Oxidative cyclisation and methylene insertion in 1,3-indandione derivatives: The mechanistic studies.

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Abstract
Dimethyl sulphoxide activated by acetic-anhydride introduces methylthiomethyl group into phenols, oxidises certain medicinally useful secondary alcohols to their corresponding ketones and brings about oxidative rearrangements in different substrates. It converts 4-hydroxy coumarins and dicoumarols, under varying conditions, to a variety of products of both pharmaceutical and chemical interest.

When 1,3-indandione (1) was interacted with this versatile reagent at water bath temperature, it afforded an ylide (2) and an oxidative cyclisation product (3). However, its interaction with Ar-CH = (CN)R, leads to the formation of a mechanistically interesting compound, indeno[1,2-b] 4H pyran (4).

DMSO alone has been used as a reagent and yields a number of products of mechanistic interest with different substrates. When 1,3-indandione (1) was refluxed with DMSO alone at elevated temperature, it results in the formation of poly(methylene-bis) 1,3-indandione (5) involving methylene group insertion between different 1,3-indandione moieties. Methylene insertion has been also observed when 1,3-indandione (1) was condensed with formaldehyde in presence of alkali carbonates or primary amines to yield (6) and (7) respectively.

Key words
1,3-indandione, oxidative-cyclisation, DMSO, acetic-anhydride, tetrad.

Introduction
Dimethyl sulphoxide acetic anhydride, a versatile reagent has been a subject of reviews and monographs with a wide range of chemical applications. It brings about oxidation of certain medicinally useful secondary alcohols (Xa), oxidative rearrangements (Xb), oxidative degradation and oxidative cyclisations in different β-diketones depending upon the reaction conditions and structure of the diketone. This reagent also converts 4-hydroxy coumarins and its 3-substituted derivatives, under varying conditions, to a variety of products of both mechanistic and chemical interest.

DMSO alone has been used as a reagent. It brings about methyl thiomethylation in barbituric acid (Xb) and ylide formation in oxazinones. When interacted with N,N-dimethyl aniline in presence of FeCl₃, it leads to the synthesis of N,N-Dimethyl Quinone-Imonium cations (Xc).

1,3-indandione a member of class of 1,3-diketo compounds has been found to yield a number of products of pharmacological importance with different substrates. Its interaction with cyclo pentanone and cyclohexanone furnishes the corresponding 2-cycloalkylidene-1,3-indandiones (Xd), shows Michael addition reaction with β-nitrovinyl benzene to give an adduct having fungicidal property which depends upon the type and location of the substituent on aryl residue. Several new 3-amino-2,4-dicyano-1-aryl-flourene-9-ones have been synthesized through addition of 1,3-indandione with arylidine malononitriles. With 5-bromo-furfural in ethanol it affords 5-bromo furfuryl diindandionyl-methane and furnishes a condensation product with indazoladione.

In view of this it was considered worth to investigate the reactions of DMSO/Ac₂O reagent or DMSO alone with 1,3-indandione under varying conditions.
Objective of the Research:- To synthesise novel compounds and investigate their properties applicable and beneficial to society in daytoday life.

Results and discussion

The reaction between 1,3-indandione and DMSO-acetic anhydride reagent when carried out at water bath temperature, reaches completion in 12 hours. Work up through removal of the reagent under vacuum followed by chromatography afforded compounds (2) and (3). The water-soluble constituent was readily identified as the ylide. (2) on the basis of its m.p. and spectral data which were in full agreement with those reported for this compound.

The other compound, m.p. 255°C isolated from this reaction was characterized as the oxidative cyclisation product (3).

Formation of this compound under these conditions is on expected lines. It can be assumed that apart from ylide formation of 2,2-methylene-bis-1,3-indandione is also formed at elevated temperature which suffers oxidative cyclisation to yield the oxidative cyclisation product, spiran (3). Scheme-1. Presence of two -CH₂ protons of the methylene group inserted in this group has been confirmed by ¹HNMR spectral studies. (Scheme-1)
Oxidative cyclisation has also been achieved in a one-pot synthesis of biologically active new indeno[1,2-b]-4H pyrans (4) by interacting 1,3-indandione with Ar-CH=C(CN)R\(^\text{18}\).

Plausible mechanism proposed for the formation of (4) can be depicted as below (Scheme-2).
DMSO alone has also been used as a reagent yielding a number of products with different substrates under varying conditions. When 1,3-indandione was refluxed with this reagent at 180°C for 5 hours and workup through addition of water afforded a single pale yellow coloured solid identified as poly(methylene-bis)-1,3-indandione (5) which provides an alternate procedure by for the synthesis of tetrad (5). The compound did not melt up to 355°C, so its mass spectrum could not be recorded and was found devoid of sulphur. However, on the basis of elemental analysis its molecular formula was found C_{39}H_{24}O_8 which indicates participation of four indandione nuclei in it. The remaining three carbon atoms must have been derived from DMSO most likely in the form of methylene groups and was assigned the structure (5).

The pmr spectrum of this compound recorded in CDCl_3 and DMSO-d_6, shows a sharp singlet equivalent to two protons at δ 8.26 which is assigned to two terminal methine protons. Apart from the multiplet spread over the aromatic region, the spectrum shows two singlets at δ 1.23 and 2.09 equivalent to four and two protons respectively. The former was assigned to the two terminal protons and latter to the two central protons.

Methylene insertion has also been observed when 1,3-indandione was condensed with formaldehyde in presence of 2-3% of alkali carbonates to yield 2,2'-methylene bis-1,3-indandione (6) and when the same reaction was carried out in presence of primary amines, it results in the formation of 2-spiro-indan-1,3-dione (7) indicating the involvement of methylene insertion in the adduct.
The mechanism proposed for the formation of (6) can be depicted as (Scheme -3)

Materials and General information

Solvents used were of AR grade. DMSO was carefully dried according to the standard procedure. 1,3-indandione has been used as substrate. All reactions were monitored by TLC plates precoated with Silica gel Si60 F254. Melting points were recorded on Tempo block melting point apparatus and are uncorrected.

Conclusion

Dimethyl sulphoxide has been used as reagent in presence of different activators or alone under different conditions. Its interaction with 1,3-indandione, under varying conditions afforded a series of compounds of both chemical and mechanistic interest. Spectral studies revealed the incorporation of methylene groups or oxidative cyclisation in different products of synthetic importance. Silica-gel used for chromatographic techniques worked as a good adsorbent and showed better resolution than other adsorbents.

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References

[1] T. Durst, in advance in organic chemistry; Methods and Results vol.6,p 285,1969. View at Google scholar/View at publisher

[2] W.W. Epstein, F.W; Sweat”Dimethyl sulphoxide oxidations”. Chem. Rev. 67, 247, 1967.

[3] A. J. Mancuso and D. Swern” Oxidation of long-chain and related alcohols to carbonyls by dimethyl sulphoxide”. Synthesis. 165,1981.

[4] R. F. Butterworth, S. Hanessian,”Selected methods of oxidation in carbohydrate chemistry” Synthesis , vol.1971,pp70-88,1971.

[5] J.G. Moffat, in oxidation, vol. 2. R. L. Augustine, D. J. Trecker, Eds. Marcel Dekker. Inc. Newyork ;p-1 1971. View at Google scholar/View at publisher

[6] S.Nagarajan and K.L.Rinehart Jr. J.Org.Chem; 50,380,1985. View at Google scholar/View at publisher

[7] R. J. Wikhom and H. W. Moore,”Dimethy sulphoxide acetic-anhydride oxidative rearrangements of hydroxyterphenylquinones.A possible biosynthetic model,”J. Am. Chem. Soc.94,6152, 1972.

[8] K. Z. Khan. N. Minhaj. K. Tasneem. A. Zaman and F. M. Dean, ”The reaction of Dimethyl sulphoxide and acetic anhydride with 4-hydroxy coumarin and dicoumarols” J. Chem. Soc. Perkin. Trans.-I. 841. 1983.

[9] K. Z. Khan . K. Tasneem, M. Rehman, S. Prakash and A. Zaman Ind.j.Chem.,Sect.B.,42-46, 1985 View at Google scholar/View at publisher

[10] W.Czuba,L.Kasperk et.al;Pol.J.Pharmacol.Phrm. 37,533-40,1985.

[11] D.Marji and J.Ibrahim, Tetrahedron Letters Vol.26,1145-46.1985. View at Google scholar/View at publisher

[12] F.J .Kunz and O.E. Polansky ;Reaction of ketones and ketimines with 1,3-indandione”Monatsh Chem. 100,1,95-105,1969.

[13] J.Kaminski,A. Skupni,.S.Maria ., Chem.Abst.87.,117698w,1997. View at Google scholar/View at publisher

[14] M.A Fathy, I.A Osman, et.al. Alexandria,J.Pharm.Sci.,1,44-49,1958.

[15] L. Geita and G. Vanagas;Chem.Abst.59,7458,1963.

[16] Y.A Strakov,.B.Y. Slude, M.V Petrova and Mishnew, Chem.Abst.,125,142660p,1996.

[17] A. Hochramer and F. Wessely, Monatash Chem.97,1, 1966. View at Google scholar/View at publisher

[18] M.Mashaly and M.Mashaly ,Chem.Abst.119,1600394,1993.

[19] H.Moehrle,S.Doembrack,et.al;Chem.Abst.96,104045,1982.