

Sambasiva Swaminathan

A Tribute



Swaminathan was born on April 20, 1923 at Madras (now Chennai), Tamil Nadu, India. He received his college education at Annamalai University and passed with Honours in Chemistry in 1943. Immediately thereafter, he joined the Indian Institute of Science, Bangalore, where he worked with Prof. P C Guha and was awarded his Associateship of the Institute, equivalent to a Masters degree by thesis.

In those days it was rather unusual for a talented young man to take to a career in science and it was the Civil Service that was most attractive. His passion for chemistry, however, propelled him to take up a career in chemistry. Swaminathan was offered a Government of India Scholarship to work with Prof. H. R. Snyder at the University of Illinois. After being awarded the PhD degree he moved to the Ohio State University to work as a post doctoral fellow with Prof. M. S. Newman for three years. Subsequently he worked as a Research Chemist for a few months with Upjohn & Co. At this stage Swaminathan decided to go back to India and start his independent academic research. In 1953 he joined the Department of Organic Chemistry, University of Madras as a Reader and he has continued this association for over five decades.

He took upon himself the task of building up a modern organic chemical research laboratory in Madras. In 1960 he became Professor and Head of the Department and in the following years the department became one of the most active and visible centers of research in organic chemistry. Although he retired formally in 1983 he continues his research with considerable enthusiasm and in 2004 he published a research paper on asymmetric synthesis, after his 80th birthday!

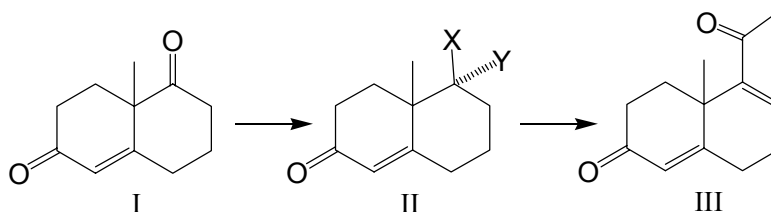
Swaminathan received many awards and recognitions for his outstanding contributions to organic chemistry including the Prof. T. R. Govindachari award (1980), the Sir P. C. Ray medal (1981), a Life-time achievement award of the Chemical Research Society of India (2001), Fellowship of Indian Academy of Sciences and Fellowship of the Indian National Science Academy. He has directed over 35 Ph.D projects and many of his students now occupy important positions in industry and academia.

He was one of the five Founder Trustees of the National Organic Symposium Trust (NOST) formed in 1983 for periodically organizing Symposia in Organic Chemistry in India. This organization continues to promote interactions among active research workers both from India and outside of India. He has been actively associated with the Madras Science Association formed in 1969 to promote the popularization and teaching of science.

Research Interests:

Swaminathan has made significant contributions in the following areas: (1) Synthetic approaches to non-aromatic steroids; (2) molecular rearrangements; (3) alicyclic chemistry; (4) chemistry of indole and related heterocycles; (5) stereochemistry of hindered benzophenones and related compounds; and (6) asymmetric synthesis.

(1) Synthetic Approaches to Non-aromatic Steroids. The main objective of the work in this area was to utilize 1,6-dioxo-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (I) as the starting material for the synthesis of non-aromatic steroids. This was elaborated to 1-acetyl-6-oxo-8a-methyl-3,4,6,7,8,8a-hexahydronaphthalene (III) as follows.¹



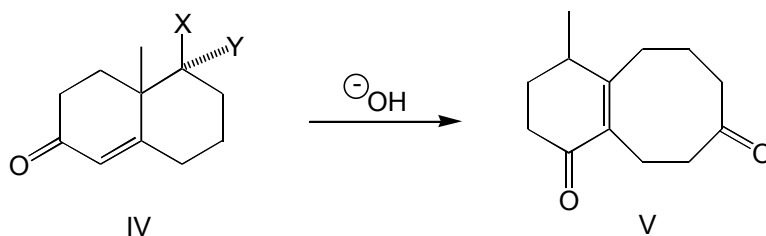
a, X = -OH, Y = -C≡CH

b, X = -C≡CH, Y = -OH

In other variations arrived at utilizing IIa and IIb, they were reduced to the corresponding allyl alcohols IVa and IVb. The carbinol IVa was treated with 2-methylcyclopentane-1,3-dione under selected conditions to furnish a tetraketone which cyclized readily to an -oxo-steroid.²

(2) Molecular Rearrangements. Perhaps the most important contribution made by Swaminathan and his group was the discovery in 1962 of a novel molecular rearrangement.³ He has reviewed contributions from his laboratories and from elsewhere in the above area up to

1983.⁴ The first report described the rearrangement of the allyl alcohols IVa (and its epimer IVb) to the ring enlarged dione V when treated with a base.

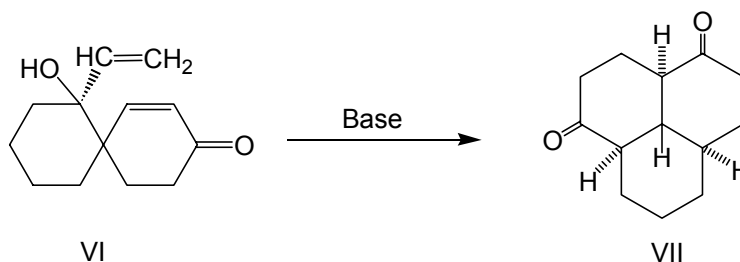


IV a, X = OH, Y = -CH = CH₂

IV b, X = -CH = CH₂, Y = -OH

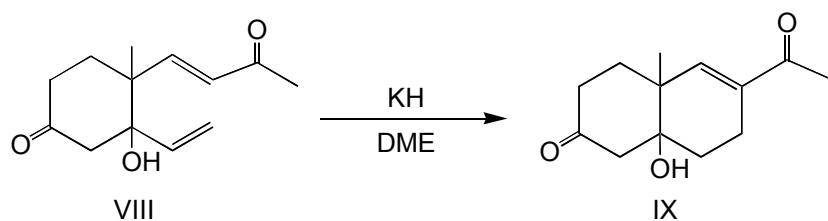
Several studies bearing on the scope of this rearrangement and also its mechanistic aspects have been carried out. Incidentally, the rearrangement of IVa to V is the first example reported in the literature of an anionic oxy-Cope rearrangement. Such anionic oxy-Cope rearrangements have come into great prominence since 1975 for the synthesis of carbocyclic systems. From further studies of the rearrangements, Swaminathan reported that transannular interactions occur along with ring expansions.^{5,6} Transannular reactions of a similar type were also encountered in metal-ammonium reduction of dione V.⁷

In other studies of base-catalyzed rearrangements of oxy-Cope systems, Swaminathan and his colleagues have shown that the spiro system VI rearranges to the perhydrophenalene dione VII in the presence of a base.⁸



He also worked out the synthesis of benzotropones based on the anionic oxy-Cope rearrangement. A novel synthesis of *trans*-octalenones of type IX by a base catalysed rearrangement of the oxy-Cope system VIII has also been reported by him.⁹

He demonstrated that the mechanism of the base catalyzed rearrangement of an oxy-Cope system could be either concerted or stepwise, depending on the solvent and the reagent used.¹⁰



Incidental to the above studies, it was found that 2-bromocyclohexane-1,3-dione suffered ring contraction on treatment with organic bases. Swaminathan has made significant contributions to the chemistry of cyclic 1,3-ketones and also to the chemistry of acetylenic compounds in the course of the above rearrangement studies.

In other studies on acetylenic compounds, Swaminathan reinvestigated the Diels-Alder reaction of acetylenic ketones with cyclopentadiene and showed that the adducts were dimers, the structures of which were determined. The photochemistry of these dimers has also been reported.¹¹

(3) Alicyclic Chemistry. With a view to extending the scope of the anionic oxy-Cope rearrangement, Swaminathan synthesized a number of bicyclic diketones of potential use in the synthesis of natural products and new carbocyclic systems. Incidental to this synthesis, a reagent for a facile 5-carbon annelation of a cyclonone was found.¹² Other studies in alicyclic chemistry included a facile 4-carbon annelation sequence involving a Wittig reaction, a one-pot synthesis of 2-alkyl cyclohexanones and a Diels-Alder reaction.

(4) Chemistry of Indole and Related Heterocycles. Swaminathan and his group were the first to show that contrary to the earlier belief, 3-substituted indoles undergo the Mannich reaction to give *N*-Mannich bases.¹³ He also developed new practical syntheses of thieno [2,3-*b*] and thieno [3,2-*b*] pyrrole systems.¹⁴ His work on the synthesis of 6-aryl-4-methoxy- α -pyrones turned out to be very useful because these compounds are analogues of the naturally occurring marindenin and as such are potential tranquilizers.

(5) Stereochemistry of Hindered Benzophenones and Derivatives. Swaminathan's group has made a significant contribution to the field of stereochemistry. He demonstrated for the first time the existence of optical isomerism caused by steric interactions in suitably substituted benzophenone derivatives.¹⁵ Interest in the stereochemistry of similarly substituted diphenyl ethers led Swaminathan to obtain evidence for the participation of an *ortho*-substituted carbonyl group in aromatic nucleophilic substitution reactions. This was the first convincing chemical evidence for the participation of a neighboring group in aromatic nucleophilic substitution reactions.¹⁶

(6) Asymmetric Synthesis. Swaminathan and his group have reported asymmetric synthesis without solvent of the well known Wieland-Miescher and Hajos' diketones.¹⁷ They proposed a template mechanism for the formation of asymmetric aldol products in the above synthesis.¹⁸

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Selected Publications:

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7. Balasubramanian K, Chandrasekaran S, Rajagopalan K & Swaminathan S, *Tetrahedron*, **34** (1978) 1561.
8. Seshu Sekhara Rao C, Kumar G, Rajagopalan K & Swaminathan S, *Tetrahedron*, **38** (1982) 2195.
9. Thangaraj K, Srinivasan P C & Swaminathan S, *Tetrahedron Lett.*, **23** (1982) 2195.
10. Uma R, Swaminathan S & Rajagopalan K, *Tetrahedron Lett.*, **25** (1984) 5825.
11. Venkataramani P S, Chandrasekaran S & Swaminathan S, *Tetrahedron*, **28** (1972) 1249.
12. Ravikumar V T, Swaminathan S & Rajagopalan K, *Tetrahedron Lett.*, **25**, (1984) 6045.
13. Swaminathan S & Ranganathan S, *J. Org. Chem.*, **22** (1957) 70.
14. Srinivasan K, Srinivasan K G, Balasubramanian K K & Swaminathan S, *Synthesis*, (1973) 313.
15. Narayanan K V, Selvarajan R & Swaminathan S, *J. Chem. Soc (C)*, (1968) 540.
16. Muthukrishnan R, Kannan R & Swaminathan S, *J. Chem. Soc Perkin Trans. 1*, (1973) 2949.
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