Tetrahedron Letters,Vol.26,No.12,pp 1581-1584,1985 0040-4039/85 $3.00 + .00
Printed in Great Britain

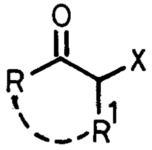
A SIMPLE SYNTHESIS OF α,β-UNSATURATED ALDEHYDES BY 1,3-CARBONYL TRANSPOSITION THROUGH ONE CARBON HOMOLOGATION

Ratna Dasgupta and Usha Ranjan Ghatak*

Department of Organic Chemistry, Indian Association for the
Cultivation of Science, Jadavpur, Calcutta - 700 032, India

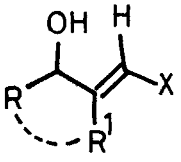
Summary : *α,β-Unsaturated aldehydes are conveniently prepared from ketones through their β-diethoxymethyl derivatives by sodium borohydride reduction followed by acid-catalysed rearrangement of the resulting diacetal carbinols.*

The homologation of carbocyclic[1] or aromatic conjugated cyclic and acyclic[2] ketones (A), having an active methylene group, to the α,β-unsaturated aldehydes (C) has been achieved[1,2] through acid-catalysed rearrangement of the respective 2-(alkylthio)-methylene carbinols (B), derived from the ketones in several steps. These methods, however, require strong basic reagents for introduction of the functionalised β-carbon residue into the ketones. We wish to report here an alternate and simple approach to the transformations of cyclic and acyclic ketones having the general structure (A) to the respective α,β-unsaturated aldehydes (C) through the easily accessible β-keto-acetals (D) under mild reaction conditions[3,4], which appears to offer a considerable promise as a general synthetic procedure.



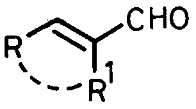
(A) : X = H

(D) : X = $CH(OEt)_2$



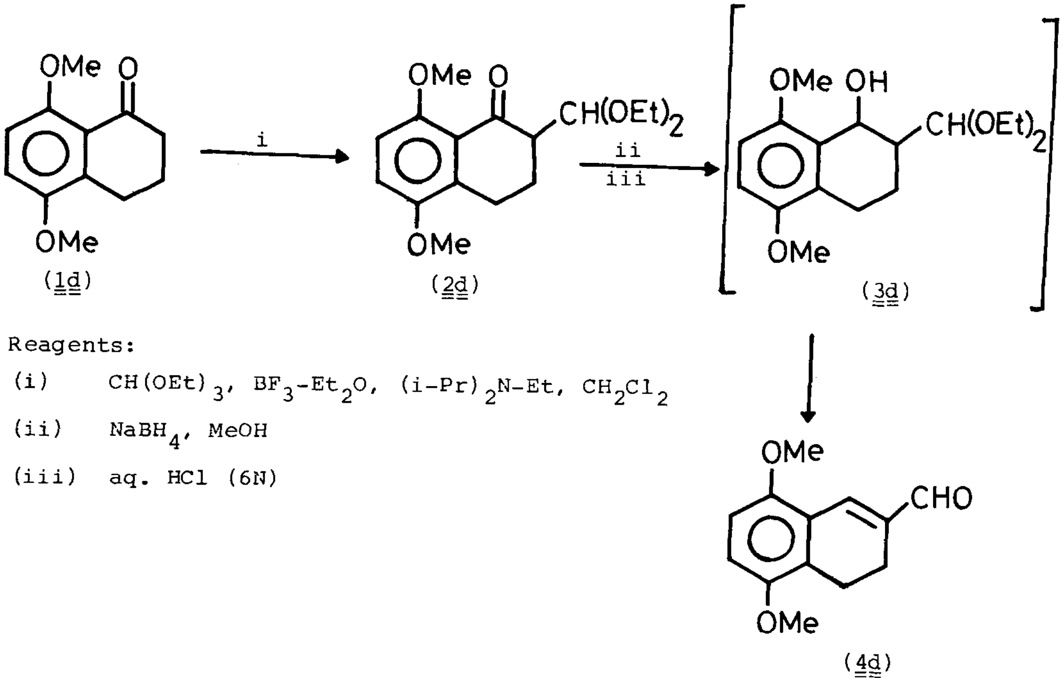
(B) : X = SMe or SBu^n

(E) : X = OEt



(C)

As a typical example, conversion of the tetralone (1d)[5] into the dihydronaphthaldehyde (4d)[6,7], a key intermediate in the synthesis of anthracyclines[6,7], via the β-ketoacetal (2d) and the carbinol (3d), is shown here.



Reagents:

(i) $CH(OEt)_3$, BF_3-Et_2O, $(i\text{-}Pr)_2N$-Et, CH_2Cl_2

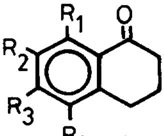
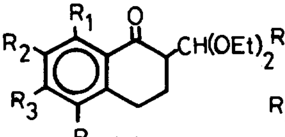
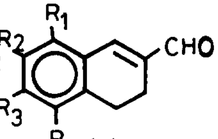
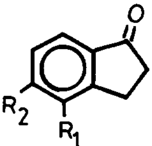
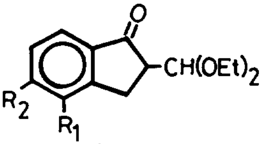
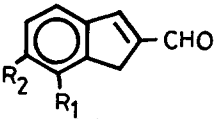
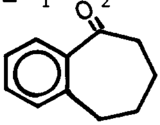
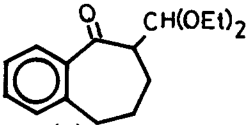
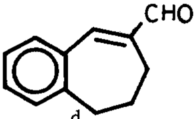
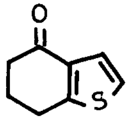
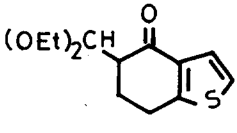
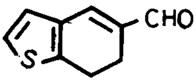
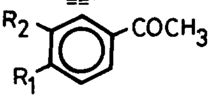
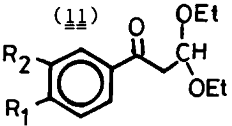
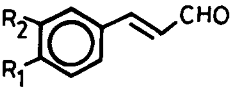
(ii) $NaBH_4$, MeOH

(iii) aq. HCl (6N)

The reaction of the tetralone (1d) with diethoxycarbonium fluoroborate [prepared in situ from $BF_3.Et_2O$ and $HC(OEt)_3$] in the presence of N,N-diisopropylethylamine in CH_2Cl_2 at -78°C (10 min) followed by -20 to -10°C for 2 hr according to Mock and Tsou[3], afforded the β-ketoacetal (2d) as a dark red viscous oil in 95% yield. This relatively unstable intermediate was characterised by the spectral data; IR (neat) 1660, 1610 cm^{-1}; ^1H NMR (CCl_4) δ 0.93-1.3 (m,6H), 1.87-3.66 (m,9H), 3.73 (s,6H,2-OCH_3), 4.83 (d,1H), 6.46-6.9 (dd,2H,ArH). Reduction of crude (2d) with an excess of $NaBH_4$ in methanol to the carbinol (3d) followed by decomposition of the reaction mixture with an excess of ice-cold aq-HCl (6N) followed by stirring at room temperature for 2 hr and purification of the resulting product (extracted with Et_2O) by short-path filtration through a silica-gel column afforded the known aldehyde (4d), m.p. 90-92°C (reported[6,7] m.p. 91-92°C) in 80% yield. Possibly, the acid-catalysed transformation of the carbinol-acetal (3d) proceeds through the rearrangement of an intermediate such as (E), similar to the sulphur analogue (B)[1,2].

The sequence was demonstrated on several other tetralones (1a-c),indanones (4a-d) and benzosuberone (7) to the respective α,β-unsaturated aldehydes (3a-c), (6a-d) and (9) in good to excellent yields (entries 1-8 in Table). The ketoacetals (14a) and (14b) derived from the respective arylmethyl ketones(13a) and (13b) gave the E-isomers (15a) and (15b) exclusively, as appeared from the ^1H NMR spectra (entries 11 and 12 in Table). The tetrahydro-4-oxo-benzo[b] thiophene (10) also yielded the previously unknown[8] α,β-unsaturated aldehyde (12) in excellent yield (entry 10 in the Table).

Table. Transformations of the ketones to α,β-unsaturated aldehydes.

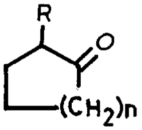
Entry	Starting Ketone	β-Ketoacetal[a]	α,β-Unsaturated Aldehyde	Yield[b] (%)	m.p.
	 (1)	 (2)	 (3)		
1	a,$R_1=R_2=R_3=R_4=H$	a,$R_1=R_2=R_3=R_4=H$	a,$R_1=R_2=R_3=R_4=H$	92	Oil
2	b,$R_1=R_2=R_4=H$ $R_3=OMe$	b,$R_1=R_2=R_4=H$ $R_3=OMe$	b,$R_1=R_2=R_4=H$ $R_3=OMe$	73	48-49°C (lit.^{11}m.p.49°C)
3	c,$R_1=R_3=R_4=H$ $R_2=OMe$	c,$R_1=R_3=R_4=H$ $R_2=OMe$	c,$R_1=R_3=R_4=H$ $R_2=OMe$	68	oil (lit.^{11}b.p. 125-130°C/2mm Hg
4	d,$R_2=R_3=H$, $R_1=R_4=OMe$	d,$R_2=R_3=H$, $R_1=R_4=OMe$	d,$R_2=R_3=H$, $R_1=R_4=OMe$	80	91-92°C (lit^{6}m.p.91-92°C)
	 (4)	 (5)	 (6)		
5	a,$R_1=R_2=H$	a,$R_1=R_2=H$	a,$R_1=R_2=H$	50	Oil
6	b,$R_1=Me,R_2=H$	b,$R_1=Me,R_2=H$	b,$R_1=Me,R_2=H$	75	80°C
7	c,$R_1=OMe,R_2=H$	c,$R_1=OMe,R_2=H$	c,$R_1=OMe,R_2=H$	79	98°C
8	d,$R_1=H,R_2=OMe$	d,$R_1=H,R_2=OMe$	d,$R_1=H,R_2=OMe$	82	64°C
9	 (7)^c	 (8)	 (9)^d	72	Oil
10	 (10)^e	 (11)	 (12)	81	low melting solid
	 (13)	 (14)	 (15)		
11	a,$R_1=OMe,R_2=H$	a,$R_1=OMe,R_2=H$	a,$R_1=OMe,R_2=H$	62	59-60°C (lit^{12}m.p.59°C)
12	b,$R_1=H,R_2=OMe$	b,$R_1=H,R_2=OMe$	b,$R_1=H,R_2=OMe$	67	oil

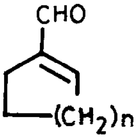
---

[a] Characterised by IR and ^{1}H NMR spectra; [b] Yields refer to the isolated pure compounds fully characterised by UV,IR, ^{1}H NMR (at 200 MHz) and elemental analyses; [c] We thank Dr.S.Ghosh and Miss. S. Saha for a generous gift of this compound; [d] This compound is susceptible to oxidation to the corresponding carboxylic acid in air; [e] We thank Dr.A.De and Mrs.S.Dutta for a generous gift of this compound.

The preliminary results indicated that the sequence of reactions developed for the aromatic conjugated ketones are also useful for the transformation of cyclohexanone (16) and cyclopentanone (17) to the respective α,β-unsaturated aldehydes (20) and (21) in ca. 50% overall yield from the ketones via the β-ketoacetals (18)[3] and (19)[3].

(16),n=2; R=H
(17),n=1; R=H
(18),n=2; R=$CH(OEt)_2$
(19),n=1; R=$CH(OEt)_2$





(20),n=2
(21),n=1

The simplicity and mild reaction conditions of our method and the ease with which it can be applied to the preparation of α,β-unsaturated aldehydes by one carbon homologation with 1,3-carbonyl transposition suggests that it will be the method of choice for such synthetic operation[9].

The easily accessible β-ketoacetals (D) are also useful intermediates for the synthesis of substituted α,β-unsaturated aldehydes and benzoannelated derivatives[10] through their reactions with organometallic reagents and these aspects will be reported in due course.

Acknowledgements

Financial support from the SERC/DST (New Delhi) under Grant No.23(3p-8)/81-STP/II is gratefully acknowledged.

REFERENCES AND NOTES

1. (a) R.E. Ireland and J.A. Marshall, *J.Org.Chem.*, 27, 1620 (1962);
   (b) R.F. Church and R.E. Ireland, *Tetrahedron Lett.*, 495 (1961);
   (c) S. Akiyama, S. Nakatsuji, and T. Hamamura, Ibid., 2809 (1979);
   (d) J.A. Marshall and P.C.Johnson, *J. Org. Chem.*, 35, 193 (1970);
   (e) T. Nishio and Y. Omoto, *Chemistry Lett.*, 365 (1979).
2. B.Myrboh, H. Ila, and H. Junjappa, *J. Org. Chem.*, 48, 5327 (1983).
3: W.L. Mock and H.R. Tsou, *J. Org. Chem.*, 46, 2557 (1981).
4. For other methods see: (a) O. Takazawa and T. Mukaiyama, *Chemistry Lett.*, 1307 (1982); (b) T. Mukaiyama and M. Hayashi, *Chemistry Lett.*, 15 (1974).
5. J.A. Moore and M. Rahm., *J. Org. Chem.*, 26, 1109 (1961).
6 M.P. Reddy and G.S. Krishna Rao, *Tetrahedron Lett.*, 22, 3549 (1981).
7. A.V.Rama Rao, J.S.Yadav, K.B.Reddy, and A.R.Mehendale, *J.Chem.Soc.Chem.Commun.*, 453 (1984); and the references cited therein.
8. Attempted formylation of (10) by Vilsmeier method gave either a mixture of products /¯D.T.Drewry and R.M.Scrowston, *J.Chem. Soc.*, (C), 2750 (1969) _7.
9. For cyclohexenone annulation by similar method see: R. Dasgupta, B. Ranu, and U.R.Ghatak, *Indian J.Chem.*, 22B, 619 (1983).
10. (a) M.A. Tius, *Tetrahedron Lett.*, 22, 3335 (1981); (b) M.A. Tius and S. Ali, *J. Org.Chem.*, 47, 3163 (1982); (c) M.A. Tius and S. Savariar, *Synthesis*, 467 (1983); (d) M.A. Tius and A. Thurkauf, *J. Org.Chem.*, 48, 3839 (1983).
11. P.A. Reddy and G.S. Krishna Rao, *Indian J.Chem.*, 20B, 100 (1981).
12. A. Horeau, *Bull. Soc. Chim. Fr.*, 414 (1948).

(Received in UK 15 January 1984)