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A NEW APPROACH TO REGIOCONTROLLED ENONE TRANSPOSITIONS BASED ON THE FACILE CONVERSION OF α,β-ENONE TOSYLHYDRAZONES TO THE TRANSPOSED ALLYLIC SULFIDES

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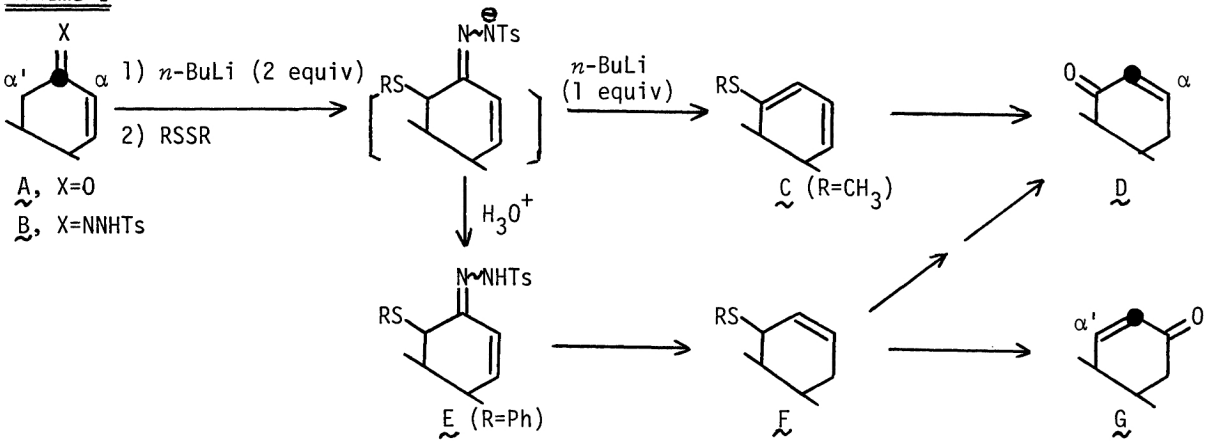
A new, facile method for the conversion of α,β-enone tosylhydrazones to the transposed allylic sulfides is described which combines sulfenylation of the hydrazone dianions with hydride reduction of the α'-sulfenylated hydrazones. This novel route to allylic sulfides can constitute the sequences for the two directionally different types of enone transposition with 1,2-carbonyl shift.

The importance of α,β-enone synthons in organic chemistry makes the ability to transpose the conjugated enone function within a molecule an important and challenging problem.[1] Although numerous methods are available for effecting such enone transposition with 1,3-carbonyl shift,[1,2] there have existed only a limited number of methods for enone transposition with 1,2-carbonyl shift.[3] Recently we have developed a facile procedure for the 1,2-enone transposition represented by the conversion A ⟶ D (Scheme I).[4] The synthetic sequence, though operationally simpler and shorter than existing ones,[3] suffers from a serious limitation: this procedure is not applicable to Δ^2-cyclohexenones in which any ring-methylenes are not *geminally* substituted because of the spontaneous aromatization of the dienol thioether (C). To solve the problem, we have now explored

Scheme I



the conversion of the easily isolable α'-sulfenylated hydrazones (E) to the allylic sulfides (F) since F could be elaborated to either the transposed enones D or G.

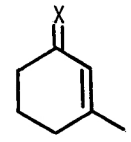
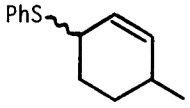
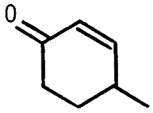
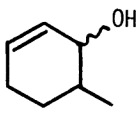
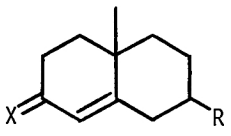
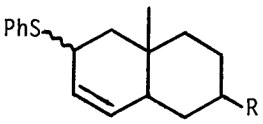
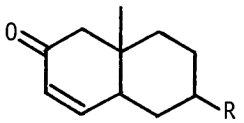
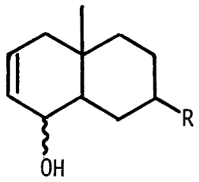
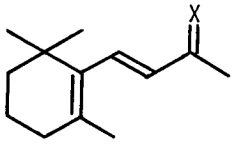
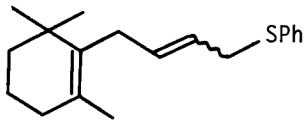
This report presents the successful realization of the conversion of E to F with sodium borohydride in acetic acid, thereby providing the synthetic sequences for the two directionally different enone transpositions leading to either D or G. The requisite α'-phenylthio hydrazones (E) were obtained quantitatively via direct sulfenylation of the dianions generated from B with diphenyl disulfide followed by quenching with aqueous ammonium chloride.[5] In view of the successful utility of sodium borohydride (SBH)[6] and sodium cyanoborohydride (SCBH)[7] in acetic acid for the reduction of simple α,β-enone tosylhydrazones to the transposed olefins, we studied the crucial reduction of E with the two reagent systems in some details. We found that more than a 10-fold excess of SBH was required for completion of the reduction. No distinct advantage was found with more expensive SCBH which gave results comparable to SBH.

The following procedure is illustrative of the optimal reduction of E. SBH (90 mmol) was added by portions to a solution of E (8.0-9.0 mmol) in 100 ml of glacial acetic acid at room temperature and the mixture was stirred at 70°C for 4 h. The mixture was poured onto ice, treated with aqueous sodium hydroxide, and extracted with ether. Evaporation followed by column-chromatographic purification (alumina) afforded the product sulfide (F). Representative examples are given in Table 1.

With the successful development of the facile conversion of E to F, our efforts were next directed toward the elaboration of F to the transposed enones D and G. Elaboration of F to D was easily accomplished by oxidation of F to the sulfoxide (H) followed by application of the Trost's procedure originally developed for 1,3-carbonyl transposition.[8] Typical procedures employed for the elaboration are shown in Scheme II. On the other hand, the sulfoxide H was subjected to the [2,3]sigmatropic rearrangement[9] to afford the allylic alcohol (J), thus furnishing the other enone transposition (Scheme II). We found that the rearrangement was most conveniently perfomed in tetrahydrofuran by using thiophenol (1 equiv) and potassium *t*-butoxide (5 equiv).[10] Representative examples of the two transpositions are given in Table 1.

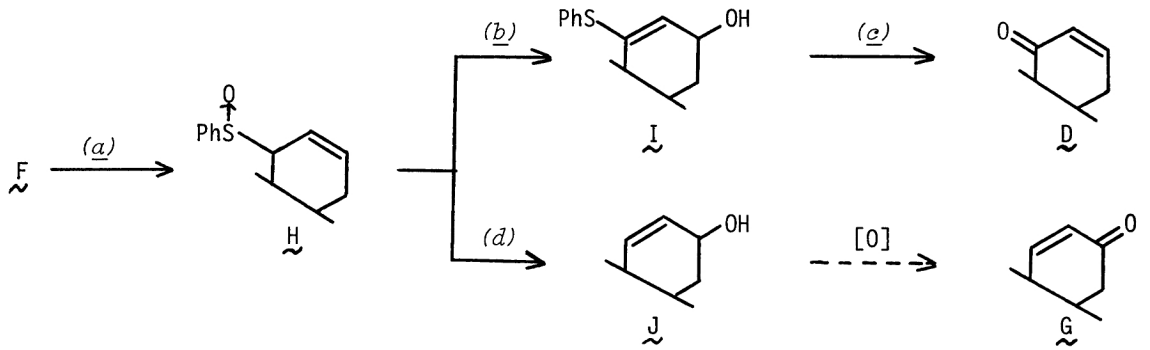
The present approach to the 1,2-enone transposition of A→D, though more lengthy than our previous one,[4] can remove the serious limitation associated with the latter. Entry 1 particularly illustrates the versatility of the present one since application of the previous one to this cyclohexenone system failed, leading instead to the formation of the thioanisole derivative.[4] In addition, the present approach provides the remarkable flexibility, thereby making it possible to prepare either the isomeric enones D or G from the single intermediate. Of particular interest is the feasibility of the novel enone transposition of A→G in which the carbonyl group migrates

Table 1

Entry	Tosylhydrazone (B) (X = NNHTs)	Allylic Sulfide (F)[a] (%Yield of E→F)[b]	Transposed Enone (D)[a] (%Yield of F→D)[b]	Transposed Alcohol (J)[a] (%Yield of F→J)[b]
1		 (78)	 (60)	 (71)
				
2	R = H	(84)	(52)	(96)
3	R = $C(CH_3)=CH_2$	(95)	(43)	(78)
4			(84)[c] [E/Z = 1.0][d]	

[a] All products exhibited spectral (IR and NMR) data in accord with the assigned structures. The spectral data will be described in a full paper. The exact stereochemistry, if any, of the product has not been determined yet. [b] Refers to isolated yield via column chromatography or TLC; not optimized yet. [c] Based on the reacted hydrazone. In this case, the reduction was quite sluggish and the starting hydrazone was recovered in 38% yield under the standard condition. [d] Determined by NMR assay.

Scheme II



(a): MCPBA, CH_2Cl_2, -78°C; (b): $LiN(C_2H_5)_2$, THF, -78°C→PhSSPh→room temp.;

(c): $HgCl_2$(3 equiv), aq. CH_3CN, 70°C, 5 h; (d): PhSH (1 equiv)/*t*-BuOK (5 equiv), THF, refl., 5 h.

to the position formerly occupied by the olefinic carbon. Furthermore, the fact that all intermediates in the sequences are stable, easily isolable compounds allows for the possibility of other structural modifications. Further applications of these methods are in progress.

References

1) For a general review on carbonyl transposition including enone transposition, see T. Nakai and T. Mimura, *Yuki Gosei Kagaku Kyokai Shi*, 35, 964 (1977).

2) For a list of recent references, consult ref 4.

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

4) T. Mimura and T. Nakai, *Chem. Lett.*, 1980, 1099.

5) Typically, a solution of diphenyl disulfide (1.0 equiv) in tetrahydrofuran (THF) was added dropwise to a red solution of the dianion of E generated by the reported method (ref 4) in THF-*N,N,N',N'*-tetramethylethylene diamine (2 : 1 (*vol*)) and the mixture was stirred at that temperature. The mixture was quenched with saturated aqueous ammonium chloride followed by usual extractive work-up gave the monosulfenylated hydrazone (E) in 91-99% of isolated yields.

6) R. O. Hutchins and N. R. Natale, *J. Org. Chem.*, 43, 2299 (1978).

7) R. O. Hutchins, C. A. Milewski, and B. E. Maryanoff, *J. Am. Chem. Soc.*, 95, 3662 (1973); R. O. Hutchins, M. Kacher, and L. Rua, *J. Org. Chem.*, 40, 923 (1975); E. J. Taylor and C. Derassi, *J. Am. Chem. Soc.*, 98, 2275 (1976). Catecolborane is also effective for a similar reduction of enone tosylhydrazones: G. W. Kabalka, *Org. Prep. Proced. Int.*, 9, 133 (1977).

8) B. M. Trost and J. L. Stanton, *J. Am. Chem. Soc.*, 97, 4018 (1975).

9) Review: D. A. Evans and G. C. Andrews, *Acc. Chem. Res.*, 7, 147 (1975).

10) Originally, trimethyl phosphite has been used as the thiophilic agent (ref 9).

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