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THE DEGRADATION OF STENHOUSE SALTS UNDER ACETYLATION CONDITIONS

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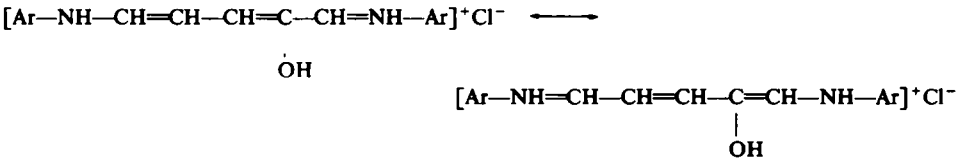
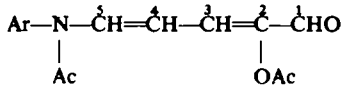
Abstract—Reinvestigation of the products formed in the treatment of Stenhouse salts (I) with acetic anhydrine–pyridine has shown that the previously assigned structures, based on a 2-hydroxypenta-2,4-dienal skeleton, should be revised to the isomeric 4-hydroxypenta-2,4-dienal type. A method of preparation of compounds having the authentic 2-hydroxypenta-2,4-dienal structure has been discovered.

STENHOUSE salts are readily prepared from the reaction between furfuraldehyde (1 mole) and an aromatic amine (2 moles) in the presence of one mole of mineral acid.[1] While it has been suggested[2,3] that these salts are of triphenylmethane type, structure I, initially proposed by Zincke and Mühlhausen[4] and supported by later workers,[5–7] seems to have become generally accepted. However, most interpretations of the reactions[4,6,8,9] of Stenhouse salts seem to have been made only in terms of the L.H.S. formula of the resonance hybrid I.



Ia: Ar = Ph; Ib: Ar = *p*-Me—C_6H_4; Ic: Ar = *p*-Cl—C_6H_4

The degradation of the purple Stenhouse salt Ia under acetylating conditions was first observed by Aschan and Schwalbe[8] who, by treatment of this salt with acetic anhydride and sodium acetate obtained a mixture from which three colourless compounds, A (m.p. 174°, major component), B (m.p. 145°) and C (m.p. 132°) were isolated. Compound A which from its analysis contained two acetyl groups, formed a semicarbazone and a phenylhydrazone and was formulated as IIa.



IIa: Ar = Ph IIb: Ar = *p*-Me—C_6H_4; IIc: Ar = *p*-Cl—C_6H_4.

Compounds B and C were assumed to be the two possible monoacetyl derivatives corresponding to IIa since, on treatment with aniline hydrochloride, both were converted into red salts, the analyses of which indicated the presence of one acetyl group only.

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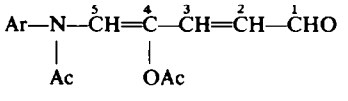
Subsequently McGowan[9] treated the salt (Ia) with pyridine–acetic anhydride and isolated the compound A (m.p. 175°), apparently free from the partially acetylated compounds which Aschan and Schwalbe had obtained. McGowan accepted structure IIa and extending the pyridine–acetic anhydride decomposition to salts Ib and Ic obtained products to which he assigned structures IIb and IIc. The UV spectrum of IIc was in reasonable agreement with that expected[10] for such a substituted conjugated dienal.

During a systematic investigation which we have begun[11] into several of the reactions of Stenhouse salts we repeated the degradation of Ia, Ib and Ic under McGowan's conditions and isolated compounds whose physical data agreed with previous values.[9] The UV maxima were at slightly lower wavelengths but the IR spectra showed peaks assignable to enolic acetate, unsaturated aldehyde, double bond of enolic acetate and tertiary amide in agreement with II. The NMR spectrum of A however clearly showed that structure IIa was incorrect. In particular the aldehyde proton signal at δ 9·43 was a doublet with a coupling of 7·5 c/s, comparable with that observed between the α-proton and the aldehyde proton in various substituted acroleins,[12, 13] and the signal at δ 7·68, assigned to a vinyl proton on carbon attached to nitrogen[14] was a singlet. The chemical shifts and splittings of the remaining protons indicated that A possessed the isomeric formula IIIa and the UV and IR data agreed equally well with this.



IIIa: Ar = Ph IIIb: Ar = *p*-Me—C_6H_4; IIIc: Ar = *p*-Cl—C_6H_4

The UV, IR and NMR spectra of the compounds formed in the similar degradation of Ib and Ic were very similar to the corresponding spectra of A and it is clear that the previously assigned structures[9] should be revised to IIIa, b and c, which are the structures which would result from the splitting off of amine from the R.H.S. resonance contributor to structure I.

It would not have been surprising if a mixture of the two possible substances IIa and IIIa had been formed. However, in the pyridine–acetic anhydride procedure used, the crude solid first isolated showed no sign of contamination with isomeric material [the presence of which would have been easily recognized from its singlet aldehyde proton signal in the NMR spectrum (see later)]. Alternative work up by evaporation under vacuum of the reaction mixture also yielded a crude product showing only a doublet signal for the aldehyde proton.

During a re-examination of the sodium acetate catalysed acetylation procedures used by Aschan and Schwalbe,[8] modified conditions were found which gave from Ia a good yield of colourless material m.p. 147° in agreement with that of product B.[8] Aschan and Schwalbe had not analysed their compound but analysis of our material indicated that it was isomeric with A and that its UV and IR spectra were also very similar to those of A. The NMR spectrum showed that product B was a diacetyl derivative and that it possessed the structure IIa originally assigned to A. The NMR spectra of both A and B are compared in Table 1.

TABLE 1. COMPARISON OF THE NMR SIGNALS OF THE ISOMERIC DIENALS (IIa AND IIIa)

	H1	H2	H3	H4	H5	N—Ac	OAc
A (IIIa)	9·43 d (7·5)	5·75 q (15, 7·5)	7·03 d (15)	—	7·68 s	1·90 s	1·43 s
B (IIa)	9·10 s	—	6·78 d (11)	5·13 q (14, 11)	8·10 d (14)	1·92 s	2·03 s

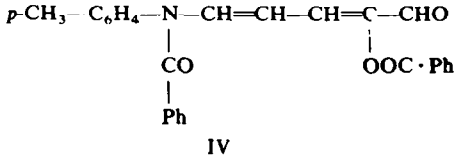
Figures in parentheses are coupling constants in c/s.
s = singlet. d = doublet. q = quartet.

Acetylation of salts (Ib and Ic) under similar conditions furnished the new dienals (IIb and IIc) whose structures followed from their UV, IR and NMR spectra..

It is apparent that the isomeric dienals (IIa and IIIa) possess an extended coplanar diene structure and probably are in the *trans–trans* configuration. The values of the coupling constants for H2–H3 in IIIa and for H4–H5 in IIa are normal for the *trans* configurations in similar compounds.[13,15] The coupling of H3–H4 in IIa is also in agreement with the value quoted by Elvidge and Ralph[15] as being characteristic of the *trans* coupling across a single bond in the similar extended conjugated system of the muconic esters. The 3 proton singlet at δ 1·43 in the dienal (IIIa) is assigned to the Me of the O-acetyl group. The marked shielding (0·6 ppm) in this case compared with the corresponding signal of IIa is worthy of comment. It appears from models of IIIa* that, with two bulky substituents attached to C4 and C5, the aromatic ring is held in a relatively fixed orientation roughly at right angles to the plane of the —NRAc system. In this situation the methyl of the O-acetyl group lies in the shielding zone[16] of the aromatic ring. Support for the suggested orientation of the aromatic ring may be derived from the UV absorption spectrum of IIIa where no maximum absorption near 240 mμ is observed. At 242 mμ ε is 4400 whereas acetanilide shows λ_{max} 242 mμ (ε 12,000).[10]

In the sodium acetate catalysed degradation of Ia there was isolated from the crystallization mother liquors a product of broad m.p. (ca. 133–138°), corresponding, possibly, to compound C of Aschan and Schwalbe.[8] The NMR spectrum of this material indicated that it was a mixture of the two diacetylated dienals (IIa and IIIa) and thus in this procedure both possible products are formed. The isolation of the single product (IIIa) in the acetylation in pyridine solution was surprising. Acetylation at both oxygen and nitrogen centres apparently occurs before final fission of the anil group, as on one occasion a quantity of diacetylated anil was isolated. The graded acetylation of Stenhouse salts and the reason for the specificity of the pyridine–acetic anhydride reaction are under investigation.

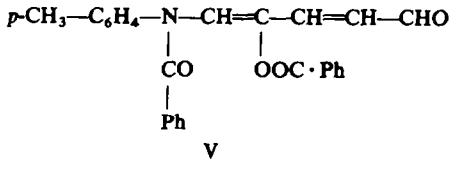
McGowan[9] also examined the degradation of Stenhouse salts (Ia and Ib) using benzoyl chloride and pyridine and isolated from Ib a crystalline product to which he assigned structure IV analogous to that of the diacetyl derivative IIb.



IV

* Courtauld Atomic models.

We found that the NMR spectrum of the dibenzoyl derivative showed a doublet (J = 7·7 c/s) at δ 9·52 for the aldehyde proton. It would appear that decomposition with benzoyl chloride in pyridine solution has proceeded as in the case of the acetylation in pyridine and that the dibenzoyl derivative should be assigned structure



V

EXPERIMENTAL

IR spectra were determined for Nujol mulls with a Grubb–Parsons GS-2 grating spectrophotometer; major peaks only are recorded except where the assignment of a minor peak was obvious. NMR spectra were obtained for solns in $CDCl_3$ at 60 Mc/s. with a Varian HA-60-IL instrument. TMS (δ = 0) was used as internal reference. UV spectra were measured for solns in 95% EtOH with a Perkin–Elmer 350 spectrophotometer. M.ps were determined on a Kofler micro hot-stage and are uncorrected. Microanalyses were performed by the Australian Microanalytical Service, Melbourne.

Stenhouse salts (I). These were prepared by the method of Williams and Wilson.[6] The precipitated purple salts were filtered off, washed with three portions of alcohol and then thoroughly with ether. This material was dried and used for the acetylations.

Acetylation using pyridine and acetic anhydride. A modification of the method of McGowan[9] was used. The Stenhouse salt (5 g) was slowly added with stirring to pyridine (50 ml) containing Ac_2O (12 ml). Decolourization was very rapid. The soln was allowed to stand at R.T. for ca. 2 hr and then added dropwise over about 1 hr to a well stirred mixture of crushed ice (400 g) and water (400 g). The sandy ppt was filtered off and washed thoroughly by re-suspending in water and refiltering. This washing was repeated several times.

N,O-*Diacetyl-5-anilino-4-hydroxypenta-2,4-dienal* (IIIa) formed colourless flat needles from EtOH m.p. 176–177° (lit.[9] m.p. 175°). (Found: C, 66·0; H, 5·5; N, 5·1; O, 23·2. $C_{15}H_{15}NO_4$ requires: C, 65·9; H, 5·5; N, 5·1; O, 23·4%). λ_{max} 320 mμ (log ε 4·42), ν_{max} 3060, 2738, 1764, 1712, 1692, 1640, 1616 *sh*, 1599, 1208, 962, 823 cm^{-1}. NMR (see Table 1) and aromatic protons δ 7·1–7·5 (5H, m). (IIIa) on treatment with phenylhydrazine in AcOH formed a phenylhydrazone, pale yellow flat needles m.p. 205–206° (from alcohol) (lit,[8] m.p. 206°).

N,O-*Diacetyl-5-p-toluidino-4-hydroxypenta-2,4-dienal* (IIIb) crystallized as white needles from EtOH, m.p. 162–163° (lit,[9] m.p. 165°). (Found: C, 66·6; H, 6·3; N, 4·9; O, 22·0. $C_{16}H_{17}NO_4$ requires: C, 66·9; H, 6·0; N, 4·9; O, 22·3%), λ_{max} 320 mμ (log ε 4·40), ν_{max} 3077, 2732, 1773, 1696, 1677, 1628, 1616 *sh*, 1517, 1205, 978, 831 cm^{-1}; NMR δ 1·40 (3H, s), 1·87 (3H, s), 2·37 (3H, s), 5·72 (1H, q), 6·98 (1H, d), 6·9–7·4 (4H, m), 7·65 (1H, s), 9·43 (1H, d), $J_{1,2}$ = 7·5 and $J_{2,3}$ = 15 c/s.

N,O-*Dibenzoyl-5-p-toluidino-4-hydroxypenta-2,4-dienal* (V) was prepared following McGowan[9] and had m.p. 200–202° (dec) (very pale yellow needles from EtOH) (lit,[9] m.p. 206°). (Found: C, 75·6; H, 5·3; N, 3·2. $C_{26}H_{21}NO_4$ requires: C, 75·9; H, 5·1; N, 3·4%), λ_{max} 332, 229 mμ (log ε 4·40, 4·23) [lit,[9] λ_{max} 330 mμ (log ε 4·20)], ν_{max} 3099, 3077, 3030, 2817, 2750, 1748, 1684, 1637, 1623, 1610, 1517, 1319, 1244, 1212, 977, 830, 715, 704 cm^{-1}; NMR δ 1·82 (3H, s), 5·96 (1H, q), 6·65–7·6 (16H, m), 9·52 (1H, d), $J_{1,2}$ = 7·7 and $J_{2,3}$ = 15·7 c/s. The dibenzoyldienal (V) on treatment with phenylhydrazine in AcOH yielded the phenylhydrazone as yellow plates m.p. 187–188° (from EtOH) (lit.[9] m.p. 188°).

N,O-*Diacetyl-5-p-chloranilino-4-hydroxypenta-2,4-dienal* (IIIc) formed colourless needles from EtOH m.p. 170–172° (lit.[9] m.p. 172°). (Found: C, 58·4; H, 4·6; Cl, 11·1; N, 4·6. $C_{15}H_{14}ClNO_4$ requires: C, 58·5; H, 4·6; Cl, 11·5; N, 4·6%), λ_{max} 319·5 mμ (log ε 4·43) [lit,[9] λ_{max} 322 mμ (log ε 4·40)], ν_{max} 3084, 2736, 1771, 1698, 1680, 1630, 1617 *sh*, 1495, 1190, 977, 830 cm^{-1}; NMR δ 1·53 (3H, s), 1·92 (3H, s), 5·75 (1H, q), 7·00 (1H, d), 7·05–7·5 (4H, m), 7·65 (1H, s), 9·48 (1H, d), $J_{1,2}$ = 7·5 and $J_{2,3}$ = 15·5 c/s.

Acetylation of Stenhouse salts using acetic anhydride–sodium acetate–acetic acid. The Stenhouse salt (3 g) was added to a mixture of Ac_2O (10 ml), glacial AcOH (20 ml) and NaOAc (4·0 g) and the mixture triturated in a mortar. The purple salt slowly dissolved and the purple red soln became deep red and finally faded to a yellow brown colour over ca. 3 hr. The mixture was allowed to stand for a further 2 hr and

then treated with 1:1 aqueous AcOH until precipitation of solid occurred. The crude solid was filtered off, washed with aqueous acetic acid then with water and dried. It was usually contaminated with the corresponding acetanilide (peaks near 3378, 1660 and 1560 cm^{-1} in the IR spectrum).

N,O-*Diacetyl-5-anilino-2-hydroxypenta-2,4-dienal* (IIa). Colourless plates (from EtOH) m.p. 145–147°. (Found: C, 66·5; H, 5·7; N, 5·2; O, 23·2. $C_{15}H_{15}NO_4$ requires: C, 65·9; H, 5·5; N, 5·1; O, 23·4%), λ_{max} 325 mμ (log ε 4·34), ν_{max} 3067, 2725, 1770, 1701, 1689 *sh*, 1636, 1613, 1599, 1498, 1205, 964, 836, 795, 722, 702 cm^{-1}; NMR see Table 1, aromatic protons δ 7·05–706 (5H, m).

N,O-*Diacetyl-5-p-toluidino-2-hydroxypenta-2,4-dienal* (IIb). Fine needles (from EtOH) m.p. 144–145°. (Found: C, 67·5; H, 6·0; N, 4·9; O, 21·9. $C_{16}H_{17}NO_4$ requires: C, 66·9; H, 6·0; N, 4·9; O, 22·3%), λ_{max} 326 mμ (log ε 4·39), ν_{max} 3067, 3046, 2732, 1763, 1700, 1691 *sh*, 1633, 1607, 1515, 1205, 1000, 966, 940, 833, 727 cm^{-1}; NMR δ 1·92 (3H, s), 2·07 (3H, s), 2·43 (3H, s), 5·17 (1H, q), 6·80 (1H, d), 6·95–7·40 (4H, m), 8·12 (1H, d), 9·17 (1H, s) $J_{3,4}$ = 11·2 and $J_{4,5}$ = 14 c/s.

N,O-*Diacetyl-5-p-chloranilino-2-hydroxypenta-2,4-dienal* (IIc). Colourless plates (from EtOH) m.p. 134–135°. (Found: C, 58·5; H, 4·6; Cl, 11·5; N, 4·5. $C_{15}H_{14}ClNO_4$ requires: C, 58·5; H, 4·6; Cl, 11·5; N, 4·6%), λ_{max} 324 mμ (log ε 4·40), ν_{max} 3080, 3040, 2727, 1773, 1694, 1681 *sh*, 1628, 1613, 1595, 1499, 1490, 1196, 961, 840, 743, 725 cm^{-1}; NMR δ 1·92 (3H, s), 2·08 (3H, s), 5·22 (1H, q), 6·84 (1H, d), 7·10–7·58 (4H, m), 8·12 (1H, d), 9·19 (1H, s), $J_{3,4}$ = 11·6 and $J_{4,5}$ = 14·4 c/s.

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REFERENCES

[1] J. Stenhouse, *Liebigs Ann.* **156**, 199 (1870).
[2] [a] H. Schiff, *Ibid.* **201**, 355 (1880).
[b] H. Schiff, *Ibid.* **239**, 349 (1887).
[3] E. R. Riegel and M. Hathaway, *J. Am. Chem. Soc.* **63**, 1835 (1941).
[4] T. Zincke and G. Mühlhausen, *Chem. Ber.* **38**, 3824 (1905).
[5] W. Dieckmann and L. Beck, *Ibid.* **38**, 4122 (1905).
[6] G. Williams and C. L. Wilson, *J. Chem. Soc.* 506 (1942).
[7] W. König, *Chem. Ber.* **67**, 1274 (1934).
[8] O. Aschan and A. Schwalbe, *Ibid.* **67**, 1830 (1934).
[9] J. C. McGowan, *Chem. & Ind.* 523 (1956).
[10] A. I. Scott, *Interpretation of the Ultraviolet Spectra of Natural Products* p. 58. Pergamon Press, London (1964).
[11] K. G. Lewis and C. E. Mulquiney, *Chem. & Ind.* 1249 (1968).
[12] A. A. Bothner-By, *Advances in Magnetic Resonance* Vol. 1, p. 195. Academic Press, New York (1965).
[13] G. Scheibe, W. Seiffert, G. Hohlneicher, C. Jutz and H. J. Springer, *Tetrahedron Letters* 5053 (1966).
[14] T. J. Mabry, H. Wyler, I. Parikh and A. S. Dreiding, *Tetrahedron* **23**, 3111 (1967).
[15] J. A. Elvidge and P. D. Ralph, *J. Chem. Soc.* (C), 387 (1966).
[16] L. M. Jackman, *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry* p. 125. Pergamon Press, London (1959).