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ORIGINAL PAPER

2,2′-(Arylmethylene)bis(3-hydroxy-5,5-dimethylcyclohex-2-enone) crystals formation via atom economy reaction and their antioxidant activity

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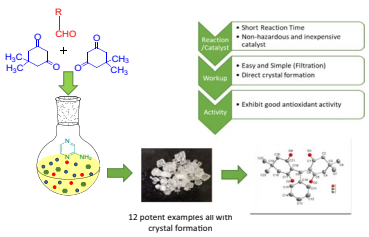
Abstract

Tetraketones with their diversified biological potencies became a highly significant class of oxygen-containing organic compounds. These are prepared by applying a simple Knoevenagel-Michael cascade procedure with 1,3-dicarbonyl compound and aldehydes. In the due course of time, numerous methods for the synthesis of these compounds, have been developed which having their own advantages and disadvantages. So, the development of an efficient, simple, and ecologically benign method for their preparation in the presence of the novel catalytic agent is still in great demand. In the present report, direct crystals of 2,2′-(arylmethylene)bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) (a tetraketone) were obtained via a simple procedure using 2-aminopyrazine as a catalyst. The prepared compound shows significant antioxidant checked by different procedures like DPPH, ABTS, and TAC.

Graphic abstract



Keywords Lewis base · Multi-component reaction · Dimedone · Anti-oxidant activity · Single crystal XRD · 2D NMR

Introduction

Multi-component reactions (MCRs), which are also known as the Multi-component Assembly Process (MCAP) [1], are progressively becoming one of the frontiers of organic synthesis [2–4], as they address the complexity and diversity in organic transformations [5, 6]. By varying reagents, molecular complexity, diversity, as well as predefined functionality, can be easily attained in MCRs [7]. In MCRs, the condensation of three or more than three components takes place without the introduction of the poisonous intermediate in the atmosphere such that the product contains a notable portion of atoms got from the entirety of the beginning material [8]. Strecker firstly reported primary MCR, i.e., synthesis of α-aminocyanides from carbonyl compounds, ammonia, and hydrogen cyanide [9]. Nowadays, combinatorial synthesis [10] and diversity-oriented synthesis [11] are preferred via MCRs because they reduce the number of reaction steps, waste creation, human labor, the expense of building highly diverse and complex molecules. Due to their experimental simplicity, they have the chance of automatization [12] and allow experimental variations.

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Multi-component reactions have been broadly applied to the preparation of bioactive [13] and complex molecules [14]. MCRs play a significant function in different examination fields like biomedical, synthetic organic, industrial chemistry, and so forth.

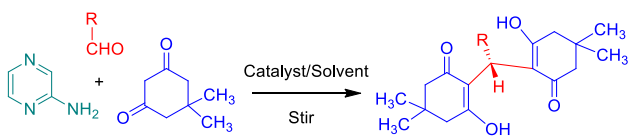
Two organic molecules hanged with the help of single aldehyde units is a widely explored research area in synthetic organic chemistry. These molecules find various applications in the biological and pharmacological fields. These compounds are found effective as tyrosinase inhibitors and also have considerable applicability in laser technology [15, 16]. Synthesis of numerous tetraketone which includes condensation of dimedone and aldehydes under varied reactions conditions and catalysis like sodium dodecyl sulfate (SDS) [17], molecular iodine [18], silica-diphenic acid [19], hexaflouro-2-propanol [20], [$HClO_4$-SiO_2] [21], and ethylenediammonium diacetate (EDDA) [22] have been reported in the literature. The existing methods have advantages one over other but still the urge for neat and clean procedures is the demand of an hour. So, in search of new methodology and in continuation on our previous work [23, 24], we are reporting a convenient, simple, and economical procedure for the production of 2,2′-(phenyl methylene)bis(3-hydroxy-5,5-dimethylcyclohex-2-enone) molecules into highly purified form, i.e., crystals.

Result and discussion

Chemistry

Starting with the intent of synthesizing fused ring 1,4-dihydropyridine via Hantzsch one-pot multi-component condensation reaction of dimedone, 2-aminopyrazine, and substituted aromatic aldehyde. After running the reaction for few hours and leaving it overnight, crystals were observed. During the early investigation of spectral data, it was observed some signature peaks were missing. Further analysis confirmed that the ring cyclization was not completed and the desired 1,4-DHP molecule was not formed. Rigorous brainstorming led us to the idea that 2,2′-(phenylmethylene)bis(3-hydroxy-5,5-dimethylcyclohex-2-enone) were obtained, justifying the low isolated yield too. The curiosity to understand the reaction behaviors completely changed the direction of our research.

Scheme 1



Effect of catalysis and solvent

To standardize the reaction conditions, to get an appropriate combination of catalyst, reaction time, percentage yield, and solvent, various combinations were investigated multiple times under varied conditions (Scheme 1). However, none of the combinations replicated the same results, as only raw solid was observed on working up with tedious methods and still satisfactory results were not obtained even after recrystallization (Table 1, entries 1–8). Further, the obtained yield with various combinations of solvent and catalysts were low in contrast to the combination of 2-aminopyrazole with ACN (Table 1, entry 9).

Effect of temperature

Thereafter, to produce the best results in context to perfect temperature and time duo, it was observed that stirring at 80 °C for 2 h gave 96% yield (Table 2, entry 4). Afterward, no increase in the yield was observed at 90 °C (Table 2, entry 5). However, on further increase in the temperature,

Table 1 Various combinations of catalyst-solvents to optimize the condition and get the optimal time and percentage yield

Entry	Catalyst	Solvent	Time/h	Yield[a]/%
1	–	Ethanol	9	68
2	β-Cyclodextrin	Ethanol	7	78
3	SDS	Water	11	37
4	Al(DS)3	Water	12	49
5	Sc(DS)3	Water	12	45
6	Piperidine	Ethanol	7	65
7	β-Cyclodextrin	ACN	6	74
8	Piperidine	ACN	4	67
9	2-Aminopyrazine	ACN	2	96

[a]Yield refers to the pure isolated product

[b]Reaction was performed in a silicon oil bath to maintain reaction temperature

Table 2 Reaction conditions optimization in terms of appropriate temperature, yield, and time

Entry	Temperature/°C	Yield[a] /%	Time/h
1	50	76	9–10
2	60	81	7
3	70	85	6
4	80	96	2
5	90	96	3
6	100	94	3
7	110	90	3

[a]Yield refer to combined amounts of different crops

the compound starts decomposing and crystallization was also affected. At lower temperatures, the reaction was not complete even after providing the extended hours (Table 2, entries 1 and 2).

Synthesis of various tetraketones *3a-3l*

Several aromatic aldehydes were selected to undergo the Knoevenagel condensation with dimedone in the presence of 2-aminopyrazine in ACN at 80 °C and results were given in Table 3. This efficient methodology affords products in excellent yield from 90 to 97%. However, the electron-withdrawing substituents on the aldehyde ring accelerate the reaction process in shorter times to produce a high yield of the product; on the contrary, the electron-donating group decelerates the reaction. Therefore, in Table 3 the substrates **3b**, **3f** with electron-withdrawing substitutions give a higher yield up to 97%, while substrates **3c**, **3d** having electron releasing group produced lower yield.

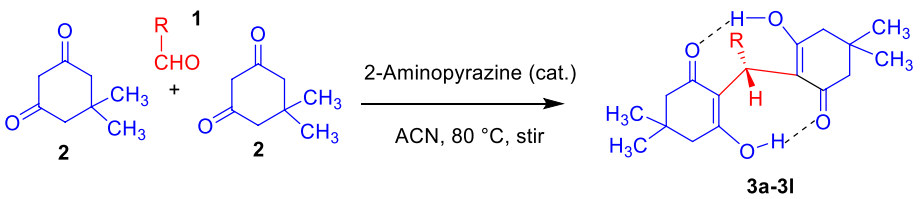
Proposed mechanism

In the probable depicted mechanistic pathway (Scheme 2), initially, the aldehyde carbonyl group is activated by the hydrogen bond formation with the amino group of 2-aminopyrazine. This activation leads to the insertion of one molecule of dimedone **II** to form intermediate **III**. In resulted intermediate **III** deprotonation of active methylene by lone pair of 2-aminopyrazine results in the formation of Knoevenagel adduct **IV** with the removal of a water molecule. Then intermediate **IV** is further activated by another molecule of 2-aminopyrazine followed by the insertion of the second dimedone molecule **II**. After that, lone pair of activated intermediate abstracts hydrogen from tautomeric enol form of dimedone leading to electron shift to form carbanion. Then resulted carbanion undergoes Michael addition gives the compound **V**. Afterward, final molecule **VI** is obtained by tautomerization of compound **V**.

The structure of the compounds **3a-3l** was examined by IR, NMR (^{1}H, ^{13}C, COSY, NOSY, HSQC), mass, elemental analysis, and single-crystal XRD. The data obtained from the infrared spectrum are very helpful in structure elucidations of these compounds. The characteristic data obtained from the infrared spectrum exhibit bands for four main functional groups at 3430–3650 (O–H), 3087–3055 (C=C–H), 2981–2867 (sp^3 C–H), and 1608–1558 cm^{-1} (C=O). In its ^{1}H NMR spectrum (500 MHz, $CDCl_3$), a singlet due to OH group appeared at 11.92–11.70 ppm.

In compound **3a,** the protons of aromatic phenyl region (H-2″, H-6″) gives doublet at 7.10–7.08 ppm (J_o = 8.40 Hz), while a clear triplets of proton H-3″, H-5″, and H-4″ observed at 7.25–7.24, 7.17–7.15 ppm. In *p*-substituted

Table 3 Structures of various tetraketone derivatives **3a-3l** from three-component aldehydes, dimedone, 2-aminopyrazine at ambient temperature in acetonitrile

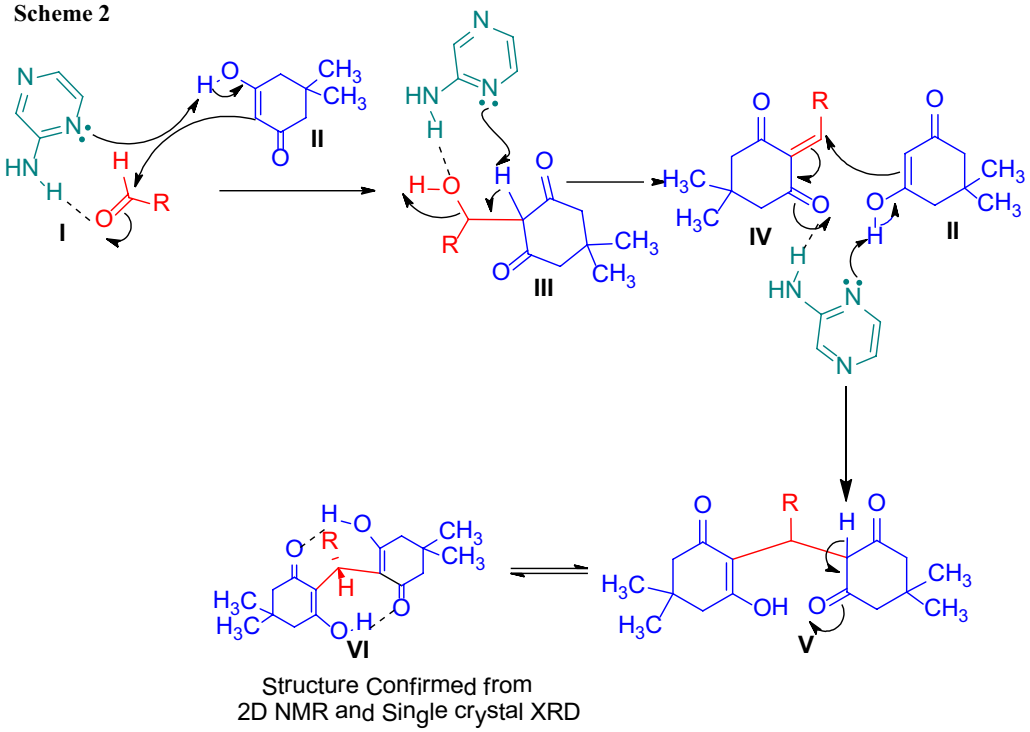


Compound	*R*	Yield[a]/%	M.p./°C	Lit. m.p./°C[b]
3a	C_6H_5	96	191	190–192 [25]
3b	4-NO_2–C_6H_4	97	169	167–171 [25]
3c	4-Me–C_6H_4	94	128	126–128 [25]
3d	4-OMe–C_6H_4	94	148	142–144 [25]
3e	4-Br–C_6H_4	96	172	172–174 [25]
3f	3-NO_2–C_6H_4	97	196–198	201–203 [26]
3g	2-OH–C_6H_4	95	199	205–206 [27]
3h	4-OH–3-OMe–C_6H_3	93	188–190	193–195 [26]
3i	C_6H_4–CH=CH	90	213	215–217 [27]
3j	Pyridin-2-yl	92	177	175–177 [28]
3k	2-Furyl	94	210	207–209 [25]
3l	Thiophen-2-yl	95	159–161	155–157 [29]

[a]Yield refers to the pure isolated product

[b]Products were characterized with spectral techniques and compared with authentic samples

Scheme 2



compound, **3b** protons H-3′′, 5′′, and H-2′′, 6′′were present at 8.13 (d, $J_o = 6.9$ Hz) and 7.26 ($J_o = 6.5$ Hz) ppm, respectively. While in compound, **3i** protons present at carbon (C-1′′′), (C-2′′′) appeared at 6.82 ($J_{trans} = 15.1$ Hz) and δ 7.01 ($J_{trans} = 15.4$ Hz) ppm. The signal of benzylic methene proton as a singlet appeared at 5.60–5.49 ppm. In dimedone ring, a multiplet at 2.55–2.20 ppm observed due to four methylene groups present at (C-4,4′–C-6,6′) respectively. The two sharp singlets observed from 1.06 to 1.30 ppm could be ascribed to two CH_3 groups at C-5,5′, respectively.

The characteristics spectroscopic ^{13}C NMR data of compounds **3a**-**3l** showed that the signals of enone moiety were present at 190.98–190.40 ppm. The signal of C-3 appeared at 189.5–189.2 ppm due to the direct attachment of the electronegative oxygen atom of the hydroxyl group. Signals resonating at 115.7–114.9 ppm are assigned to C-2 and the signals at 47.4–46.1 and 46.5–46.4 ppm represent C-6, C-4, respectively. Moreover, the carbon C-5 appeared upfield at 41.8–31.1 ppm owing to the presence of two electron-donating methyl groups. In the aromatic region, the signal of carbon atom C-4′′ was found as high as 146.54 ppm with nitro substitutions and as low as 124.8 ppm with methoxy group substitution. Similarly, the signal for other carbon atoms appeared in the range of 128.2–146.14 ppm for C-3′′,5′′, 127.6–138.1 ppm for C-1′′, and 123.5–135.3 ppm for C-2′′,6′′ as per the various group's substitution. While the upfield signals of benzylic methylene carbon and carbon of two methyl groups (C-5,5′–2CH_3) resonating at 32.2–33.5 and 27.30–29.80 ppm, respectively. Finally, the ESI–MS spectrum of compounds **3a**-**3l** proved concrete evidence in support of the dimeric existence of these compounds with the (M + 1), (M + Na) peaks along with (2M + 1), (2M + Na).

Antioxidant activity

Examination of the antioxidant potential of the tetraketone derivatives **3a**-**3l** was carried out using phosphomolybdenum reducing assay, ABTS, and DPPH free radical scavenging assays. The results of different antioxidant assays were presented in Table 4. The antioxidant potential of DPPH, ABTS, and TAC assays was ranged between 17.96 ± 3.23 and 93.77 ± 0.51%, 0 and 61.68 ± 1.68%, and 0 and 63.5 ± 0.42 mg of AAE/1 g of the compound, respectively. The highest DPPH radical scavenging potential was shown by tetraketone derivative **3h** (93.77 ± 0.51), followed by **3a** (66.20 ± 0.22), **3i** (65.32 ± 0.073), **3g** (59.16 ± 0.22), **3d** (54.15 ± 0.17), and **3k** (48.24 ± 0.59) respectively. DPPH scavenging potential of **3h** was higher than the standard used, i.e., gallic acid (91.76 ± 0.62). On the other hand, **3a** and **3i** exhibited the comparable DPPH scavenging potential with that of the standard used, while derivative **3l** showed the lowest DPPH scavenging potential. Alike results were also reported in case of tetraketones derivatives 4-(*N*,*N*-dimethylamino)phenyl-2,2′-methylenebis-(5,5-dimethylcyclohexane-1,3-dione) (67%), 2-chlorophenyl-2,2′-methylenebis-(5,5-dimethylcyclohexane-1,3-dione) (77%), and 4-methoxyphenyl-2,2′-methylenebis-(5,5- dimethylcyclohexane-1,3-dione) (84%) at concentration of 1 mM by

Table 4 The results of various antioxidants assay for different synthesized compounds

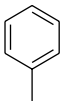
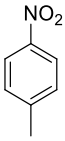
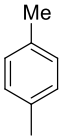
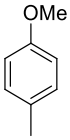
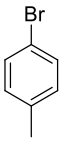
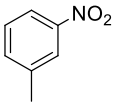
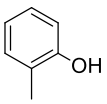
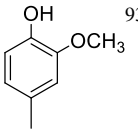
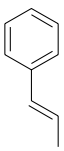
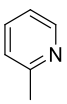
Compound	*R*	DPPH	ABTS	TAC
3a		66.20 ± 0.22	34.79 ± 0.67	7.45 ± 0.08
3b		45.38 ± 1.24	61.68 ± 1.68	–
3c		46.77 ± 0.15	30.92 ± 1.17	2.84 ± 0.12
3d		54.15 ± 0.17	40.16 ± 1.34	4.10 ± 0.37
3e		45.08 ± 0.366	39.49 ± 0.34	15.50 ± 0.06
3f		35.04 ± 0.29	57.31 ± 1.00	3.59 ± 0.40
3g		59.16 ± 0.22	43.19 ± 3.36	13.47 ± 0.08
3h		93.77 ± 0.51	46.55 ± 1.00	8.12 ± 0.10
3i		65.32 ± 0.073	37.98 ± 4.20	17.36 ± 0.12
3j		36.24 ± 0.78	-	12.93 ± 0.08
3k		48.24 ± 0.59	41.68 ± 5.55	63.5 ± 0.42
3l		17.96 ± 3.23	44.20 ± 2.35	6.94 ± 0.14
Gallic acid		91.76 ± 0.62	96.53 ± 0.15	83.17 ± 0.08
Ascorbic acid		89.52 ± 0.89	97.65 ± 0.15	–

Table 4 (continued)

The results of DPPH and ABTS assays were expressed as % inhibition and that of TAC as mg AAE/g compound

TAC total antioxidant capacity, *ABTS* 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid), *DPPH* 2,2-diphenyl-1-picrylhydrazyl radical scavenging assay

[30]. Further, [16] also reported comparable results of the antioxidant potential of various tetraketone derivatives.

In ABTS scavenging assay, compound **3b** (61.68 ± 1.68) exhibited the highest scavenging potential followed by **3f** (57.31 ± 1.00), **3h** (46.55 ± 1.00), **3l** (44.20 ± 2.35), and **3g** (43.19 ± 3.36), respectively, while no ABTS scavenging potential was observed in the case of **3j**. The order of present results of ABTS scavenging potential for various synthesized compounds was different from that of DPPH scavenging potential this may be attributed to a different mechanism of action and reaction conditions. Alike results were also given by [31], where various substituted benzilic acid derivatives have a different order of antioxidant potential in the case of DPPH and ABTS assay.

In the case of TAC, **3k** (63.5 ± 0.42) showed the highest TAC values, whereas **3b** showed the lowest TAC values. In comparison with **3k**, the TAC values of other derivatives are very low and lie in the range from 0 to 17.36 ± 0.12. These values of TAC are much lower than the standard used. The results of TAC values in the case of **3k** were comparable to the results of TAC values observed in the case of several methanol extracts acquired from various parts of *Nepeta leucophylla*, while the results of the rest of the derivatives were comparable to the TAC values of hexane and chloroform extracts obtained from various parts of *Nepeta leucophylla* [32, 33].

The results of various antioxidant assays reveal that these synthesized tetraketones derivatives have the tremendous potential to act as an antioxidant, however, the necessary investigation (in vivo evaluation and toxicological studies) must be performed before proceeding further.

Conclusion

In conclusion, we have reported a novel route for the preparation of various tetraketones by condensation of dimedone and aldehydes using 2-aminopyrazine via the Knoevenagel-Michael cascade procedure. In this report, 12 examples of tetraketones were collected in the form of pure crystals. The yields of products varied from 90 to 97% depending upon the substitutions on the aldehyde group. It was also observed that the yield obtained through the electron-withdrawing group is higher in comparison with electron releasing groups. Moreover, the characteristic data obtained through XRD, and ESI–MS shows that in the solvent medium the

final structure exists in dimeric form. On the other hand, in crystal form monomer molecule exists with intramolecular hydrogen bonding. The evaluated data of antioxidant assay show that these synthesized tetraketone derivatives have the tremendous potential to acts as an antioxidant.

Experimental

The chemicals were obtained from Sigma Aldrich and they were utilized as such. Solvents used in reaction and washing of products were of analytical grade. For the preparation of all the aqueous solutions, double distilled water was utilized. Melting points were taken in an open capillary using digital melting point apparatus. IR spectra were taken on Perkin Elmer (spectrum II) using ATR mode. NMR (^{1}H, ^{13}C-NMR, COSY, NOSY, HSQC) were recorded on a Bruker Advanced NEO 500 MHz NMR spectrometer in $CDCl_3$ and using TMS as the internal standard. Coupling constants are expressed in unit Hertz. The MS analysis was performed on LC–MS Spectrometer Model Q-ToFMicromass, Waters. Single-crystal XRD data were examined at 298 K on a Rigaku SuperNova HyPix3000 diffractometer with monochromatic Mo-Kα radiation ($\lambda = 0.71073$ Å).

General experimental procedure for synthesis of 2,2′-(arylmethylene)-bis(3-hydroxy-5,5-dimethylcyclohex-2-enone)

In a one-pot synthesis of tetraketones, an aldehyde (5 mmol), dimedone (10 mmol), and 2-aminopyrazine (3 mmol) were mixed in an unproportionate ratio in ACN and stirred at 80 °C for 2–3 h (TLC: ethyl acetate: *n*-hexane 7:3). Thereafter the obtained mixture, after the reaction completion, was allowed to cool at room temperature and allow standing for overnight. Next day crystals of tetraketones were collected by washing with ethanol. Colorless crystals were collected for structure elucidation.

XRD structure

Single crystals of **3a** are suitable for the X-ray structure examination. Single-crystal XRD data were obtained at 298 K on a Rigaku SuperNova HyPix3000 diffractometer with monochromatic Mo-Kα radiation ($\lambda = 0.71073$ Å). The CIF has been deposited with the Cambridge Crystallographic Data Centre. From the Cambridge Crystallographic Data Centre www.ccdc.cam.ac.uk/data_request/cif, the data can be obtained without any charge. Single-crystal XRD analysis revealed that compound **3a** crystallized in the tetragonal system with the $I4_1/a$ space group. The asymmetric unit contained two molecules with lattice parameters $a = 20.9226(4)$ Å, $b = 20.9226(4)$ Å, $c = 36.9382(9)$ Å, and 16,169.9(7) Å^3 is unit cell volume. The C–C bond distance ranges from 1.359(4) Å to 1.536(3) Å and C–O bond lengths range from 1.262(2) Å to 1.318(2) Å. The detailed bond lengths and bond angles are attached to the supplementary file. The compound **3a** CCDC no. is 1992004. Compound **3a** crystal data details are given in Table 5.

Antioxidant potential

Determination of DPPH free radical scavenging potential

The free radical scavenging activity DPPH was done according to the method given by [32]. According to the reported procedure, 4 mg of DPPH was mixed in 100 cm^3 of methanol and the prepared solution was kept in dark for further use. The standard solution and sample were prepared by dissolving 1 mg of sample or standard in 1 cm^3 of DMSO. 200 mm^3 of sample or standard or blank (DMSO) was mixed with 3 cm^3 of DPPH methanolic solution. Then, for 30 min all the samples were incubated in dark at room temperature. After incubation, sample absorbance was recorded at 517 nm using a UV–Visible spectrophotometer. The calculation of

Table 5 Details of crystal Structure and compound Refinement of **3a**

Empirical formula	$C_{23}H_{28}O_4$
Formula weight	368.45
Temperature/K	293(2)
Crystal system	Tetragonal
Space group	I41/a
a/Å	20.9226(4)
b/Å	20.9226(4)
c/Å	36.9382(9)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	16,169.9(7)
Z	32
ρ_{calc}/g cm^{-3}	1.211
μ/mm^{-1}	0.082
F(000)	6336.0
Radiation	MoKα ($\lambda = 0.71073$)
2Θ range for data collection/°	6.542–54.776
Index ranges	$-26 \le h \le 23$, $-26 \le k \le 26$, $-46 \le l \le 42$
Reflections collected	76,130
Independent reflections	8701 [$R_{int} = 0.0984$, $R_{sigma} = 0.0750$]
Data/restraints/parameters	8701/0/499
Goodness-of-fit on F^2	0.998
Final R indexes [$I >= 2\sigma(I)$]	$R1 = 0.0622$, $wR2 = 0.1420$ Final R indexes [all data] $R1 = 0.1564$, $wR2 = 0.1823$
Largest diff. peak/hole/e Å^{-3}	0.18/− 0.18

(I %) inhibition of DPPH free radical for different samples was done according to the given equation:

$$I\%\,[\text{DPPH free radical}] = \left[\left(A_C - A_S\right)/A_C\right] \times 100$$

where A_S and A_C stand for absorbance of standards/samples and control, respectively. Results for I% of standards/samples were represented as the mean ± standard deviation of three values.

Determination of ABTS free radical scavenging potential

The free radical scavenging potential ABTS was evaluated according to the method given by [34]. To prepare ABTS stock solution, equal volume (1 cm^3 each) of 2 mM PPS (potassium persulfate) solution and 7 mM ABTS solution was mixed. The final solution was incubated for 12 h at room temperature in dark. Afterward, the preparation of the final working solution is done by mixing 1 cm^3 of the incubated stock solution and 22 cm^3 of distilled water. After this, standard (1 mg/cm^3) or 400 mm^3 of samples (1 mg/cm^3) or blank (DMSO) were allowed to react with an equal volume (400 mm^3) of working solution. Then at room temperature, the prepared samples were incubated for 7 min and finally, the absorbance was recorded spectrophotometrically at 734 nm. The scavenging percentage (I%) was calculated as explained above in the DPPH assay. Results for I% standards/samples were illustrated as the mean ± standard deviation of three values.

Total antioxidant capacity (TAC) assay

The TAC results of various compounds and standards were determined according to phosphomolybdenum reducing assay as demonstrated by [33]. 3 cm^3 of reagent solution (prepared by mixing an equal amount of 28 mM sodium phosphate, 4 mM ammonium molybdate, and 0.6 M sulfuric acid) was mixed with 300 cm^3 of samples (1 mg/cm^3) or standards (ascorbic acid, 60–300 mg/dm^3). Further, at 95 °C all the resulting solutions were incubated for 90 min. The volume of the prepared samples was kept constant and also the samples were contained in capped test tubes during the incubation period. Afterward, all samples were cooled at room temperature and absorbance was recorded at 695 nm using a UV–Visible spectrophotometer. TAC results were illustrated as mg of AAE (ascorbic acid equivalent)/1 g of the compound (mean ± standard deviation of three values). The results of (TAC) assay were calculated using the standard linear equation $y = 6.065x + 0.007$ and the R^2 was equal to 0.999.

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References

1. Sahn JJ, Granger BA, Martin SF (2014) Org Biomol Chem 12:7659
2. Sahn JJ, Su JY, Martin SF (2011) Org Lett 13:2590
3. Hardy S, Martin SF (2011) Org Lett 13:3102
4. Goodnough AM, Sahn JJ, Martin SF (2020) Tetrahedron Lett 61:151777
5. Lepovitz LT, Martin SF (2019) Tetrahedron 75:130637
6. Khan MM, Khan S, Saigal S, Iqbal S (2016) RSC Adv 6:42045
7. Shaaban S, Abdel-Wahab BF (2016) Mol Divers 20:233
8. Cimarelli C (2019) Molecules 24:2372
9. Strecker A (1850) Justus Liebigs Ann Chem 75:27
10. de Graaff C, Ruijter E, Orru RVA (2012) Chem Soc Rev 41:3969
11. Spandl RJ, Bender A, Spring DR (2008) Org Biomol Chem 6:1149
12. Cargill JF, Lebl M (1997) Curr Opin Chem Biol 1:67
13. Colombo M, Peretto I (2008) Drug Discov Today 13:677
14. Touré BB, Hall DG (2009) Chem Rev 109:4439
15. Khan KM, Maharvi GM, Khan MTH, Shaikh AJ, Perveen S, Begum S, Choudhary MI (2006) Bioorg Med Chem 14:344
16. Maharvi GM, Ali S, Riaz N, Afza N, Malik A, Ashraf M, Iqbal L, Lateef M (2008) J Enzyme Inhib Med Chem 23:62
17. Liu LB, Jin TS, Han LS, Meng L, Na Q, Li TS (2006) E-J Chem 3:117
18. Kidwai M, Bansal V, Mothsra P, Saxena S, Somvanshi RK, Dey S, Singh TP (2007) J Mol Catal A Chem 268:76
19. Vaid R, Gupta M, Kant R, Gupta VK (2016) J Chem Sci 128:967
20. Maleki B, Raei M, Akbarzadeh E, Ghasemnejad-Bosra H, Sedrpoushan A, Ashrafi SS, Dehdashti MN (2016) Org Prep Proced Int 48:62
21. Kantevari S, Bantu R, Nagarapu L (2007) J Mol Catal A Chem 269:53
22. Jung DH, Lee YR, Kim SH, Lyoo WS (2009) Bull Korean Chem Soc 30:1989
23. Malhi DS, Kaur M, Sohal HS (2019) ChemistrySelect 4:11321
24. Sohal HS, Kaur M, Thakur AR, Parmar P (2016) Pharm Chem 8:148
25. Zhang Y, Shang Z (2010) Chin J Chem 28:1184
26. Ilangovan A, Malayappasamy S, Muralidharan S, Maruthamuthu S (2011) Chem Cent J 5:1
27. Horning EC, Horning MG (1946) J Org Chem 11:95
28. Khurana JM, Vij K (2012) J Chem Sci 124:907
29. Navarro CA, Sierra CA, Ochoa-Puentes C (2016) RSC Adv 6:65355
30. Iqbal L, Lateef M, Ali S, Rigaz N, Maharvi GM, Ashraf M, Afza N (2007) J Chem Soc Pakistan 29:51
31. Sudha R, Kanakam CC, Nithya G (2016) Asian J Pharm Clin Res 9:1
32. Sharma A, Cannoo DS (2016) RSC Adv 6:78151
33. Sharma A, Cannoo DS (2017) J Food Biochem 41:1
34. Bhardwaj P, Thakur MS, Kapoor S, Bhardwaj AK, Sharma A, Saxena S, Chaurasia OP, Kumar R (2019) Pharmacogn J 11:536