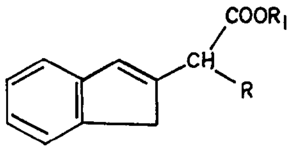
Tetrahedron Letters No.28, pp. 2331-2334, 1969. Pergamon Press. Printed in Great Britain.

A NOVEL SYNTHESIS OF STYRYLACETIC ACID SYSTEMS

S. K. Dasgupta, S. R. Ghosh and A.S. Sarma
Department of Organic Chemistry, Indian Association for
the Cultivation of Science, Jadavpur, Calcutta-32, INDIA

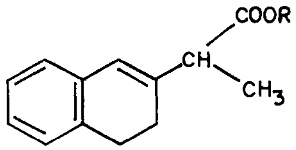
(Received in UK 8 April 1969; accepted for publication 9 May 1969)

The importance of styrylacetic acid systems as potential intermediates in organic syntheses has already been demonstrated in our previously reported[1] synthesis of tricarbocyclic resin acid derivatives and related compounds. In connection with our programme on syntheses of alicyclic compounds related to giberellins, we needed the unsaturated acid (Ia), apparently containing the styrylacetic acid moiety, so far not reported in the literature. It could not be prepared by Reformatsky reaction of 2-indanone[3] with esters of α-bromopropionic acid, in contrast to the successful conversion[2] of 2-tetralone to the related acid (IIa) under similar reaction conditions. This, however, resulted in the exclusive formation of the indenylindanone derivative[4] (III). Failure to attain this objective led us to search for an alternative general method, preferably starting from more readily available phenyl ketones (vide infra), for syntheses of structurally related representative compounds including Ic and IIa. This has now been successfully realised in quite high yields (see Tables 1 and 2) through acid-catalysed alcoholysis (MeOH), under refluxing conditions, of suitably substituted phenylbutyrolactone systems (IVa, IVb and V) followed by alkaline hydrolysis. These acids were characterised through elemental analyses, spectral properties and comparison of the melting points with the recorded data, if known, in the literature. The results including characteristic physical properties are reported in Table I of the present communication. Attempted alkaline hydrolysis of the lactones followed by acidification, however, failed to cleave these to the desired unsaturated acids, while the parent compounds are recovered unchanged.



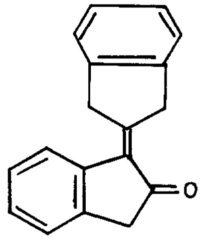
I

a, R=CH$_3$, R$_1$= H
b, R=CH$_3$, R$_1$= CH$_3$
c, R=H, R$_1$= H
d, R=H, R$_1$= CH$_3$

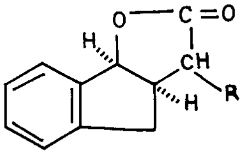


II

a, R = H
b, R = CH$_3$

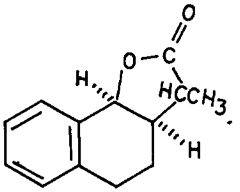


III

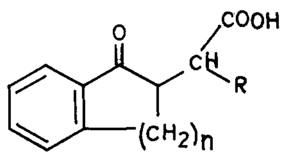


IV

a, R = CH$_3$
b, R = H



V



VI

a, R= CH$_3$, n = 1
b, R= H, n= 1
c, R= CH$_3$, n = 2

Table I

(Conversion of lactones to the desired styrylacetic acid systems)

Lactone	Unsaturated ester(yield)	Physical properties of the unsaturated ester	Unsaturated acid(yield)	Physical properties of the unsaturated acid	
		b.p., $\nu_{max}^{CHCl_3}$ in cm^{-1}		m.p.,	λ_{max}^{EtOH} in mμ
IVa	Ib (90%)	135°/0.6 mm., 1725	Ia (85%)	106-106.5°	260
					log ε (4.16)
IVb	Id (89%)	132°/0.6 mm., 1728	Ic (90%)	124-125°	259
				lit.[3] 116-117°	log ε (4.14)
V	IIb (92%)	136°/0.6 mm., 1730	IIa (90%)	118-119°	266
				lit.[2] 118-119°	log ε (4.04)

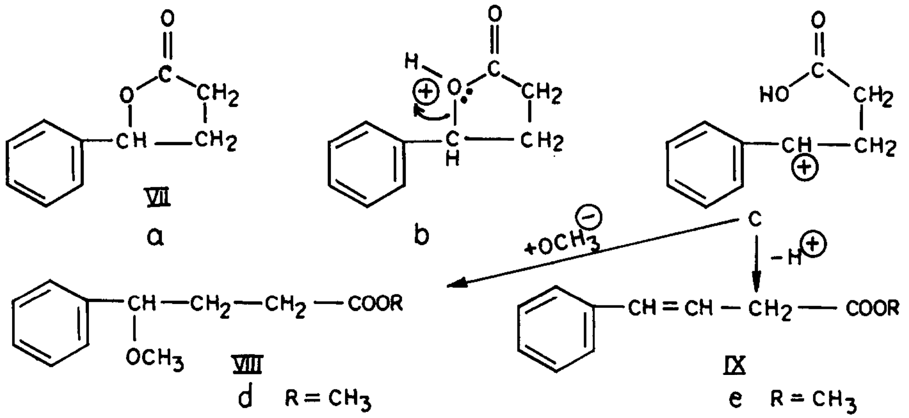
The required lactones (IVa, IVb and V; see Table 2) were prepared by the reduction of the previously known keto acids VIa[5], VIb[5],[6] and VIc[5] respectively with sodium borohydride in the following general manner. To a solution of keto acid in 40% aqueous sodium hydroxide an excess of sodium borohydride was added in three or four proportions at room temperature and the mixture left for 48 hours. It was then decomposed with ice-cold hydrochloric acid (6N) and left for 7 days. After extraction with ether and the usual work up, removal of the solvent afforded a lactone in more than 80% yield. The present result is in marked contrast to the 20% yield as recorded by House et al[6] in the conversion of the keto acid (VIb) to the lactone (IVb). The physical properties of the lactones are described below in Table 2.

Table 2

(Conversion of keto acids to cis[7]-fused lactones)

Keto acid	Lactone	Physical properties of the lactones		
		m.p.	λ_{max}^{EtOH} in mμ	$\nu_{max}^{CHCl_3}$ in cm^{-1}
VIa	IVa	52-53°	260 (log ε 2.84) 266 (log ε 3.03) 273 (log ε 3.06)	1760
VIb	IVb[6]	65-66° lit.[6] 65-66°	same as recorded in ref. 6	1760
VIc	V	80-82°	265 (log ε 2.73) 274 (log ε 2.81)	1765

When γ-phenylbutyrolactone (VII) was subjected to acid-catalysed methanolysis (vide supra), the product b.p. 105°/2 mm. (90%) was identical through spectral properties $\nu_{max}^{CHCl_3}$ 1730 cm-1, and its conversion to γ-phenylbutyric acid (m.p. and mixed m.p.51°[8]) by catalytic reduction (10% Pd/C) followed by hydrolysis, as a methoxyl methyl ester (VIII) rather than the expected styrylacetic acid derivative (IX). The NMR spectra of (VIII) revealed a characteristic triplet centered at τ5.89, J= 6.c.p.s., due to the single benzyl proton at the carbon atom bearing a methoxy group, a singlet at τ6.83 (3H) due to the methyl ether protons and another singlet at τ6.4 (3H) due to the ester methyl. It is of interest to note that the difference in behaviour of the fused ring lactones (IVa, IVb and V) and γ-phenylbutyrolactone (VII) during methanolysis lies in the fact that in the former case the benzyl carbonium ion (stage c) generated on protonation is stabilised by elimination of a proton, affording an



olefinic methyl ester (stage e), while a substitution reaction by a OMe⁻ accounts for the formation of the methoxylated methyl ester(VIII) in the latter.

Acknowledgements : The authors wish to express their gratitude to Dr. T.R. Govindachari, Director, Ciba Research Centre, Goregaon, Bombay for NMR spectra. Thanks are also due to Professor P.C.Dutta for his interest in the work and Dr. A. Chatterjee of Jadavpur University, Calcutta for the gift of a few keto acid as starting materials.

References

1. S.K. Dasgupta and P.C. Antony, Tetrahedron Letters, No. 41, 4997 (1966).
2. S.K. Dasgupta and P.C. Antony, Chem. Comm., 485 (1966).
3. (a) H.Ahmed and N. Campbell, J.Chem.Soc., 4115 (1960); (b) Reformatsky reaction of 2-indanone with bromoacetic acid ester has been reported to afford the unsaturated acid (1c) in unspecified yield.
4. W. Triebs and W. Schroth, Annalen, 639, 204 (1961).
5. A. Chatterjee, D. Banerjee and S. Banerjee, Tetrahedron Letters, 3851 (1965) and the references cited therein.
6. H.O. House, H.Babad, R.B.Toothhill and A.W.Noltes, J.Org.Chem.,27,4141(1962).
7. cis-Fused structures have been based on the results derived by House et al in the reduction of (VIb) to (IVb), cf., ref. 6. Detailed stereochemistry on the basis of NMR and stability studies will be reported later.
8. E. L. Martin, "Org. Syntheses", Coll. Vol. 2, p. 499, John Wiley and Sons, Inc., New York.