

**Communication**

**Asymmetric [3, 3]-Sigmatropic Rearrangement  
of Allylic Enamine**

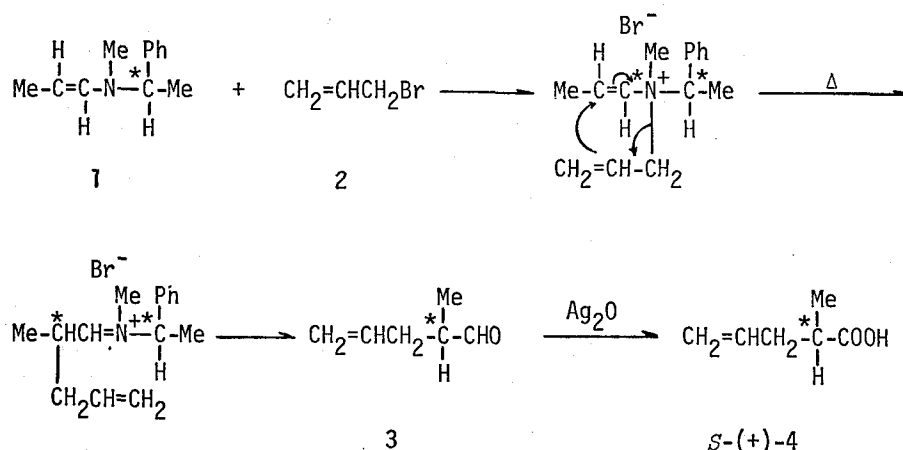
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In the series of asymmetric synthesis studies, we reported some achievements in alkylation of chiral enamines.<sup>1)</sup>

This paper deals with another asymmetric synthesis by the use of chiral enamine eventually to give a chiral aldehyde. (*R*)-(+)-*N*-methyl-phenylethylamino-*E*-propene (**1**, 17.5 g, 0.1 mole), prepared from (*R*)-(+)-*N*-methyl-benzylamine ( $[\alpha]_D^{25}$  54.5°) and propanal, when heated with allyl bromide (**2**, 12 g, 0.1 mole) in acetonitrile (30 ml), followed by hydrolysis, yielded 2-methyl-4-pentalenal (**3**). This was immediately converted without purification by silver oxide oxidation into (+)-2-methyl-4-pentenoic acid (**4**, 7.18 g, 63% yield, bp 110–112°C (30 Torr),  $[\alpha]_D^{25}$  3.6° (*c*, 0.356; MeOH)) of the established *S*-configuration:<sup>2)</sup> amide; mp 75.5–76°C, Found. C; 63.58, H; 9.52, N; 12.21. Calcd for C<sub>6</sub>H<sub>11</sub>NO: C, 63.71; H, 9.73; N, 12.39%. The optical purity proved to be 45% on the basis of the reported maximum rotation, ±7.97°.<sup>2)</sup> It then follows that the parent aldehyde (+)-**3** can be assigned the *S*-configuration and should have the optical purity of 45%.

With (*S*)-(–)-**1** used as the starting material, the enantiomeric product, (*R*)-(–)-**4**, was obtained in a comparable asymmetric bias, ( $[\alpha]_D^{25}$  –3.4°; 42.6% optical purity).



[3, 3]-Sigmatropic Rearrangement of Allylic Enamine

In the light of analogous enamine reactions in literature,<sup>3)</sup> the direct *C*-alkylation seems very unlikely in the present system. Alternative mechanism would probably be that which involves the initial *N*-alkylation, followed by either [3, 3]sigmatropic rearrangement or dissociation-nucleophilic displacement.

It should be noted that the initial *N*-quarternization induces an additional chirality on the  $sp^3$ -N atom, thus producing two possible diastereomeric intermediates ( $C_R:N_S$ ) and ( $C_R:N_R$ ) in an equilibrium dependent on relative conformational stabilities.

The [3, 3] shift process can be looked upon as constituting a self-immolative asymmetric synthesis, in which the chirality originally residing on nitrogen is transferred to  $sp^2$ -carbon at the expense of the former. The [3, 3] shift would be preferred in view of the ease with which the concerted mechanism operates under the reaction conditions employed here. Consistently, Brannock<sup>4)</sup> proposed the allylic rearrangement of the initially formed quarternary ammonium salt in an analogous achiral system which involved *N,N*-dimethylaminobutene and crotyl bromide.

Should the [3, 3] sigmatropic rearrangement be valid in the present case, chair-like transition state conformers A, B, C, A', B', and C', could reasonably be assumed to be in operation for thermally allowed process. This is cogently supported by the theoretical consideration based on the Woodward-Hoffmann rule as well as by analogy to the stereochemical outcome observed in closely similar allylic enamine<sup>5)</sup> and its carbon analog.<sup>6)</sup>

Each three staggered conformations are conceivable for diastereomeric intermediates ( $C_R:N_S$ ) and ( $C_R:N_R$ ) and their relative conformational stabilities were

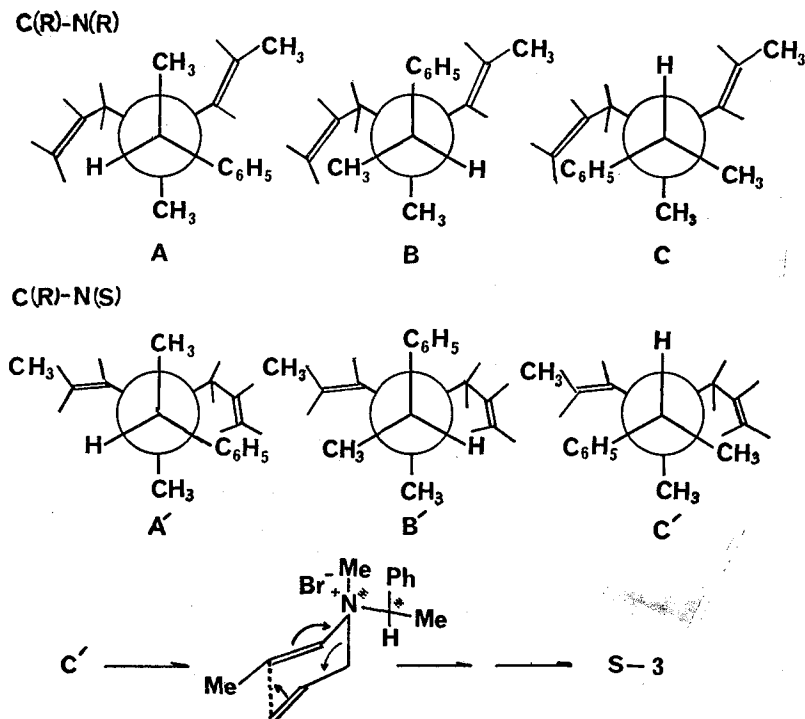


Fig. 1.

assessed qualitatively by comparing the total sum of gauche interactions between ligands around the C\*-N\* bond. This indicated the relative conformational stabilities to be in the order B>A'=B'>A>C>C' and the main path of this rearrangement to proceed through thermodynamically the most stable C' in a 6-membered cyclic transition state conformation. The Woodward-Hoffmann rule of conservation of orbital symmetry, as applied to the thermal process of the C<sub>R</sub>:N<sub>S</sub> conformer (C'), predicts the transfer of S-chirality on the sp<sup>3</sup>-N to the sp<sup>2</sup>-C, giving rise to the tetrahedral carbon with S-configuration, in good agreement with the finding.

In view of the fact that the transfer of chirality is nearly quantitative in general [3, 3]sigmatropic rearrangements, the asymmetric yield 45% found for the present system is the direct reflection of the distribution of diastereomeric transition state conformers  $\Sigma N_{\text{O}_{\text{RNS}}}: \Sigma N_{\text{O}_{\text{RRR}}}=72.5:27.5$  ( $\Delta\Delta G^\ddagger=0.58$  Kcal/mol).

Finally, it seems very likely that the doubly suprafacial mode would be reasonably preferred for the present rearrangement to the doubly antarafacial path, because of the geometric and therefore energetic stringency of the latter.

#### REFERENCES

- (1) J. Oda, T. Igarashi, and Y. Inouye, *Bull. Inst. Chem. Res., Kyoto Univ.*, **50**, 222 (1972); *Agr. Biol. Chem.*, **34**, 811 (1970).
- (2) Stallberg-Stenhagen, *Ark. Kemi.*, 23A, No. 15 (1946); G. Stallberg, *Acta Chem. Scand.*, **11**, 1430 (1957); G. I. Fray and N. J. Polgar, *J. Chem. Soc.*, 2036 (1956).
- (3) U. K. Pandit, W. A. Zwart Voorspuij, and P. Houdewind, *Tetrahedron Letters*, 1997 (1972); P. Houdewind and U. K. Pandit, *ibid.*, 2359 (1974).
- (4) K. C. Brannock and R. D. Burpitt, *J. Org. Chem.*, **26**, 3576 (1961).
- (5) R. K. Hill and N. W. Gilman, *Tetrahedron Letters*, 1421 (1967).
- (6) R. K. Hill and N. W. Gilman, *Chem. Commun.*, 619 (1967).