Tetrahedron. Vol. 29, pp. 359 to 362. Pergamon Press 1973. Printed in Great Britain

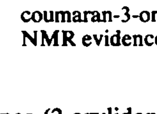
THE CONFIGURATION OF AURONES[1]

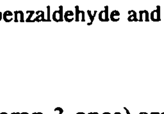
B. A. BRADY, J. A. KENNEDY and W. I. O'SULLIVAN*
Department of Chemistry, University College, Belfield, Dublin 4, Ireland

(*Received in the UK* 28 *August* 1972; *Accepted for publication* 30 *September* 1972)

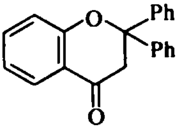
Abstract—The configurations of 6-methoxyaurone prepared by the condensation of 6-methoxycoumaran-3-one and benzaldehyde and of its photoisomer are assigned on the basis of chemical and NMR evidence.

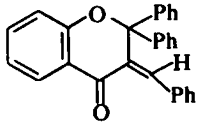
Aurones (2-arylidenecoumaran-3-ones) are usually prepared[2] by acid or base catalysed condensation of coumaran-3-ones with aromatic aldehydes. They have also been prepared by treatment of suitably substituted chalcones with alkaline hydrogen peroxide,[3] by reaction of certain chalcone dibromides with ethanolic potassium hydroxide,[2b] by dehydration of 2-hydroxy-2-benzylcoumaran-3-ones,[4] by treatment of 2-benzylcoumaran-3-ones with N-bromosuccinimide followed by ethanolic potassium hydroxide[5] and by base catalysed cyclisation of *o*-hydroxybenzoylphenylacetylenes.[6] In all cases only one of the two possible geometric aurone isomers (1 and 2) was isolated even when the same aurone was prepared by two or more alternate syntheses. The naturally occurring aurone, leptosidin[7] (3',4',6-trihydroxy-7-methoxyaurone) was found to have the same configuration as that synthesised by acid catalysed condensation of protocatechuic aldehyde and 6-hydroxy-7-methoxycoumaran-3-one.[8]


1


2

From a consideration of the concept of overlap control,[9] the expected products of condensation of coumaran-3-ones and other methylene ketones with aromatic aldehydes are the *trans*-arylidene isomers.† The arylidene derivatives of acetophenones,[10] cyclohexanones,[11] tetralones,[12] flavanones[13] and indanones[12] as usually prepared, have all been shown to be *trans*-isomers except when a high degree of steric overcrowding renders the *trans*-isomers unstable. For example, the condensation of 2,2-diphenylchormanone (3) with benzaldehyde gave only the *cis*-chromindogenide (4); the *trans*-isomer is not known. The assignment of configuration to the compounds mentioned above was made on the basis of the chemical shifts of the β-protons which in the *trans*-isomers gave signals at considerably lower fields than the signals of the corresponding protons in the *cis*-isomers (Table 1).


3


4

With a view to applying this method of structure determination to aurones, the second isomer of 6-methoxycoumaran-3-one was prepared by UV irradiation of the product synthesised by base catalysed condensation of 6-methoxycoumaran-3-one with benzaldehyde. The isomerisation was carried out in benzene solution by means of a high-pressure mercury-vapour lamp using a pyrex filter to give a *ca.* 1:1 equilibrium mixture of the *cis* and *trans*-isomers which was separated on alumina. The identity of the new compound as an isomer of 6-methoxyaurone was inferred from elemental analysis, IR, UV, NMR spectra; from its almost quantitative isomerisation into the original synthetic isomer on treatment with hot ethanolic NaOH, and from the fact that both isomers gave the same epoxide on treatment with alkaline H_2O_2.[1]

The chemical shift of the β-proton of the synthetic 6-methoxyaurone was τ 3·20 while that of the product of irradiation was τ 3·14. Because the signals of these protons occurred in the same region of the NMR spectra as those of the C-5 and C-7 protons, their positions were verified by an examination of the NMR spectra of the corresponding β-deuterated aurones which were prepared respectively by condensation of 6-methoxycoumaran-3-one with benzaldehyde-d and by the subsequent UV irradiation of the product obtained to the geometric isomer. The absence of a peak at τ 3·20 in the spectrum of condensation product

---

*Address enquiries to this author.

†The terms *cis* and *trans* used in this paper refer to the relative positions of the carbonyl and side chain aryl groups.

Table 1. Chemical shifts for β-protons in exocyclic α,β-unsaturated ketones

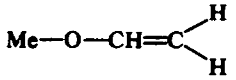
	Isomer		
	trans	*cis*	Ref.
2-Benzylidene-1-indanone	< 2·7*	3·11 (2·98)†	12
2-Benzylidene-3,3-dimethyl-1-indanone	2·35	3·20	12
2-Benzylidene-6,6-diphenylcyclohexanone	3·0*	3·67	11
2-Benzylidene-4,4-dimethyl-1-tetralone	2·29	3·37	12
3-Benzylideneflavone	1·92	3·30	13

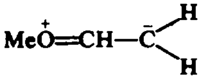
*Masked by aromatic protons.
†Our Reading.

and at τ 3·14 in the spectrum of the product of irradiation showed that the chemical shift assignments were correct.

The configuration of the two isomeric aurones could not be assigned on the basis of the chemical shifts of the β-protons because of the small difference between them. However, the lower τ-value (τ 1·85; deshielding by the carbonyl group) of the 2′,6′-protons in the photoisomer compared with a value of τ 2·10 for the corresponding protons in the condensation product indicates that this product is the *cis*-isomer and that the latter is the *trans*-isomer.* This conclusion is in agreement with the results obtained with other α,β-unsaturated ketones; namely, that the thermodynamically less stable isomer obtained on UV irradiation of the more stable isomer has the *cis*-configuration.[10,11,12,13]

The chemical shift of the β-proton in *cis*-6-methoxyaurone (τ 3·14) is close to that of the β-proton (τ 2·98) in the homocyclic analog, *cis*-2-benzylidene-1-indanone. However, the chemical shift of the β-proton in *trans*-6-methoxyaurone occurred at considerably higher field (τ 3·20) than that of the corresponding proton in *trans*-2-benzylidene-1-indanone which occurred at less than τ 2·7 (Table 1). Examination of Fieser models of the two *trans*-compounds shows that the β-protons are equidistant from the carbonyl groups and consequently should be deshielded to the same extent by these groups. The higher τ-value of the β-proton in *trans*-6-methoxyaurone is attributed to the shielding influence of the heterocyclic oxygen atom in the aurone molecule. Evidence in support of this view is obtained from the NMR spectra of many vinyl ethers which have been examined[14] and found to have high chemical shifts for the terminal ethylene protons when compared with the shifts of terminal protons in olefins not having alkoxyl substituents. The origin of the high shielding of these protons is thought[14] to lie in delocalisation effects involving the resonance forms;





It was found that the protons *trans* to the oxygen atom were shielded to a greater extent than protons *cis* to this atom. It was noted that the 2′,6′-protons in *trans*-2-benzylidene-1-indanone had a chemical shift of τ 2·13 while the corresponding protons in the *cis*-isomer absorbed at τ 1·9. These values are in line with those observed in the NMR spectra of the aurones.

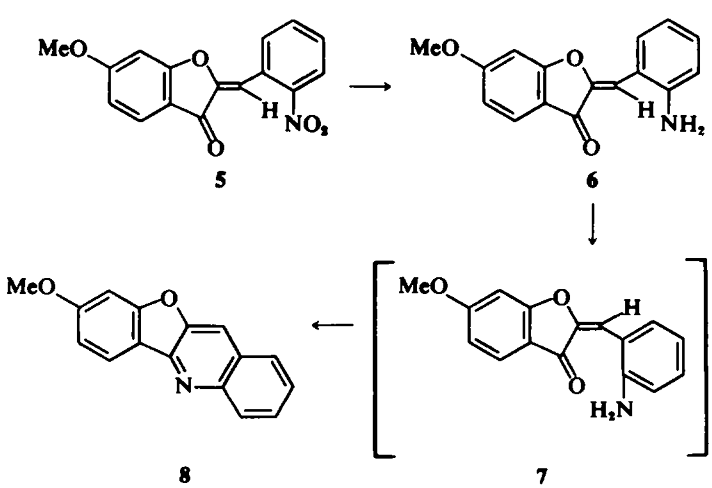
The assignment of configuration to the aurones was supported by the chemical evidence described below (Scheme). 6-methoxy-2′-nitroaurone (5) on treatment with $SnCl_2$ and HCl at room temperature gave 2′-aminoaurone (6). The latter on irradiation with UV light gave quinoline **8**, presumably *via* the *cis*-aminoaurone **7**, which on formation cyclised immediately. Isolation of quinoline **8** rather than the *cis*-aminoaurone **7** indicated that the aminoaurone **6** and consequently the nitroaurone **5** were both *trans*-isomers.

2-(2-aminobenxylidene)-1-tetralones were also found to cyclise to the corresponding quinoline derivatives on UV irradiation.[15] 2-Arylidenetetralones as usually prepared were subsequently shown to have the *trans*-configuration.[12]

Coumaranoquinoline **8** was obtained directly on reduction of nitroaurone **5** with sodium dithionite in boiling EtOH. That the *trans*-aminoaurone **6** was an intermediate in the reaction was supported by the fact that this compound (**6**) on treatment with sodium dithionite under the same conditions gave the quinoline derivative **8**. Since aminoaurone **6** was recovered unchanged on treatment with boiling EtOH and since the condensations of ketones with amines are not normally base catalysed,[16] it is suggested that the dithionite anion or some other basis species in the reaction

---

*The 2′,6′-protons in 4′-methoxy-5-methylaurone and in 4,6-dimethoxyaurone, prepared in the usual way, gave signals in each case at τ 2·1; in the UV irradiated products of these compounds the signals of 2′,6′-protons shifted down field to τ 1·7 and τ 1·84 respectively. M. Bennett, this department, personal communication.



medium was responsible for the isomerisation of the *trans*-aminoaurone to the less stable *cis*-isomer which on formation cyclised to coumaranoquinoline **8**.

EXPERIMENTAL

M.ps are uncorrected. The NMR spectra were taken at 60 MHz in the solvents stated containing TMS as internal reference.

Preparation of trans-*2-benzylidene-6-methoxycoumaran-3-one.*[17] NaOH aq (4·8 ml; 50%) was added slowly to a soln of 6-methoxycoumaran-3-one (19 g) and benzaldehyde (15 g) in EtOH (150 ml) at 60°. The product began to separate almost immediately as fine needles. The mixture was kept at 60° for 1·5 hr. The product was collected and washed successively with MeOH, dil H_2SO_4 and water and crystallized (EtOH) to yield colourless needles of *trans*-2-benzylidene-6-methoxycoumaran-3-one (17·6 g; 61%), m.p. 147–148° (lit.[17] m.p. 148°), λ_{max} (MeOH) 340 mμ (ϵ, 32,000); ν_{max} (KBr) 1710, 1654 cm^{-1}; τ ($CDCl_3$), 6·12 (s, 3H, 6-OMe), 3·28 (q, *J* 8·8 and 2·2 Hz, 5-H), 3·25 (d, *J* 2·2 Hz, 7-H), 3·20 (s, β-H) 2·58 (m, 3′, 4′, 5′-Hs), 2·31 (d, *J* 8·8 Hz, 4-H) and 2·10 (m, 2′, 6′-Hs).

trans-*2-(α-Deuterobenzylidene)-6-methoxycoumaran-3-one.* (12 g; 56%) was prepared in the same way from 6-methoxycoumaran-3-one (14 g) and benzaldehyde-d[18] (11·1 g); m.p. 147–148° alone or when mixed with a non-isotopic sample.

Photochemical isomerisation of trans-*2-benzylidene-6-methoxycoumaran-3-one.* A soln of *trans*-2-benzylidene-6-methoxycoumaran-3-one (10 g) in dry benzene (2·5 l) was irradiated for two weeks through a pyrex sleeve using a Philips HPK 125 W. mercury vapour lamp. The solid obtained on removal of solvent was chromatographed on standard alumina (Merck, active grade II-III; benzene). Removal of benzene from the first band eluted afforded a solid which on crystallisation (benzene/petroleum; b.p. 80–100°) yielded green-yellow needles of cis-*2-benzylidene-6-methoxycoumaran-3-one* (4·5 g; 45%), m.p. 136–137°. (Found: C, 75·77; H, 4·82. $C_{16}H_{12}O_3$ requires: C, 76·18; H, 4·80%); λ_{max} (MeOH) 337 mμ (ϵ, 28,000); ν_{max} (KBr) 1685, 1640 cm^{-1}; τ ($CDCl_3$) 6·14 (s, 3H, 6-OMe), 3·4 (d, *J* 2·2 Hz, 7-H), 3·14 (s, β-H), 3·30 (q, *J* 8·8 and 2·2 Hz, 5-H), 2·33 (d, *J* 8·8 Hz, 4-H), 2·61 (m, 3′, 4′, 5′-Hs) and 1·85 (m, 2′, 6′-Hs). The *trans*-isomer was eluted from the column with ether. It crystallised (EtOH) as colourless needles (5 g) m.p. and m.m.p. 147–148°.

cis-*2-(α-Deuterobenzylidene)-6-methoxycoumaran-3-one.* (0·6 g; 30%) was obtained in the same way on irradiation of *trans*-2-(α-deuterobenzylidene)-6-methoxycoumaran-3-one (2 g) for 10 days; m.p. 136–137° alone as when mixed with a non-isotopic sample.

Base catalysed isomerization of cis-*2-benzylidene-6-methoxycoumaran-3-one.* (a) A mixture of *cis*-2-benzylidene-6-methoxycoumaran-3-one (20 mg), NaOH aq (0·1 N; 1·5 ml) and EtOH (3 ml) was heated under reflux for 10 min, allowed to cool and added to ice and water. The resulting precipitate was collected, washed with water and crystallized (EtOH) as needles of *trans*-2-benzylidene-6-methoxycoumaran-3-one (16 mg; 80%), m.p. and m.m.p. 147–148°.

(b) *cis*-2-Benzylidene-6-methoxycoumaran-3-one (100 mg) was dissolved in pyridine (10 ml) at room temp and aliquots examined by TLC (silica: benzene) at intervals of 2 hr. The starting aurone was completely isomerized into its *trans*-isomer (R_f, colour under a UV lamp at 254 and at 350 nm) within 48 hr.

When the *trans*-isomer was similarly treated it remained unchanged.

trans-*2-Benzylideneindan-1-one.* The title compound was prepared as previously described,[19] m.p. 108–110° (lit.[19] m.p. 109–111°) ν_{max} (KBr), 1709 cm^{-1}; τ ($CDCl_3$) 6·0 (d, *J* 2·0 Hz, 2H, $\rangle CH_2$), 2·13 (m, 2H, 2′,6′-Hs), 2·23–2·76 (m, 8H, aromatic and β-proton).

cis-*2-Benzylideneindan-1-one.*[12] *trans*-2-Benzylideneindan-1-one (10 g) in MeOH (3 l) was irradiated with a Philips HPK 125w. mercury lamp for 7 days. Removal of the solvent gave a solid* which was separated by PLC (Merck silica gel; CH_2Cl_2). The upper band was $CHCl_3$ extracted and yielded, on solvent removal and crystallisation of the oil obtained from dil MeOH, yellow needles of *cis*-2-benzylideneindan-1-one (4·3 g; 43%). m.p. 95

---

*Integration of the areas under the peaks due to the hydrogens at the 3-position indicated a product ratio of 47·5% *cis* to 52·5% *trans*-isomers.

(lit.[12] m.p. 95–96°); τ ($CDCl_3$) 6·08 (d, J 1 Hz, 2H, $>CH_2$), 2·97 (5, 1H, β-H) 1·9 (m, 2H, 2′,6′-Hs), 2·14–2·7 (m, 7H, aromatic).

The lower band yielded the *trans*-isomer (4·8 g; 48%), m.p. 108–109°.

trans-2-(2-*Nitrobenzylidene*)-6-*methoxycoumaran*-3-*one* (**5**). Dry HCl was passed into a hot soln of 6-methoxycoumaran-3-one (8 g) and 2-nitrobenzaldehyde (11 g) in absolute EtOH until saturation. The product separated immediately as a grey precipitate, which was collected, washed with water and crystallized from acetone-EtOH (charcoal) to give fluffy yellow needles of nitroaurone **5**, m.p. 201–202°. (Found: C, 64·70; H, 3·77; N, 4·73. $C_{16}H_{11}NO_5$ requires: C, 64·64; H, 3·73; N, 4·71%); τ ($CDCl_3$) 2·67 (s, 1H, β-H). UV irradiation of nitroaurone **5** afforded decomposition products; the reaction was not further pursued.

trans-2-(2-*Aminobenzylidene*)-6-*methoxycoumaran*-3-*one* (**6**). A suspension of $SnCl_2$ (10 g) in glacial AcOH (140 ml) was brought into soln by saturating the mixture with dry HCl and the resulting soln was cooled to below 10°. *trans*-2-(2-Nitrobenzylidene)-6-methoxycoumaran-3-one (5 g) was added to the soln in small amounts and when it was all dissolved, the mixture was kept, with occasional shaking, at room temp for 16 hr. The yellow precipitate which separated was collected, suspended in water and neutralized with NaOH aq (10%). The copious red precipitate which formed was collected, washed with water and recrystallized from acetone to give fluffy orange needles of *amino-aurone* **6** (3·8 g; 85%), m.p. 215°. (Found: C, 71·9; H, 4·7; N, 5·4. $C_{16}H_{13}NO_3$ requires: C, 71·9; H, 4·9; N, 5·2%); τ (DMSO-d_6), 6·02 (s, 3H, 6-OMe), 4·0 (s, borad, 2H, 2′-NH_2), 2·85 (s, β-H).

2,3-(6-*Methoxycoumaran*-3,2)*quinoline* (**8**). (a) A sat soln of sodium dithionite was added to a suspension of *trans*-2-(2-nitrobenzylidene)-6-methoxycoumaran-3-one (1 g) in boiling EtOH (50 ml), giving the soln an orange-red colouration. Sodium dithionite was added until the orange colour disappeared, indicating complete reduction of the nitroaurone. The cooled mixture was filtered and diluted with water. The precipitate obtained was collected and crystallised from EtOH to give yellow needles of quinoline **8**, (0·3 g; 36%), m.p. 171°. (Found: C, 77·11; H, 4·67; N, 5·90. $C_{16}H_{11}NO_2$ requires: C, 77·09; H, 4·45, N, 5·62%); τ ($CDCl_3$) 6·02, (OMe) 1·77–3·01 (aromatic protons).

(b) A sat soln of sodium dithionite (1·5 ml) was added gradually to a soln of aminoaurone **6** (50 mg) in EtOH (5 ml) at reflux temperature. When the orange red colour of the mixture disappeared (*ca.* 3 hr), the soln was cooled and the solid which separated collected and dried, m.p. 168–170°. A second crop, m.p. 166–168° (total yield, 0·35 mg) was obtained on dilution of the filterate. Mixture m.ps with samples of quinoline **8** in each case showed no depression.

When a soln of aminoaurone **6** (50 mg) in EtOH (5 ml) was heated under reflux for 2 h, it was recovered unchanged (m.p. and m.m.p. 215°) on work up.

Acknowledgements—The authors express their gratitude to Professor E. M. Philbin for her interest and encouragement. Two of us (B.A.B. and J.A.K.) thank the Minister for Education, Republic of Ireland, for maintenance grants.

REFERENCES

[1] B. A. Brady, M. M. Healy, J. A. Kennedy, W. I. O'Sullivan and E. M. Philbin, *Chem. Comm.* 1435 (1970).

[2a] P. Friedländer and L. C. Schnell, *Ber. Dtsch. Chem. Ges.* **30**, 2150 (1897); [b] L. Kesselkaul and St. V. Kostanecki, *Ibid.* **29**, 1888 (1896); G. Woker, St. V. Kostanecki and J. Tambor, *Ibid.* **36**, 4235 (1903).

[3] B. Cummins, D. M. X. Donnelly, J. F. Eades, H. Fletcher, F. O'Cinneide, E. M. Philbin, J. Swirski, T. S. Wheeler and R. K. Wilson, *Tetrahedron* **19**, 499 (1963).

[4] J. Chopin, P. Durual and M. Chadenson, *Bull. Soc. Chim. Fr.* 3572 (1965).

[5] S. K. Grover, V. N. Gupta, A. C. Jain and T. R. Seshadri, *J. Sci. Ind. Research* **19B**, 258 (1960).

[6] Y. Okajima, *Yakagaku Zasshi* **80**, 318 (1960).

[7] T. A. Geissman and C. D. Heaton, *J. Am. Chem. Soc.* **65**, 677 (1943).

[8] T. A. Geissman and W. Mojé, *Ibid.* **73**, 5765 (1951).

[9a] H. E. Zimmerman and L. Aheramjian, *Ibid.* **81**, 2086 (1959); [b] H. E. Zimmerman, L. Singer and B. S. Thyagarajan, *Ibid.* **81**, 108 (1959).

[10] W. B. Black and R. E. Lutz, *Ibid.* **77**, 5134 (1955).

[11] A. Hassner and T. C. Mead, *Tetrahedron* **20**, 2201 (1964).

[12] D. N. Kevill, E. D. Weiler and N. H. Cromwell, *J. Org. Chem.* **29**, 1276 (1964).

[13] J. R. Doherty, D. D. Keane, K. G. Marathe, W. I. O'Sullivan, E. M. Philbin, R. M. Simons and P. C. Teague, *Tetrahedron* **26**, 2545 (1970).

[14] J. W. Emsley, J. Feeney and L. H. Sutcliff, *High Resolution Nuclear Magnetic Resonance Spectroscopy* Vol. 2, p. 721. Pergamon Press.

[15] V. L. Bell and N. H. Cromwell, *J. Org. Chem.* **23**, 789 (1958).

[16] R. L. Reeves, *The Chemistry of the Carbonyl Group*, p. 567. S. Patai Ed. Interscience Publishers, London (1966).

[17] K. v. Auwers and P. Pohl, *Annalen* **405**, 243 (1915).

[18] A. Streitwieser, Jr. and J. R. Wolfe, Jr., *J. Am. Chem. Soc.* **79**, 903 (1957).

[19] A. Hassner and N. H. Cromwell, *Ibid.* **82**, 1452 (1960).