Professor S. V. Kessar

A Tribute

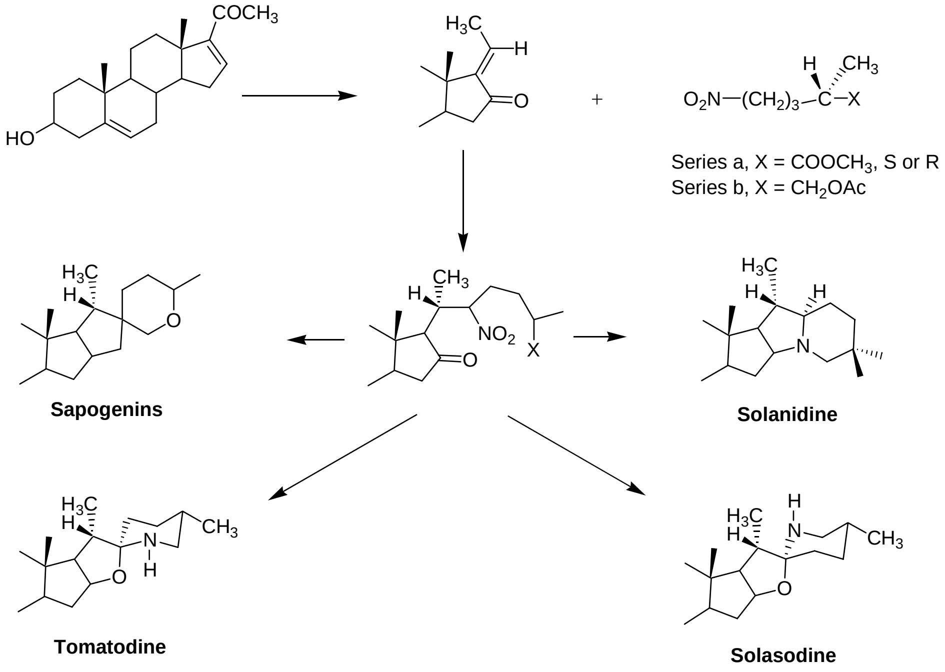
Satinder Vir Kessar was born to Susheela Devi and Durga Dass at Hoshiarpur (India) in June 1932. Though his father was a very successful lawyer, he deeply regretted his choice of profession believing that he would have been much happier administering to the sick rather than to the litigant even if that was less lucrative. This perhaps made young Satinder grope for the right profession. After a short stint at the National Military Academy and a later competitive entry into the much-coveted Civil Service, he realized that scientific research/teaching was his true calling. Ever since, he stuck to it so tenaciously that his long time colleague Prof. Harkrishan Singh once jokingly remarked that Kessar is too focused and too cunning to be trapped in by the glitter of high administrative positions.

After early schooling at D.A.V. high school, Kessar entered the Department of Chemistry of the Panjab University as a B.Sc. student and thus began an association, which is now into its sixth decade. Graduating in 1953 with a first class first, he worked under the supervision Prof. S.M. Mukherji for an M.Sc. degree by research and published his first joint paper in *Nature* in 1954.[1] Immediately afterwards he joined the Ph.D. programme of University of Southern California at Los Angles. His dissertation on the synthesis of pyrrolines was guided by Prof. M.C Kloetzel.[2] This and a brief post-doctoral tenure with Prof. S.W. Benson, an authority in kinetics, evoked his fascination for synthetic methodology and reaction mechanisms, areas in which he has been working since then. I am giving here a brief description of his research activities over the decades under three sub-headings:

a) Total synthesis of heterosteroids, steroidal alkaloids and sapogenins

Around the time of Kessar's return to the Panjab University in 1959, there was world-wide interest in the synthesis of heterosteroids and, thus, he also decided to join this club. His early contribution in this area included the syntheses of 13, 16-aza and 15-thia equilenins. A semi-chair conformation for ring C of these molecules was established by extensive NMR studies.[3-6]

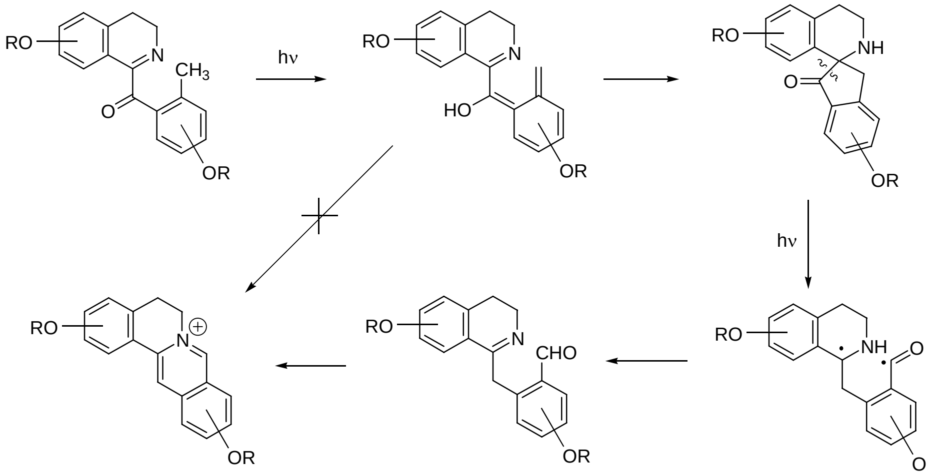
In the sixties, steroidal alkaloids and sapogenins with additional rings, heteroatoms and stereogenic centers were considered a formidable synthetic challenge. The first formal total synthesis of diosogenin by Sondheimer was considered a landmark in this sense. It involved step-by-step elaboration of a four ring relay material and in its final stage, crystals of C-26 diastereomers were separated by hand picking. Soon afterwards Kessar's group disclosed an approach to diosogenin which was short, allowed control at all stereocentres and was versatile enough to provide access not only to other members of the sapogenin family but also to two other important groups of steroidal alkaloids.[7]



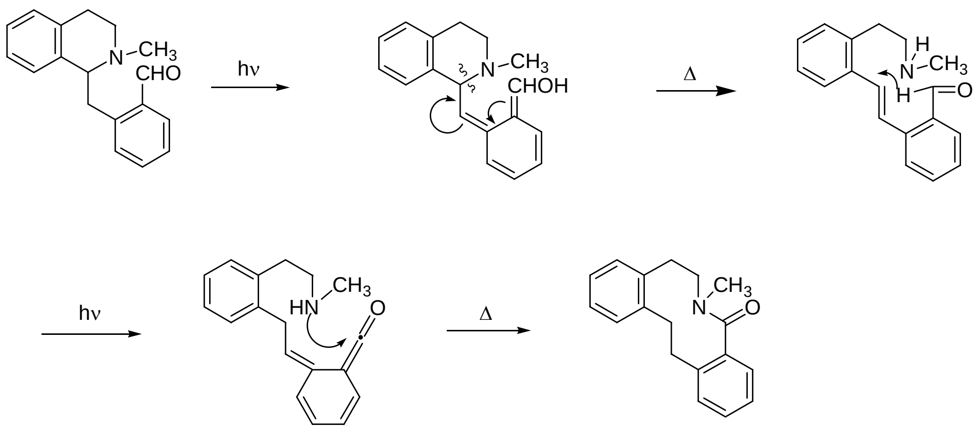
Thereafter followed a series of papers on the synthesis of kryptogenin, yamogenin, isonorthogenin, septrumgenin, solanidine, solasodine and tomatodine.[8-11] This strategy of steroselective stitching of a relay α,β-unsaturated ketone and a nitroalkane with appropriate masked functionalities was conceived four decades ago and still provides the most effective access to hexacyclic steroidal natural products.

b) Photochemical and thermal generation of reactive intermediates and their novel transformations

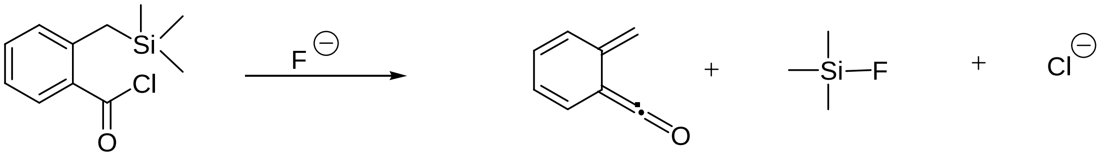
Kessar's early work in photochemistry was concerned with the synthesis of benzophenanthridine alkaloids, which were attracting attention due to promising anticancer activity. His route involved photolysis of halogenated benzanilides which underwent direct or aryl radical mediated cyclization.[12-13] His research interest then shifted towards synthesis through unusual phototransformations of quinodimethane intermediates formed by γ-hydrogen abstraction. For example, it was shown that irradiation of keto-imines can lead to berberines through a spiro intermediate. Direct electrocyclization of the first formed triene intermediate was ruled out by substituent labelling of ring D.[14] In fact Japanese workers later used this reaction to synthesize spiroisoquinoline alkaloids.



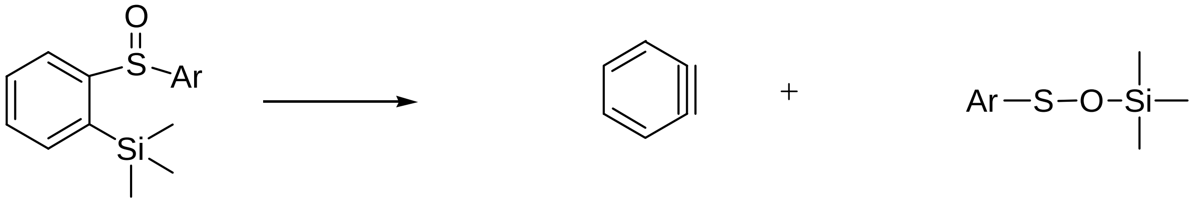
Perhaps even more fascinating was the Kessar group's photoconversion of a related aminoaldehyde to a 10-membered ring alkaloidal framework.[15] This reaction was shown by deuterium labeling to involve the cascade of transformations given below. Formation of an oxoquinodimethane, through an unprecedented acyl hydrogen abstraction by a styryl carbon, was firmly established by flash photolysis and infrared study of matrix isolated transients.[16]



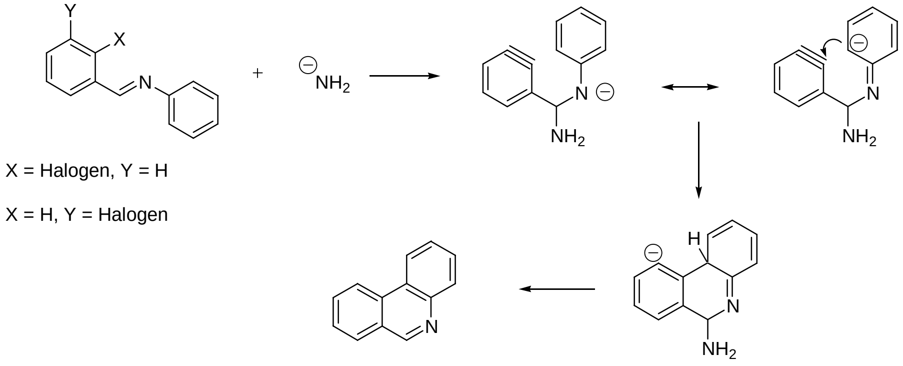
essar has also investigated new thermal routes for generating oxoquinodimethane intermediates e.g. by fluoro desilylation.[17-20]

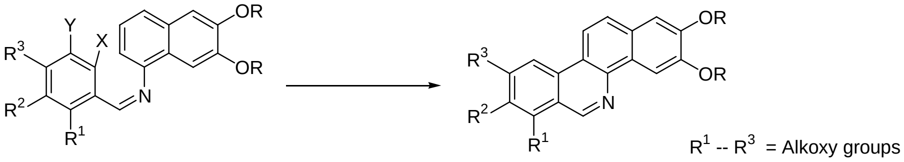


Intramolecular desilylation of arylsulphoxides was shown to proceed readily affording a most convenient and safe route for benzyne generation under neutral conditions.



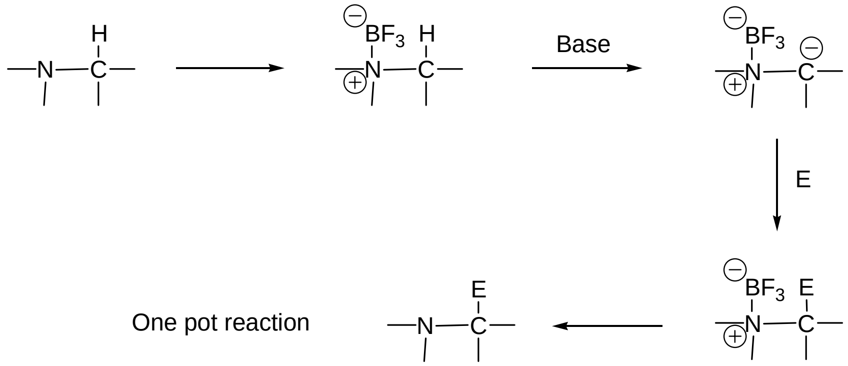
In fact Kessar's group has made another very significant contribution to benzyne chemistry by showing that intramolecular linking of this intermediate with aryl rings is possible provided anionic activation is inbuilt into the cyclisation substrate.[21-24] A most useful illustration of this principle, covered in an Accounts of Chemical Research article,[25] is cyclisation of halogenated anils to phenanthridines. This reaction has found extensive use in the synthesis of alkaloids and condensed polynuclear compounds.[26-27]



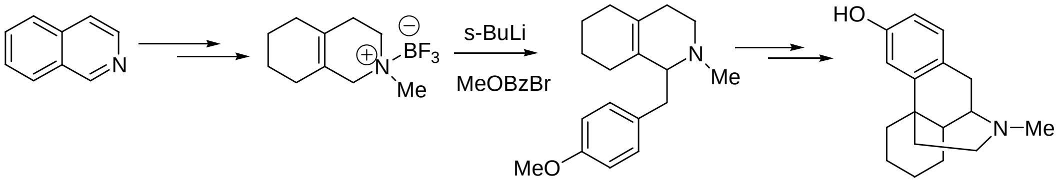


c) Lewis acid activation of tertiary amines

For the last decade, the Chandigarh group has been trying to develop a viable procedure for forming new bonds at weakly acidic α-carbon centres of amines. This is a challenge because nitrogen unlike other heteroatoms does not promote α-deprotonation and thus, the lithiation-electrophile reaction protocol is not generally useful for amines. Prof. Kessar has cleverly designed amine complexation with a Lewis acid to increase α-acidity of the methylene moiety which avoids the obvious problem of attack of the deprotonating base on the Lewis acid due to mismatch in steric or softness-hardness terms.[28-29]



This rather bold approach worked remarkably well in practice and has already grown into a widely used methodology for elaboration of tertiary amines and nitrogen hetreocycles.[30-34] Its principle, applications and potential for stereocontrol have been discussed in an article in Chemical Reviews.[32] The remarkably short synthesis of dextrophan is given below as an illustrative example.



In summary, Kessar and associates, especially Paramjit and Kamal Nain, have made significant contributions to diverse facets of synthesis. The common thread running through their work is high originality and a deep mechanistic insight.

Professor Kessar has also been active in promoting Science and Technology in India by working in the committees of University Grant Commission (UGC), Council of Scientific and Industrial Research (CSIR), Department of Science and Technology (DST) etc. He has also served as Vice-President of Indian National Science Academy (INSA), Chairman of the National IUPAC Committee, Chairman of the Research Council of a CSIR laboratory and Chairman of PAC for Organic Chemistry of the DST. He has been elected to various fellowships including that of TWAS, all the three Indian National Science Academies, Punjab Academy of Sciences, University (now Wolfson) College Cambridge (1971) and UGC National Fellowship (1976-78). Prof. Kessar has received numerous scientific awards and prizes which include Prem Singh Medal, Basudev Banerjee Medal, Bhatnagar Prize, Hari Om Award, Jawaharlal Nehru National Science Award, Goyal Prize, INSA Golden Jubilee Medal and INSA Meghnad Saha Medal for life time contribution to Science. He was also invited to the first CSIR Distinguished Professorship.

Satinder Kessar is married to Urmi who is a professor of art history at Panjab University. They have two daughters. The elder one, Bindu, is into cultural heritage work and has just authored a book on the fascinating city of Jaisalmer. Younger, Radha has opted for mathematics and is currently a fellow of the University College, Oxford. The Kessars share an interest in English literature and Hindustani Classical music and also confess to individual addictions - TV serials hers and golf-bridge his.

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Selected publications of Professor Kessar and associates referred to in this tribute

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27. Benzyne cyclisation route to benzophenanthridine alkaloids *J. Org. Chem.* **1988**, *53*, 1708.
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