmospheric oxygen.

In summary, the one-pot conversion of Δ^2-cyclohexenone tosylhydrazones to the dienol thioethers which relies upon the direct sulfenylation of the dianions followed by the Shapiro reaction of the sulfenylated dianion provides a short, efficient method for the regioselective 1,2-carbonyl transposition, ultimately yielding the positionally isomeric Δ^2-cyclohexenones. Further improvement and extensions of the method outlined here are in progress.

Table 1

Entry	Enone Tosylhydrazone[a] (X=NNHTs)	Dienol Thioether[b] (% yield)[c]	Transposed Enone[b] (% yield)[c]
1		 (75)	 (68)
2	 [d]	 (80)	 (73) (*cis*/*trans*=1:3)[e]
3	 [f]	 (36)	 (91)[g]
4	 (4-Cholesten-3-one)	 (94)	 (80)[h] (*cis*/*trans*=1:1)[i]
5		 (28)  (39)	 (<5)[j]
6	 $R^1=CH_3$, $R^2=H$	 (31)[l]	
7	$R^1=H$, $R^2=CH_3$[k]	(42)[l]	

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[a] Unless otherwise noted, tosylhydrazones were prepared by the standard method and their mp's were in accord with the reported ones. [b] All products exhibited spectral data in accord with the assigned structures or with the reported values. [c] Isolated yeilds after TLC or column chromatography; no attempts were made to optimize yields. [d] Mp 152.8-156.1°C [e] Determined by NMR assay. For the NMR data, see ref 9. [f] Mp 74.1-79.5°C [g] For the stereochemical argument, see ref 10. [h] The hydrolysis was carried out in aqueous dioxane in place of aqueous acetonitrile. [i] Determined by NMR assay. For the NMR data, see ref 11. [j] Aromatization also took place during the hydrolysis. [k] Mp 155.7-158.0°C [l] No dienol thioether was isolated.

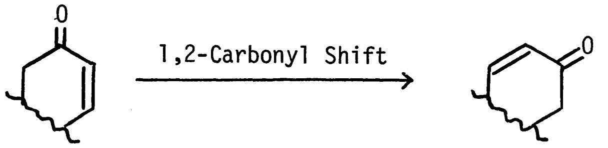
References and Notes

1) For a general review on carbonyl transposition, see T. Nakai and T. Mimura, *Yuki Gosei Kagaku Kyokaishi (J. Synth. Org. Chem., Jpn.)*, 35, 964 (1977).

2) Representative examples: P. S. Wharton and D. H. Bohlen, *J. Org. Chem.*, 26, 3615 (1961); G. Büchi and J. C. Vederas, *J. Am. Chem. Soc.*, 94, 9128 (1972); B. M. Trost and J. L. Stanton, *ibid.*, 97, 4018 (1975); W. G. Dauben and D. M. Michno, *J. Org. Chem.*, 42, 682 (1977); T. Nakai, T. Mimura, and T. Kurokawa, *Tetrahedron Lett.*, 1978, 2895.

3) (a) B. M. Trost, K. Hiroi, and N. Holy, *J. Am. Chem. Soc.*, 97, 5873 (1975); (b) W. Oppolzer, T. Sarkar, and K. Mahalanabis, *Helv. Chim. Acta*, 59, 2012 (1976).

4) Reusch[5)] recently reported the synthetic sequence for another interesting type of 1,2-carbonyl transposition of Δ^2-cyclohexenone systems as depicted by eq 3.



(3)

5) K. M. Patel and W. Reusch, *Synth. Commun.*, 5, 27 (1975).

6) T. Nakai and T. Mimura, *Tetrahedron Lett.*, 1979, 531; *Chem. Lett.*, 1980, 931.

7) For generations of dianions of enone tosylhydrazones and their Shapiro olefin forming reactions, see W. G. Dauben, G. T. Rivers, and W. T. Zimmerman, *J. Am. Chem. Soc.*, 99, 3414 (1977); A. R. Chamberlin, J. F.Stemke, and F. T. Bond., *J. Org. Chem.*, 43, 147 (1978), and references cited therein.

8) It is worthy of note that each of the organolithium species has the characteristic color shown in Scheme 1 and hence the reaction sequence was easy to monitor by the color changes.

9) NMR (CCl_4, TMS):δ 0.92 (s, *trans*-CH_3), 1.16 (s, *cis*-CH_3), 5.98 (d, J=10.35 Hz, *cis*-4-H), 6.00 (d, J=10.50 Hz, *trnas*-4-H), 6.22 (dd, J=10.50 and 1.95 Hz, *cis*-3-H), 6.84 (dd, J= 10.35 and 1.50 Hz, *trans*-3-H). For the NMR assignments, see J. A. Marshall and R. A. Ruden, *J. Org. Chem.*, 37, 659 (1972).

10) The presence of the single peak (at δ0.98) due to the angular methyl indicates that only the *trans*-fused isomer was formed.

11) Mp 105.2-109.0°C (lit. mp 109°C for the *trans*-fused isomer: E. Mincione,G. Ortaggi, and A. Sirna, *Synthesis*, 1977, 773); NMR (CCl_4, TMS):δ 6.48 (dd, J=10.05 and 1.80 Hz, *cis*- 4-H), 6.55 (dd, J=10.05 and 1.95 Hz, *trans*-4-H), 5.96 (d, J=10.05 Hz, *cis* -3-H), 6.00 (d, J=10.05, *trans*-3-H).

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