International Journal of Advance Research in Science and Engineering
Vol. No.4, Issue 11, November 2015
www.ijarse.com
IJARSE
ISSN 2319 - 8354

SYNTHESIS OF 2-CINNAMYLIDENE- 3(2H) – BENZOFURANONES AND ^{13}C-NMR SPECTRAL STUDIES OF (i) 2-CINNAMYLIDENE- 3(2H) - BENZOFURANONES AND (ii) 2ˈ-HYDROXY-ω-CINNAMYLIDENE ACETOPHENONES

Sharda Pasricha[1], Manasi Singhi[2]

[1]Department of Chemistry, Sri Venkateswara College , University of Delhi, New Delhi, (India)
[2]Department of Chemistry,
Ambedkar Institute of Advanced Communication Technologies and Research, Geeta Colony,
New Delhi, (India)

ABSTRACT

2-Cinnamylidene-3(2H) -benzofuranones have been synthesized in good yields by the reaction of appropriate 3(2H) - benzofuranone with cinnamaldehyde in alkaline medium in the presence of triethylbenzylammonium chloride (TEBA) as the phase transfer catalyst.

^{13}C-NMR studies of 2-Cinnamylidene- 3(2H) - benzofuranones (3) and the closely related 2ˈ-hydroxy-ω-cinnamylidene acetophenones (4) have been recorded. Their study has revealed the utility of ^{13}C-NMR over ˈH-NMR spectra for the diagnostic assignment of the four olefinic protons.

***Keywords:* 2-Cinnamylidene-3(2H) –benzofuranones,2ˈ-hydroxy-ω-cinnamylidene acetophenones, synthesis, TEBA, ^{13}C-NMR.**

I. INTRODUCTON

Aurones are biologically active compounds showing various types of biological activites viz; antileishmanial activity,anticancer, hepatitis C virus inhibitors, antibacterial and antioxidant activities[1,2,3,4]. 2-Cinnamylidene- 3(2H) -benzofuranones bear a close structural resemblance to 2'-hydroxy-ω-cinnamylidene acetophenones and are vinyl analogues of 2-benzylidene-3(2H) -benzofuranones. Because of their close structural resemblance to these two classes of compounds, it was considered to ,compare and contrast their methods of preparation.

2'- Hydroxychalcones undergo AFO- oxidation[5] at low temperature to give aurones. However 2'-hydroxy-ω-cinnamylidene acetophenones under similar conditions did not give the 2-cinnamylidene- 3(2H)-benzofuranones[6].

We report herein that 3(2H)- benzofuranones (1) undergo smooth condensation with cinnamaldehyde (2) to the corresponding 2-cinnamylidene-3(2H)- benzofuranones (3) when reacted with 30% aqueous potassium hydroxide and TEBA in ethanol at room temperature for 16-24 hrs.

^{1}H-NMR spectral studies of 2-cinnamylidene-3(2H)-benzofuranones (3) and 2'-hydroxy-ω-cinnamylidene acetophenones (4) revealed [7] that the olefinic protons can not be distinguished from one another as they merge with the aromatic protons in the region (δ6-8). Therefore assignment of any particular δ value to any of them based on ^{1}H-NMR spectra becomes extremely difficult.

Hence, it was considered to take up the study of ^{13}C-NMR spectra of some representative 2-cinnamylidene-3(2H)-benzofuranones and 2'-hydroxy-ω-cinnamylidene acetophenones in order to ascertain if it would be possible to assign separate δ values to the olefinic carbons for diagnostic purpose.

^{13}C-NMR spectra of various 2-cinnamylidene-3(2H)-benzofuranones and 2'-hydroxy-ω-cinnamylidene acetophenones have now been recorded and studied (“Table III” and “Table IV” respectively). Assignment of δ-values to various carbons has been made by making use of the correlation tables[8] of substitution chemical shifts and also by comparison with existing literature ^{13}C– NMR data of 2'-hydroxy chalcones[9] and aurones[10] which they so closely resemble.

II. MATERIALS AND METHODS

All chemicals and solvents were obtained from Merck,India,and were used as received or dried using standard procedures.

Melting points are uncorrected.

The ^{1}H-NMR spectra were recorded on a Perkin Elmer R-32 (90 MHz) instrument or on Hitachi F.T. NMR (60 MHz) instrument with tetramethylsilane (TMS) as the internal standard.

The 13C-NMR spectra were recorded on ACP Bruker F.T. (300 MHz) instrument with TMS as the internal standard.

The C, H analysis were carried out on Carlo Erba 1108 Heraeus instrument or on Pregl apparatus.

Compounds 4a-4h were prepared by the method of Makrandi et. al. [7]. Melting points of the new compounds are given in “Table II”.

2.1 General Method of Preparation of Compound 3a

6-Methoxy-3 (2H)- benzofuranone (0.5 g) was dissolved in ethanol (15ml) and cinnamaldehyde (0.57ml) was added to it along with 30 % aqueous potassium hydroxide (10ml) and triethylbenzlammonium chloride (0.70 g). The solution was magnetically stirred for 16 hrs. The solution was cooled to 0˚,diluted with water and a steady streamof sulphurdioxide gas was passed through it until it was acidic. The yellow solid obtained was filtered, washed with saturated solution of sodium bicarbonate and then with water. The solid obtained was recrystallised from ethanol to afford 2-cinnamylidene-6-methoxy-3(2H)- benzofuranone.

Compounds **3b-3d** were prepared by the similar method.

2.2.^{1}H-NMR and Elemental Analysis of New Compounds

3a: ^{1}H-NMR ($CDCl_3$): δ 3.70 (s, 3H,-OCH_3), 6.2-7.5 (m, 11H, H_5, H_7, H_A, H_K, H_D, H_4, C_6H_5).

Found: C, 77.8; H, 5.4; $C_{18}H_{14}0_3$ requires: C, 77.6; H, 5.1

3b: ^{1}H-NMR ($CDCl_3$): δ 3.7 and 3.72 (each s, 3H,-OCH_3), 5.8 (d, 1H, J=2Hz, H_5) ,6.0 (d, 1H, J=2 Hz, H_7), 6.2-7.2 (m, 8H, H_A, H_D, H_K, C_6H_5)

Found: C, 74.1; H, 5.3; C_{19} H_{16} O_4 requires C, 74.0; H, 5.2.

3c: ^{1}H-NMR ($CDCl_3$) : δ 2.45 (s, 3H,-CH_3), 7.2-7.8 (m, 11H, H_4, H_6, H_7,-CH-CH=CH- ,-C_6H_5)

Found: C, 82.4; H, 5.4; C_{18} $H_{14}O_2$ requires C, 82.4; H, 5.4.

3d: ^{1}H-NMR ($CDCl_3$) : δ 6.75-7.7 (m, 11H, H_4, H_6, H_7,-CH-CH=CH- ,-C_6H_5)

Found: C, 72.2; H, 3.9;$C_{17}H_{11}O_2Cl$; requires:C,72.2;H,3.9.

4c: ^{1}H-NMR ($CDCl_3$) : δ 3.80 (s, 3H,-OCH_3), 6.05-7.45 (m, 12H, H_4', H_3', H_5',-CH=CH-CH=CH,-C_6H_5) and 14.11 (s,,1H,OH).

Found: C,77.3; H, 6.0. C_{18}, H_{16}, O_3 requires C, 77.1; H, 5.8%

4g: ^{1}H-NMR ($CDCl_3$) : δ 3.66 and 3.75 (each s of 3H,2xOCH_3),5.75 and 5.85(each d of 1H,J=2Hz, H_3'and H_5'), 6.60-7.45 (m, 9H, ,-CH=CH-CH=CH,-C_6H_5) and 14.11 (s,,1H,OH).

Found: C,73.3; H, 6.1. C_{19}, H_{18}, O_4 requires C, 73.5; H, 5.9%

4h: ^{1}H-NMR ($CDCl_3$) : δ 2.00(s,3H,CH_3), 3.90 (bs, 6H,2xOCH_3),6.00(s,1H, H_5'), 6.90-7.60 (m, 9H,-CH=CH-CH=CH,-C_6H_5) and 14.00 (s,,1H,OH).

Found: C,73.8; H, 6.4. C_{20}, H_{20}, O_4 requires C, 74.0; H, 6.2%

III. RESULTS AND DISCUSSION

3.1. 2-Cinnamylidene-3(2H)-Benzofuranones

Carbonyl group was assigned at δ 182ppm corresponding to carbonyl resonance of aurones .C-4' in the ring B was assigned a higher δ value than C-2'/C-6' and C-3'/C-5'. This is so because during calculation of δ value for ring B the effect of only one double bond on the ring carbons was considered. Assuming the presence of another double bond in conjugation with the first one should have a deshielding effect on C-4', it has been assigned higher δ value than C-2'/C-6' or C-3'/C-5'. A high field signal at δ 55.0-55.7 is due to the methoxyl group. In compound (3c) methyl group appears at δ 20.5 which is close to the methyl carbon attached to benzene ring (δ21.2 in toluene).

C = O, C-α, C-β, C-γ and ring B carbons appear at similar δ values in all the compounds, C-α is observed around 113 ppm, C-β is around 127 ppm, C-γ is observed around 140 ppm and C-2 is around 160 ppm. Thus all four olefinic carbons in all 2-cinnamylidene-3(2H)-benzofuranones appear at widely separated δ values (110-160 ppm) showing assignment of these carbons. ^{13}C-NMR shifts are displayed in “Table III”.

3.2. 2'-Hydroxy-ω-Cinnamylidene Acetophenones

The δ values for carbon of carbonyl group of aryl and conjugated ketones is observed between 196-199 ppm[8]. However, presence of 2'- hydroxy group moves it downfield by 3-5 ppm, relative to the corresponding 2'-

methoxy and 2'- acetoxy compounds owing to the intramolecular hydrogen bonding[11]. Therefore, low intensity signal between 192-194 ppm was assigned to the carbonyl resonance of compounds **4a-4h**; this compares well with C=0 absorption of chalcones[9].

In most of the cases the four olefinic carbons, C- β and C-δ have been assigned lower field values than C-γ and C-α. This is because the two double bonds are conjugated to the carbonyl functions. Due to the delocalization of π - electrons towards oxygen atoms of carbonyl group, the electron density at C- β and C-δ would be lower than at C- α and C-c. Therefore, the four olefinic carbons in the order of increasing electron density around their nucleus are C- β < C-δ < C- γ < C- α. However, in the case of compounds **4c**, **4g** and **4h**, possessing a methoxyl group at position- 6', possibly due to loss of coplanarity between ring A and keto group, C-α, C- γ and C-4 experience net desheilding, whereas, C- β and C-δ experience net shielding w.r.t. average values of these carbons in rest of the cases.

From the “Table IV”, it is clear that δ values of all the four olefinic carbons appear at widely separated values. Also, in almost all the cases except **4d,** C- γ and C-δ appear as readily distinguishable six line multiplets in the off- resonance decoupled spectrum.

C-4 in ring B has been given higher d value than C-2/C-6 or C-3/C-5 considering the desheilding effect of two conjugated double bonds.

Compounds **4b-4d** and **4f-4h** show high field signal between δ55.0 to 55.7 due to the presence of methoxyl group in ring A. The methoxyl carbon at C-3' in **4f** appears at d 60.1 because it is ortho to another methoxyl at C-4'.

Methyl carbon in compound **4e** appears at the expected value (δ 20.5) as compared to the methyl carbon in **4h**, which appears at a very high field. The high field absorption, probably, is caused by the combined effect of the neighbouring oxygen atoms.

In compound **4b** due to the presence of methoxyl group at C-4', C-2', C-4' and C-6' move downfield, whereas, C-1', C-3' and C-5' move upfield. Similar effects were observed in **4c** and **4d** which contain one methoxyl substituent each in ring A as in **4b**.

Presence of methyl group at C-5' in **4e** causes downfield shift of C-5' by 17.5 ppm. Very little shielding effect of methyl group is observed, however, on ortho/para carbons i.e. C-4'/C-6' and C-2'. Carbons meta to the methyl group also remained unaffected.

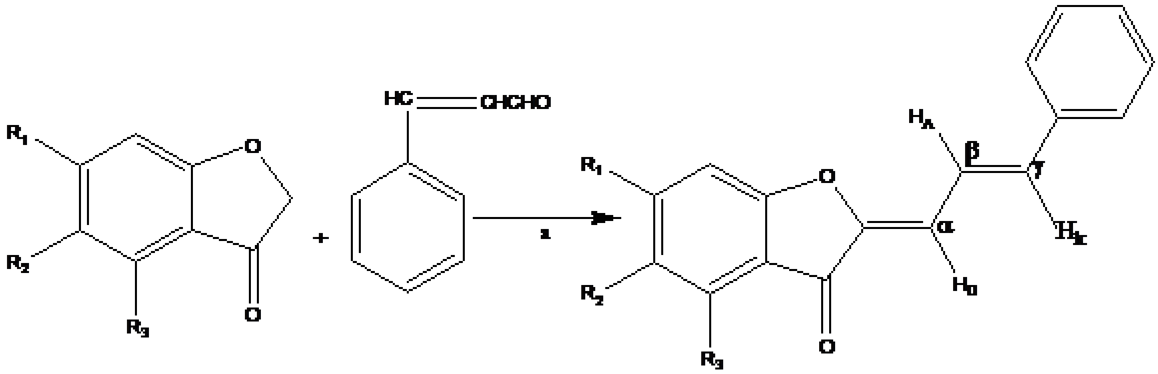
In **4f** and **4g** the combined effect of two methoxyl groups is experienced by the ring A carbons. In **4f** both C-3' and C-4', due to the presence of methoxyl groups, move downfield and rest of the ring carbons experience a shielding effect of different magnitude, which is maximum for C-5' and minimum for C-6'.

Similarly, due to combined effect of two methoxyl and one methyl group in **4h**, C-4' and C-6' move downfield, and rest of ring A carbons move up field.

All the carbons in ring B and other carbons i.e. C=0, C- α, C-β, C- γ and C-δ however appeared at similar δ values in **4a-4h**.

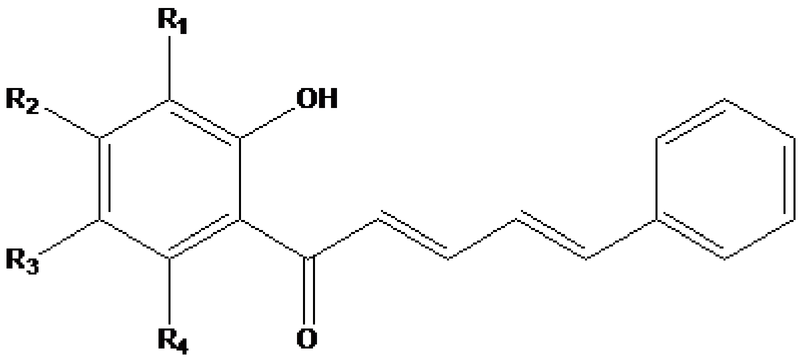
From the above ^{13}C NMR spectral studies we observe that all the four olefinic carbons appear at widely separated δ values in all the compounds **4a-4h**, and also, in almost all the cases C- γ and C-δ appear as easily distinguishable six line multiplets in the off resonance decoupled spectra.

IV. FIGURES AND TABLES



(1) (2) (3)

a:30%Aq.KOH:TEBA:C_2H_5OH:16-24 hrs.



(4)

Table –I: Physical Data of 2-Cinnamylidene-3(2H) -Benzofuranones

Comp.	R_1	R_2	R_3	m.p. (°C)	Reaction Period (hr.)	% yield
3a	OCH_3	H	H	188°	16	85
3b	OCH_3	H	OCH_3	207-08°	16	82
3c	H	CH_3	H	120°	18	85
3d	H	Cl	H	180°	24	80

Table –II: Physical Data of 2'-hydroxy-ω-Cinnamylidene Acetophenones.

Comp.	R_1	R_2	R_3	R_4	m.p. (ºC)
4a	H	H	H	H	-
4b	H	OCH_3	H	H	-
4c	H	H	H	OCH_3	124-125º
4d	H	H	OCH_3	H	-
4e	H	H	CH_3	H	-
4f	OCH_3	OCH_3	H	H	-
4g	H	OCH_3	H	OCH_3	109-110º
4h	CH_3	OCH_3	H	OCH_3	182-183º

'+' m.p. of all new compounds have been reported.

Table-III: ^{13}C –NMR Structural Data of Compounds (3a - 3d)

		Carbon atom number																
		c-1′	c-2′	c-3′	c-4′	c-5′	c-6′	c-2	c-3	c-4	c-5	c-6	c-7	c-8	c-9	c-α	C-β	c-γ
3a	X	136.4	127.3	128.8	129.1	128.8	127.3	167.3	182	120.6	111.8	167.8	96.5	148	115	112.9	125.6	140..5
	Y	137 s	128 d	128 d	126 d	128 d	128 d	160 s	181-186 s	131 d	106 d	165 s	99 d	160 s	114 s	113 d	127 d	130 d
3b	X	136.5	127.2	128.8	128.9	128.8	127.2	168.3	179.7	159.3	89.1	168.8	93.8	148.5	106	111.9	120	139.7
	Y	137 s	128 D	128 d	126 d	128 d	128 d	160 s	181-186 s	161 s	91 d	166 s	91 d	160 s	99 s	113 d	127 d	130 d
3c	X	136.4	127.4	128.8	129.2	128.8	127.4	163.9	183.9	120.8	132.9	137.8	112.3	147.9	122.4	113.9	124.1	141.4
	Y	137 s	128 d	128 d	126 d	128 d	128 d	160 s	181-186 s	130 d	136 s	135 d	114 d	157 s	122 s	113 d	127 d	130 d
3d	X	136.1	127.5	128.8	129.5	128.9	127.5	163.5	182.3	122	129.3	136.3	114	148	122	115.3	124	142
	Y	137 s	128 d	128 d	126 d	128 d	128 d	160 s	181-186 s	130 d	127 s	135 d	115 d	157 s	123 s	113 d	127 d	130 d

- X: δ observed; Y: δ calculated;
- s,d are the singlet and doublet multiplicities observed in off resonance decoupled spectrum

Table-IV: ^{13}C –NMR Spectral Data of Compounds (4a - 4b)

Comp.		Carbon atom number																	
		C-1'	C-2'	C-3'	C-4'	C-5'	C-6'	C=O	C-α	C-β	C-γ	C-δ	C-1	C-2	C-3	C-4	C-5	C-6	OMe/Me
4a	X	120.0 S	163.6 S	118.6 d	136.2 d	118.7 d	129.5 d	193.5 s	123.5 d	145.5 d	126.7 m	142.9 m	136.2 s	127.4 d	128.9 d	129.5 d	128.9 d	129.5 d	
	Y	124	156	116	135	122	130	191-196	131	151	127	130	137	128	128	126	128	128	
4b	X	114.0 s	166.2 s	101.1 d	166.7 s	107.7 d	131.1 d	191.8 s	123.8 d	144.5 d	126.8 m	142.2 m	136.1 s	127.4 d	128.9 d	129.3 d	128.9 d	127.4 d	55.5 q
	Y	116	157	101	165	107	131	191-196	131	151	127	130	137	128	128	126	128	128	55-57
4c	X	111.7 S	160.6 s	111.1 d	135.2 d	100.9 d	165.1 s	193.5 s	128.8 d	143.2 d	127.0 m	141.1 m	136.1 s	127.3 d	128.6 d	130.8 d	128.6 d	127.3 d	55.4 q
	Y	109	157	108	136	107	160	191-196	131	151	127	130	137	128	128	126	128	128	55-57
4d	X	119.3 S	151.5 s	119.2 d	123.3 d	158.0 s	112.1 d	192.8 s	123.8 D	145.3 d	126.6 d	142.6 d	135.9 s	127.3 d	128.7 d	129.3 d	128.7 d	127.3 d	55.7 q
	Y	125	148	117	120	152	115	191-196	131	151	127	130	137	128	128	126	128	128	55-57
4e	X	119.5 S	161.7 s	118.3 d	136.8 d	135.9 s	127.8 d	192.7 s	123.5 d	144.7 d	126.6 Six line	142.2 Six line	135.9 s	127.2 d	128.7 d	129.0 d	128.9 d	127.2 d	20.5 q
	Y	124	154	116	135	131	130	191-196	131	151	127	130	137	128	128	126	128	128	7-22
4f	X	115.5 s	158.2 s	136.8 s	158.4 s	102.6 d	125.3 d	191.7 s	123.5 d	144.3 d	126.6 m	141.1 m	135.9 s	127.2 d	128.6 d	129.0 d	128.6 d	127.2 d	55.6 q 60.1 q
	Y	117	142	131	150	108	123	191-196	131	151	127	130	137	128	128	126	128	128	55-57 59-63
4g	X	106.3 S	162.2 s	93.8 d	168.6 s	91.0 d	165.9 s	192.0 s	128.7 d	142.7 d	127.6 m	140.5 m	136.4 s	127.1 d	128.6 d	131.0 d	128.6 d	127.1 d	55.4 q 55.2 q
	Y	101	158	95	166	92	161	191-196	131	151	127	130	137	128	128	126	128	128	55-57
4h	X	105.8 S	160.5 s	105.8 s	164.1 s	85.7 d	162.9 s	192.1 s	128.5 d	142.2 d	128.0 m	140.1 m	136.0 s	126.8 d	128.8 d	131.0 d	128.4 d	126.8 d	7.2 q 55.2 q 55.0 q
	Y	101	158	104	166	92	159	191-196	131	151	127	130	137	128	128	126	128	128	7-22 55-57

- X: δ observed; Y: δ calculated;
- Multiplicity of signals in the off resonance decoupled spectra are shown by the symbols: s-singlet, d-doublet, q-quartet and m-six line multiplet.

V. CONCLUSION

A new efficient method for the synthesis of 2-cinnamylidene-3(2H)- benzofuranones has been developed by the smooth condensation of 3(2H)- benzofuranones with cinnamaldehyde in the presence of 30% aq.KOH+TEBA /ethanol at room temperature.

All four olefinic carbons in all the 2-cinnamylidene-3(2H)-benzofuranones appear at widely separated δ values. Similarly, in all the 2'-hydroxy-ω-cinnamylidene acetophenones all the four olefinic carbons appear at widely separated δ values and also, in almost all the cases C- γ and C-δ appear as easily distinguishable six line multiplets in the off resonance decoupled spectra. Therefore, ^{13}C NMR is much more useful than ^{1}H NMR for the diagnostic assignment of the olefinic carbons.

REFERENCES

[1] M. Roussaki, S. C. Lima, A.M. Kypreou, P. Kefalas, A.Silva and A. Detsi Int J Med Chem.,2012, 2012, 196921.

[2] A. Barakat, A. M. Al-Majid, S. M. Soliman, Y. N. Mabkhot, M. Ali, H. A. Ghabbour, H. Fun, and A. Wadood ,Chem Cent J.,9, 2015, 35.

[3] R Haudecoeur, A. Ahmed-Belkacem, W.Yi, A. Fortuné, R. Brillet, C. Belle, C.Pallier, J. Pawlotsky,and A. Boumendjel, J Med Chem., 54(15), 2011, 5395–5402.

[4] M.Braun, A. Hessamian-Alinejad , B. Lacroix 1, B.Hernandez and G. Fischer ,Molecules, 13, 2008, 995-1003

[5] V.V.S. Murty, P.V.Raman, R.S.Thakur and T.R.Sheshadri, Journal of Scientific and Industrial Research, 21B, 1962, 80.

[6] F.M.Dean and V.Podimuang , Journal of Chemical Society, 1965, 3978.

[7] J.K.Makrandi and Seema, Indian Journal of Chemistry, 30B, 1991, 788.

[8] W.Kemp, Organic Spectroscopy (ELBS, Macmillan, London, 3rd Edition,1991).

[9] R.Radeglia, W.Attenburg, W.D.Orlow and M.Reinhard , Zeitschrift für anorganische und allgemeine Chemie, 9, 1976, 363.

[10] E.Pretch,E. Buhlmann and A.Affolter , Structure determination of organic compounds(Springer, 2004).

[11] A.Pelter ,R.S.Ward and T.I.Gray, Journal of Chemical Society Perkin Transactions I, 1976, 2475.