Microwave assisted synthesis of 3,5–diaryl-6-carbethoxy cyclohex-2-en-1-ones on solventless inorganic solid support and their antibacterial activities

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Síntesis asistida por microondas de 3,5–diaril-6-carbetoxi ciclohex-2-en-1-onas en soporte inorgánico sólido sin disolvente y su actividad antibacteriana.

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Recibido: 14 de septiembre de 2011; aceptado: 11 de octubre de 2011

RESUMEN

Se han sintetizado varios derivados de 3,5–diaril–6-carbetoxi ciclohex-2-en-1-onas (4a-g), por reacción de aceto-acetato de etilo con chalconas substituidas en fase disuelta convencional (acetona y K_2CO_3 anhidro) y asistida por microondas (piperidina/Al_2O_3 básica). A partir del estudio comparativo hemos concluido que se puede llevar a cabo una síntesis eficiente en medio seco de 3,5–diaril–6-carbetoxi ciclohex-2-en-1-onas, bajo radiación con microondas, en un horno microondas doméstico, con una velocidad de reacción aumentada y mejores rendimientos. La estructura de los compuestos se justifica mediante datos analíticos y espectroscópicos. Se han estudiado también relaciones estructura-actividad de los compuestos sintetizados

Palabras clave: actividad antibacteriana, alúmina básica, chalconas , ciclohexenona, irradiación con microondas.

SUMMARY

A variety of 3,5–diaryl–6-carbethoxy cyclohex-2-en-1-ones derivatives (4a-g) were synthesized by the reaction of ethylacetoacetate with substituted chalcones in conventional (acetone & anhy. K_2CO_3) and microwave assisted solution phase (acetone & anhy. K_2CO_3) and dry media (basic Al_2O_3/piperidine). From the comparative study we have concluded that efficient dry media synthesis of 3,5–diaryl–6-carbethoxy cyclohex-2-en-1-ones under microwave irradiation can be carried out in domestic microwave oven with enhanced reaction rates and improved yields. The structure of compounds are supported by spectral and analytical data. The structure activity relationship of synthesized compounds have also been studied.

Keywords: antibacterial activity, basic alumina, chalcones, cyclohexenone , microwave irradiation

RESUM

S'han sintetitzat diversos derivats de 3,5–diaril–6-carbetoxi ciclohex-2-en-1-ones (4a-g), per reacció d'aceto-acetat d'etil amb chalcones substituïdes en fase dissolta convencional (acetona i K_2CO_3 anhidre) i assistida per microones (piperidina/Al_2O_3 bàsica). A partir de l'estudi comparatiu hem conclòs que es pot dur a terme una síntesi eficient en medi sec de 3,5–diaril–6-carbetoxi ciclohex-2-en-1-ones, sota radiació amb microones, en un forn microones domèstic, amb una velocitat de reacció augmentada i millors rendiments. L'estructura dels compostos es justifica mitjançant dades analítiques i espectroscòpics. S'han estudiat també relacions estructura-activitat dels compostos sintetitzats

Paraules clau: activitat antibacteriana, alúmina bàsica, chalcones , ciclohexenona, irradiació amb microones.

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INTRODUCTION

Green Chemistry[1-10] (environmentally benign chemistry) is not different from traditional chemistry in as much as it embraces the same creativity and innovation that has always been central to classical chemistry.

But with an increase in environmental consciousness throughout the world, there is a challenge for chemists to develop new products, processes and services that achieve necessary social, economical and environmental objectives. By using these technologies energy input reduces, improvement of selectivity, shortening of reaction time occurs. Some reactions, which are not possible with single heating, can be possible with above technique. In current aspects development of more sustainable products and energy efficient processes with reducing waste are discussed in emerging green technologies. Use of energy sources like light, microwave, ultrasound and electricity are more clean, and efficient.

As we know chalcones are valuable intermediates in organic synthesis[11] and exhibit a multitude of biological activities[12,13]. From a chemical point of view, an important feature of chalcones is the ability to act as activated unsaturated system in conjugated addition reactions of carbanions in the presence of basic catalysts. [14] This type of reaction may be exploited with the view of obtaining highly functionalized cyclohexene derivatives[15,16], but is more commonly used for the preparation of 3,5-diaryl-6-carbethoxycyclohexenones via Michael addition of ethyl acetoacetate . Cyclohexenones are efficient synthons in building spiranic compounds[17] or intermediates in the synthesis of fused heterocycles such as benzoselenadiazoles and benzothiadiazoles[18], benzopyrazoles and benzisoxazoles[19] or carbazole derivatives[20] with diverse biological activities. Further cyclohexenone have been popular substrate for the generation of variety of intermediate compounds. Some of these compounds and their derivatives posses a wide range of biological activities. Cyclohexenone are also known as a useful chiral[21] building block for preparation of asymmetric[22] enantioselective[23], stereoselective[24], regioselective[25], and substituted cyclohexenone rings[26].

In this paper we have described microwave assisted synthesis of 3,5–diaryl-6-carbethoxy cyclohex-2-en-1-ones on solventless inorganic solid support[27,28] .The antibacterial activities against four bacterial strains are also described

MATERIAL AND METHODS

General Procedures. Melting points are uncorrected and were recorded using open-end capillaries.Thin layer chromatography of synthesised compounds was performed on silicagel-G plates using benzene-ethylacetate (9:1) solvent system and iodine as visualising agent. The IR spectra of synthesised compound were recorded on DIGILAB FTS-14 or Perkin- Elmer 157P spectrophotometer in KBr (ν_{max} in cm^{-1}). ^1H NMR was recorded on $CDCl_3$ on a varian CFT-20 or Brucker DRX-300 (300 MHz) spectrometer using TMS as internal standard (chemical shifts in δ, ppm). FAB MS was recorded on Jeol SX-102 spectrometer. All compounds gave satisfactory elemental analysis and spectral data. All the reactions were carried out in a domestic microwave oven (Kenstar, output energy 1200W,frequency 2450 MHz, model No. MO9706}.

RESULTS AND DISCUSSION

In the present work we have carried out reaction for the synthesis of substituted chalcones using variously substituted benzaldehydes and acetophenones. These substituted chalcones were taken for the reaction with ethylacetoactate to give cyclohexenone derivative

The reaction of substituted chalcones and ethylacetoacetate on solid phase using basic alumina under microwave irradiation (MWI)afforded the substituted 3,5–diaryl-6-carbethoxy cyclohex-2-en-1-ones 4a-g within (4-6) min as compared to solvent phase under microwave irradiation (5-10 min) and conventionally (3-6 hrs)

It seems that under basic conditions, the active methylene group of acetoacetic ester is first converted to a carbanion species, which in turn attacks at β carbon of the enone system in a Michael type of addition reaction followed by intramolecular cyclocondensation. resulting 3,5–diaryl–6-carbethoxy cyclohex-2-en-1-ones **(**4a-g)

The structure of the synthesized compound were established on the basis of their analytical and spectroscopic data.

The infra red spectra of cyclohexenones exhibited absorbtion bands of 3600-3040 cm^{-1} (-OH),3020-2800 cm^{-1}(Ar-H and aliphatic C-H) 1730-1700 cm^{-1} (ester>c=o) and1630-1600 cm^{-1}(α, β-unsaturated >C=O). The two major aromatic c=c frequencies in the region 1600-1400 cm^{-1} are among the strongest observed occur in the region 1580-1570 cm^{-1} and 1460-1430 cm^{-1}. 1450 cm^{-1} and 1370 cm^{-1} for –CH deformation and 1240 cm^{-1} for C-O stretching vibration. IR bands in the region 860-750 cm^{-1} are due to substituted phenyl rings

The PMR spectrum showed a triplet at δ1.2-1.3(-CH_2) and quartet at 4.1-4.2 (-CH_2) for –O-CH_2-CH_3.The C_2-H olefinic proton appeared as a singlet at δ6.2-6.25. The methylene proton of C4-H were observed as two doublets at δ3.01-3.1. The C5-H appears as a multiplet at δ3.2-3.54 . While the proton at C6-H was observed as doublet at δ 3.89-4.04. Multiplets due to aromatic protons was observed at δ 6.7-7.4.

The mass spectrum supported the formation of the compound as the molecular ion peak M^+ that correspond to its molecular weight. Whereas, the base peak was observed due to the loss of ester group and other fragments of mass value.

In conclusion reation of chaclone with ethyl aceto acetate in presence of inorganic solid support (basic alumina) under MWI resulted cyclohexenone derivaties (4a-g) via Michael addition followed by an intra molecular cyclocondensation. This process has advantages over conventional methods, such as shorter reaction time, higher yield, solvent free and environmentally benign. The synthesized compounds may serve as useful intermediate for the synthesis of structurally diverse heterocycles

Antibacterial activity

All the synthesized compounds (4a-g) were screened for their in vitro antibacterial activity against gram positive S.aureus, S. Fecalis and Gram negative bacteria P.mirabilis and P. aeruginosa by the paper disc diffusion method. The zone of inhibition was measured in mm/cm. Standard drug Amicacin and Amoxyclav for gram positive and Tobramycin & Amoxicillin for gram negative were used for comparision. The zone of inhibition was compared with the standard drug after 24 hr of incubation at 25^0 c. All

the compounds (4a-g) exhibited moderate to good activity against test organism.

This observed that compound **4a** (R_3 = OH), **4b** (R_2 = OCH_3, R_3 = OH) **4c** (R_2 = R_3 = OH) **4d** (R_1 = R_3 = OH) **4e** (R_2 = R_5 = OH, R_4 = OCH_3) against S. aureus, compound **4a** (R_3 = OH) **4d** (R_1 = R_3 = OH) **4f** (R_2 = R_4 = OCH_3, R_5 = OH) **4g** (R_1 = R_5 = OH, R_4 = OCH_3) against S. fecalis, compound **4a** (R_3 = OH) **4b** (R_2 = OCH_3, R_3 = OH) **4c** (R_2 = R_3 = OH) **4d** (R_1 = R_3 = OH) **4f** (R_2 = R_4 = OCH_3, R_5 = OH) **4g** (R_1 = R_5 = OH, R_4 = OCH_3) against P. mirabilis and compound **4a** (R_3 = OH) **4b** (R_2 = OCH_3, R_3 = OH) **4c** (R_2 = R_3 = OH) **4d** (R_1 = R_3 = OH) **4g** (R_1 = R_5 = OH, R_4 = OCH_3) against P. aeruginosa are showing excellent antibacterial activity and it may be concluded that these compounds stand to be promising antibacterial agents. Results are summarized in Table 1

General Procedure for the synthesis of 3,5–diaryl–6-carbethoxy cyclohex-2-en-1-ones (4a-g)

(A) Conventional Method:

To a solution of substituted chalcones (0.1 mole) in acetone (40ml) was added ethylacetoacetate (0.2 mole) and anhydrous K_2CO_3 (0.4 mole). The reaction mixture was stirred for 3-6 hours and kept for over-night at room temperature. The mixture was filtered and the filtrate on concentration under reduced pressure give a solid, which on crystallisation from ethanol afforded analytical samples of compounds (4a-g)

(B) Microwave irradiation solution phase (acetone)

To a solution of substituted chalcone (0.1 mole) in acetone (25-30ml) was added ethylacetoacetate (0.2 mole) and anhydrous K_2CO_3 (0.4 mole). The mixture was irradiated in a microwave oven (35%microwave power) for 5-10 min. After the completion of reaction (tlc examination), the reaction mixture was cooled at room temperature and filtered. The mother liquor , evaporated to dryness. The residual

Table 1 *Antibacterial activity of synthesized 3,5–diaryl–6-carbethoxy cyclohex-2-en-1-ones (4a-g) (Zone of Inhibition in mm.): -*

Compound No. & Standard Drug	Gram Positive		Gram Negative	
	S. aureus	S. fecalis	Protius mirabilis	Psedumonas aeruginosa
4a-14	31	25	24	23
4b-15	28	11	23	21
4c-16	24	10	23	21
4d-17	23	24	25	23
4e-18	31	16	13	16
4f-19	15	34	24	10
4g-20	16	25	28	23
Amicacin	31	34	-	-
Amoxyclav	29	33	-	-
Tobramycin	-	-	28	26
Amoxicillin	-	-	29	26

Table – 2: *Comparision of reaction time & Yield of compounds (4a-g).*

Comp. No.	R_1	R_2	R_3	R_4	R_5	Reaction time			Yield (%)		
						Classical (hr.)	Sol. Phase (acetone) (min)	Solid phase Al_2O_3 (min)	Classical	Sol. Phase (acetone)	Solid phase Al_2O_3
4a	H	H	OH	H	H	4	5	4	65	78	87
4b	H	OCH_3	OH	H	H	5	8	6	63	74	79
4c	H	OH	OH	H	H	6	7	5	57	71	84
4d	OH	H	OH	H	H	4	6	5	72	80	83
4e	H	OH	H	OCH_3	OH	5	9	6	60	69	78
4f	H	OCH_3	H	OCH_3	OH	5	10	7	63	74	70
4g	OH	H	H	OCH_3	OH	3	8	6	67	76	81

crude mass is crystallized with suitable solvent to give compounds (4a-g).

(C) Solid Phase Microwave Assisted Method (Basic alumina & piperidine):

A mixture of substituted chalcone (0.01 mol), ethylacetoacetate (0.02 mol) and piperidine (1-2 ml) was dissolved in ethanol (5-10 ml) and taken in a 100 ml borosil flask. To this 4-5 gm of basic alumina was added and the reactants properly mixed with the help of a glass rod. Adsorbed material was dried in air and irradiated inside the microwave oven at medium power level (50%) intermitently at 30 sec. intervals for a period of 4-6 minute. On completion of reaction (tlc examination), the mixture was cooled at room temperature, extracted with ethanol .Removal of the solvent and subsequent recrystallization with proper solvents resulted compounds (4a-g). Reaction time & yields from different methods are summarized in table 2

The authenticity of the compounds obtained by methods (A), (B) and (C) was confirmed by m.m.ps., co-tlc and IR spectral results.

(4a) 3- Phenyl -5- (2- hydroxy phenyl) -6- carbethoxy cyclohex -2- en -1- ones

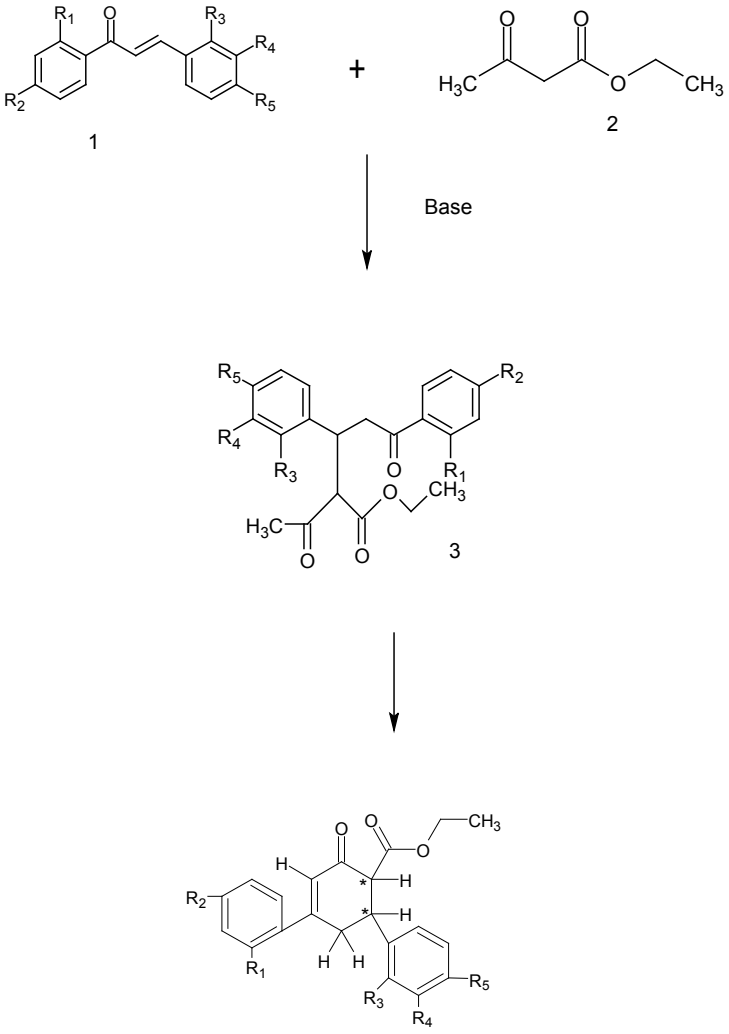
Light Yellow, m.p. 48^0 C , Anal. Calcd. For $C_{21}H_{20}O_4$ (336) : C 74.98 H 5.99 Found: 74.95 H 5.96. **IR (KBr) cm^{-1}** 3558, 3348, 3045, 2981, 2364, 1720(νc=o ester), 1660(νc=o ketone),1643, 1580, 1480, 1423, 1361, 1289, 1239, 1100, 1088, 772, 771, 624 **NMR ($CDCl_3$, δppm):** 1.32 [t, 3H, -OCH_2 – CH_3], 4.21 [q, 2H, -O –CH_2 – CH_3], 6.24 [s, 1H, C_2H, ethylene], 3.14 [dd, 1H, H_α, methylene], 3.03 [dd, 1H, H_β, methylene], 3.22-3.56 [m, 1H, C_5H methane], 3.81 [d, 1H, C_6H, methane], 6.86-7.48 [m, broad & unresolved, Ar.-H], 9.71 (s, 1H, OH] , **MS(m/z)** :336[M]$^{+\cdot}$, 321[M-CH_3]$^{+\cdot}$, 319[M-OH]$^{+\cdot}$, 232[M-$C_4H_8O_3$]$^{+\cdot}$, 307[M-C_2H_5]$^{+\cdot}$, 291[M-C_2H_5O]$^{+\cdot}$, 263[M-$C_3H_5O_2$]$^{+\cdot}$, 262[M-$C_3H_6O_2$]$^{+\cdot}$, 261[M-$C_3H_7O_2$]$^{+\cdot}$, 230[M-$C_4H_{10}O_3$]$^{+\cdot}$, 218[M-$C_5H_{10}O_3$]$^{+\cdot}$, 206[M-$C_6H_{10}O_3$]$^{+\cdot}$, 180[M-$C_8H_{12}O_3$]$^{+\cdot}$, 77[M-$C_{15}H_{15}O_4$]$^{+\cdot}$.

(4b) 3-(4'-Methoxy phenyl) -5-(2-hydroxy phenyl) -6-carbethoxy cyclohex-2-en-1- ones

Light Yellow, m.p. 60^0 C , Anal. Calcd. For $C_{22}H_{22}O_5$ (366) C 72.10 H 6.07 Found: 72.12 H 6.05. **IR (KBr) cm^{-1}** 3444, 3060, 3026, 2919, 2850, 2364, 1947, 1875, 1805, 1726(νc=o ester), 1655(νc=o ketone),1599, 1491, 1451, 1352, 1258, 1116, 1069, 1027, 906, 836, 756, 699 **NMR ($CDCl_3$, δppm):** 1.34 [t, 3H, -OCH_2 – CH_3], 4.22 [q, 2H, -O –CH_2 – CH_3], 6.24 [s, 1H, C_2H, ethylene], 3.15 [dd, 1H, H_α, methylene], 3.02 [dd, 1H, H_β, methylene], 3.21-3.56 [m, 1H, C_5H methane], 3.83 [d, 1H, C_6H, methane], 6.76-7.38 [m, broad & unresolved, Ar.-H], 9.72 (s, 1H, OH], 3.84 [s, 3H, OCH_3] **MS(m/z) :** 366[M]$^{+\cdot}$, 351[M-CH_3]$^{+\cdot}$, 337[M-C_2H_5]$^{+\cdot}$, 321[M-C_2H_5O]$^{+\cdot}$, 293[M-$C_3H_5O_2$]$^{+\cdot}$, 292[M-$C_3H_6O_2$]$^{+\cdot}$, 291[M-$C_3H_7O_2$]$^{+\cdot}$, 274[M-$C_3H_8O_3$]$^{+\cdot}$, 262[M-$C_4H_8O_3$]$^{+\cdot}$, 251[M-$C_5H_7O_3$]$^{+\cdot}$, 242[M-$C_4H_{12}O_4$]$^{+\cdot}$, 239[M-$C_6H_7O_3$]$^{+\cdot}$, 231[M-$C_5H_{11}O_4$]$^{+\cdot}$, 205[M-$C_7H_{13}O_4$]$^{+\cdot}$.

(4c) 3- (4'- Hydroxy phenyl) -5- (2- hydroxy phenyl) -6- carbethoxy cyclohex –2- en -1- ones

Yellow, m.p. 67^0 C , Anal. Calcd. For $C_{21}H_{20}O_5$ (352) C 71.60 H 5.73 Found: 71.58 H 5.72. **IR (KBr) cm^{-1}** 3600, 3251, 3048, 2981, 2365, 1730(νc=o ester), 1663(νc=o ketone), 1588, 1485, 1420, 1370, 1295, 1245, 1103, 1092, 735, 773, 630 **NMR ($CDCl_3$, δppm):** 1.33 [t, 3H, -OCH_2 – CH_3], 4.21 [q, 2H, -O –CH_2 – CH_3], 6.22 [s, 1H, C_2H, ethylene], 3.14 [dd, 1H, H_α, methylene], 3.07 [dd, 1H, H_β, methylene], 3.24-3.58 [m, 1H, C_5H methane], 3.95 [d, 1H, C_6H, methane], 6.74-7.42 [m, broad & unresolved, Ar.-H], 9.71 (s, 1H, OH], 9.46 [s, 1H, OH] **MS(m/z) :** 352[M]$^{+\cdot}$, 337[M-CH_3]$^{+\cdot}$, 323[M-C_2H_5]$^{+\cdot}$, 318[M-O_2H_2]$^{+\cdot}$, 307[M-C_2H_5O]$^{+\cdot}$, 278[M-$C_3H_6O_2$]$^{+\cdot}$, 277[M-$C_3H_7O_2$]$^{+\cdot}$, 263[M-$C_3H_5O_3$]$^{+\cdot}$, 231[M-$C_4H_9O_4$]$^{+\cdot}$, 217[M-$C_5H_{11}O_4$]$^{+\cdot}$, 205[M-$C_6H_{11}O_4$]$^{+\cdot}$, 179[M-$C_8H_{13}O_4$]$^{+\cdot}$, 92[M-$C_{15}H_{16}O_4$]$^{+\cdot}$.



(4a-g)
Reaction Scheme

(4d) 3- (2'- Hydroxy phenyl) -5- (2- hydroxy phenyl) -6- carbethoxy cyclohex -2- en -1- ones

Light Yellow, m.p. 50^0 C, Anal. Calcd. For $C_{21}H_{20}O_5$ (352) C 71.62 H 5.71 Found: 71.58 H 5.72. **IR (KBr) cm^{-1}** 3672, 3446, 3048, 2980, 2366, 1731(νc=o ester), 1667(νc=o ketone) ,1598, 1487, 1421, 1375, 1298, 1249, 1105, 1091, 735, 770, 632 **NMR ($CDCl_3$, δppm):** 1.34 [t, 3H, -OCH_2 – CH_3], 4.21 [q, 2H, -O –CH_2 – CH_3], 6.26 [s, 1H, C_2H, ethylene], 3.04 [dd, 1H, H_α, methylene], 2.96 [dd, 1H, H_β, methylene], 3.27-3.58 [m, 1H, C_5H methane], 3.99 [d, 1H, C_6H, methane], 6.83-7.39 [m, broad & unresolved, Ar.-H], 9.84 (s, 1H, OH], 11.85 [s, 1H, OH] **MS(m/z) :** 352[M]$^{+\cdot}$, 337[M-CH_3]$^{+\cdot}$, 323[M-C_2H_5]$^{+\cdot}$, 318[M-O_2H_2]$^{+\cdot}$, 307[M-C_2H_5O]$^{+\cdot}$, 279[M-$C_3H_5O_2$]$^{+\cdot}$, 278[M-$C_3H_6O_2$]$^{+\cdot}$, 277[M-$C_3H_7O_2$]$^{+\cdot}$, 231[M-$C_4H_9O_4$]$^{+\cdot}$, 229[M-$C_4H_{11}O_4$]$^{+\cdot}$, 217[M-$C_5H_{11}O_4$]$^{+\cdot}$, 205[M-$C_6H_{11}O_4$]$^{+\cdot}$, 179[M-$C_8H_{13}O_4$]$^{+\cdot}$, 92[M-$C_{15}H_{16}O_4$]$^{+\cdot}$.

(4e) 3- (4'- Hydroxy phenyl) -5- (4- hydroxy -3- methoxy phenyl) -6- carbethoxy cyclohex -2- en -1- ones

Dark Yellow,m.p. 72^0 C, Anal. Calcd. For $C_{22}H_{22}O_6$ (382) C 69.12 H 5.79 Found: 69.10 H 5.80. **IR (KBr) cm^{-1}** 3601, 3334, 3050, 3021, 2918, 2845, 2367, 1941, 1875, 1720(νc=o ester), 1660(νc=o ketone), 1583, 1478, 1433, 1352, 1258, 1107, 1055, 1011, 890, 750, 695 **NMR (CDCl$_3$, δppm):** 1.36 [t, 3H, -OCH_2 – CH_3], 4.27 [q, 2H, -O –CH_2 – CH_3], 6.21 [s, 1H, C_2H, ethylene], 3.14 [dd, 1H, H_α, methylene], 3.06 [dd, 1H, H_β, methylene], 3.23-3.54 [m, 1H, C_5H methane], 3.95 [d, 1H, C_6H, methane], 6.76-7.23 [m, broad & unresolved, Ar.-H], 9.86 (s, 1H, OH], 3.82 [s, 3H, OCH_3], 7.25 [s, 1H, OH] **MS(m/z) :** 382[M]$^{+\cdot}$, 367[M-CH_3]$^{+\cdot}$, 353[M-C_2H_5]$^{+\cdot}$, 337[M-C_2H_5O]$^{+\cdot}$, 308(M-$C_3H_6O_2$]$^{+\cdot}$, 307[M-$C_3H_7O_2$]$^{+\cdot}$, 293[M-$C_3H_5O_3$]$^{+\cdot}$, 290[M-$C_3H_8O_3$]$^{+\cdot}$, 252[M-$C_6H_{10}O_3$]$^{+\cdot}$, 247[M-$C_5H_{11}O_4$]$^{+\cdot}$, 243[M-$C_4H_{11}O_5$]$^{+\cdot}$, 230[M-$C_5H_{12}O_5$]$^{+\cdot}$, 192[M-$C_8H_{14}O_5$]$^{+\cdot}$, 126[M-$C_{12}H_{16}O_6$]$^{+\cdot}$, 88[M-$C_{15}H_{18}O_6$]$^{+\cdot}$, 76[M-$C_{16}H_{18}O_6$]$^{+\cdot}$.

(4f) 3- (4'- Methoxy phenyl) -5- (4- hydroxy -3- methoxy phenyl) -6- carbethoxy cyclohex -2- en -1- ones

Yellow, m.p. 102^0 C, Anal. Calcd. For $C_{23}H_{24}O_6$ (396) C 69.65 H 6.13 Found 69.68 H 6.10. **IR (KBr) cm^{-1}** 3601, 3404, 3061, 3020, 2918, 2848, 2364, 1945, 1876, 1805, 1725(νc=o ester), 1670(νc=o ketone), 1589, 1481, 1452, 1347, 1257, 1112, 1060, 1023, 895, 754, 700 **NMR (CDCl$_3$, δppm):** 1.37 [t, 3H, -OCH_2 – CH_3], 4.23 [q, 2H, -O –CH_2 – CH_3], 6.21 [s, 1H, C_2H, ethylene], 3.12 [dd, 1H, H_α, methylene], 3.05 [dd, 1H, H_β, methylene], 3.26-3.59 [m, 1H, C_5H methane], 3.91 [d, 1H, C_6H, methane], 6.86-7.33 [m, broad & unresolved, Ar.-H], 9.83 (s, 1H, OH], 3.85 [s,s, 2x3H, 2x -OCH_3], 3.81 [s, 3H, OCH_3] **MS(m/z) :** 396[M]$^{+\cdot}$,381[M-CH_3]$^{+\cdot}$, 367[M-C_2H_5]$^{+\cdot}$, 351[M- C_2H_5O]$^{+\cdot}$, 323[M-$C_3H_5O_2$]$^{+\cdot}$, 293[M-$C_4H_7O_3$]$^{+\cdot}$, 265[M-$C_5H_7O_4$]$^{+\cdot}$, 379[M-OH]$^{+\cdot}$, 366[M-CH_2O]$^{+\cdot}$, 317[M-$C_2H_7O_3$]$^{+\cdot}$, 252[M-$C_6H_8O_4$]$^{+\cdot}$, 239[M-$C_7H_9O_4$]$^{+\cdot}$, 237[M-$C_7H_{11}O_4$]$^{+\cdot}$

(4g) 3- (2'- Hydroxy phenyl) -5- (4- hydroxy -3- methoxy phenyl) -6- carbethoxy cyclohex -2- en -1- ones

Yellow , m.p. 62^0 C , Anal. Calcd. For $C_{22}H_{22}O_6$ (382) C 69.08 H 5.82 Found 69.10 H 5.80.

IR (KBr) cm^{-1} 3671, 3340, 3070, 2915, 2850, 2358, 1935, 1868, 1715(νc=o ester), 1662(νc=o ketone), 1580, 1475, 1430, 1345, 1257, 1101, 1053, 1008, 885, 747, 692 **NMR (CDCl$_3$, δppm):** 1.33 [t, 3H, -OCH_2 – CH_3], 4.26 [q, 2H, -O –CH_2 – CH_3], 6.23 [s, 1H, C_2H, ethylene], 3.16 [dd, 1H, H_α, methylene], 3.07 [dd, 1H, H_β, methylene], 3.23-3.59 [m, 1H, C_5H methane], 3.95 [d, 1H, C_6H, methane], 6.73-7.37 [m, broad & unresolved, Ar.-H], 9.83 (s, 1H, OH], 3.84 [s, 3H, OCH_3], 11.83 [s, 1H, OH] **MS(m/z) :** 382[M]$^{+\cdot}$, 367[M-CH_3]$^{+\cdot}$, 353[M-C_2H_5]$^{+\cdot}$, 337[M-C_2H_5O]$^{+\cdot}$, 308[M-$C_3H_6O_2$]$^{+\cdot}$, 307[M-$C_3H_7O_2$]$^{+\cdot}$, 293[M-$C_3H_5O_3$]$^{+\cdot}$, 290[M-$C_3H_8O_3$]$^{+\cdot}$, 252[M-$C_6H_{10}O_3$]$^{+\cdot}$, 247[M-$C_5H_{11}O_4$]$^{+\cdot}$, 243[M-$C_4H_{11}O_5$]$^{+\cdot}$, 230[M-$C_5H_{12}O_5$]$^{+\cdot}$, 192[M-$C_8H_{14}O_5$]$^{+\cdot}$, 126[M-$C_{12}H_{16}O_6$]$^{+\cdot}$, 88[M-$C_{15}H_{18}O_6$]$^{+\cdot}$, 76[M-$C_{16}H_{18}O_6$]$^{+\cdot}$.

ACKNOWLEDGEMENTS

The author thank the concerning authorities of BNPG college, Udaipur (Raj) for providing laboratory facilities. Our thanks are also due to the Head, RSIC, Lucknow (U.P.) India for analytical and spectral results.

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