Microwave induced synthesis and characterization of some thiazolidinone derivatives bearing benzotriazole moeity

Kirti Shrimali, Diwaker Sitha, Jitendra Vardia* and Suresh C. Ameta
Microwave Chemistry Laboratory, Department of Chemistry,
University College of Science, Mohanlal Sukhadia University,
Udaipur - 313 001 (Raj.), INDIA

Síntesis inducida por microondas y caracterización de algunos derivados de tiazolidinona que contienen el fragmento benzotriazol

Síntesi induïda per microones i caracterització d'alguns derivats de tiazolidinona que contenen el fragment benzotriazole

**Present Address:-Team Leader, P.I.Industries, Udaipur (Raj)-313001*

RESUMEN

Se describe un método extremadamente rápido y eficiente para la síntesis de algunos derivados de tiazolidinona a partir de benzotriazol mediante irradiación con microondas. Se caracteriza la estructura de los compuestos sintetizados en base a los análisis elementales y los datos espectroscópicos.

Palabras clave: Benzotriazol, tiazolidinona, irradiación con microondas.

ABSTRACT

An efficient and extremely fast method for the synthesis of some thiazolidinone derivatives starting from benzotriazole under microwave irradiation has been described. The structure of synthesized compounds have been characterized on the basis of their elemental analysis and spectral data.

Key words: Benzotriazole, thiazolidinone, microwave irradiation.

RESUM

Es descriu un mètode extremadament ràpid i eficient per a la síntesi d'alguns derivats de tiazolidinona a partir de benzotriazole mitjançant irradiació amb microones. Es caracteritza l'estructura dels compostos sintetitzats en base als anàlisis elementals i les dades espectroscòpiques.

Mots clau: Benzotriazole, tiazolidinone, irradiació amb microones.

INTRODUCTION

In recent years, benzotriazole derivatives have gained significant importance because of their wide use in organic sunthesis[1,2] and pharmaceutical chemistry.[3] It is known to exhibit a broad spectrum of biological activities such as antimicrobial[4,5], antifungal[6,7], antiinflammatory[8], analgesic[9], anticancer[10], CNS depressant[11], etc. On the other hand, thiazolidinones and their 5-arylidene derivatives are also well known for their versatile pharmacological activities[12-18] like antileukemic, anti-HIV, anticonvulsant, antimicrobial and antiviral.

With an interest in the synthesis of bioactive heterocycles and their incorporation into some established pharmacophores like thazolidinone for new drug evolution; eco-friendly synthetic methodologies have been explored under the framework of green chemistry. Microwave induced organic transformations[19-22] stands among the alternative routes proposed during the last decade or due to various reasons like higher yields in shortest possible reaction time. This paper describes the synthesis of 1,3-thiazolidin-4-ones bearing benzotriazole moeity under microwave irradiation, which is an efficient and operationally simple method of synthesis.

RESULTS AND DISCUSSION

In the present investigation, 1H-benzotriazole **(1)** on N-esterification with ethylchloroacetate in presence of K_2CO_3 as a base affords ethyl ethanoate benzotriazole **(2)**. Compound **(2)** showed characteristic IR absorption bands in

* E-mail: ameta_sc@yahoo.com

the region 1743 (C=O str), 1597 (C-N str.) and 1029 cm^{-1} (C-O str.) and 3.708 δ for $–NCH_2$ group in ^1H NMR spectrum. 2-(1, 2, 3-benzotriazol-1-yl-acetate) hydrazine carbothioamide **(3)** was prepared by condensation of **(2)** with thiosemicarbazide. Formation of **(3)** was confirmed by the presence of N-H stretching peaks at 3378 and 3237 cm^{-1} in IR and a multiplet at δ 8.3 for NH. NH.C C=S. NH_2 group in ^1H NMR spectra.

Compound **(3)** underwent ready heterocyclisation upon its reaction with chloroacetic acid in presence of sodium acetate to afford 2-[(1,2,3-benzotriazolyl) acetohydrazido]-1,3-thiazolidin. 4-one **(4)**. In the IR spectrum, band at 1712 cm^{-1} were obtained due to carbonyl stretching, ^1H NMR signals were found at δ 5.6 (s) and 4.4 (s), which showed the presence of a thiazolidinone ring. Reaction of compound **(4)** with aromatic aldehydes led to the formation of final product i.e. 2-[(1,2,3-benzotriazolyl) acetohydrazido]-5-(4-substituted benzylidene)-1,3- thiazolidin-4-ones **(5a-d).** Compounds **(5a-d)** were characterized by IR and ^1H NMR spectral data. The IR spectrum of compound **(5a)** showed the absence of carbonyl absorption of thiazolidinone at 1712 cm^{-1} and the presence of a chalcone carbonyl band (C=C-C=O) at 1685 cm^{-1}. Its ^1H NMR spectrum displayed a new singlet at δ 6.3, which may be attributed to the chalcone moeity (C=CH-absorption). The mass spectrum also supported the proposed structure by the presence of molecular ion peak at m/z 412. The physical and analytical data are presented in **Table 1** and spectral data are given in **Table 2**.

EXPERIMENTAL SECTION

General Procedure

All the reactions were carried out in a domestic microwave oven (Kenstar, Model No. OM-26 EGO, Power-1200W). Melting points were determined in open capillaries. Reactions were monitored by thin layer chromatography using silica gel-G as adsorbent using ethyl acetate : n-hexane (7 : 3) as eluent. IR spectra (KBr pellets) were recorded on Perkin-Elmer 1800 (FTIR) spectrometer. ^1H NMR spectra (DMSO-d_6) were taken a Bruker DRX spectrometer (300 MHz FTNMR) using TMS as internal standard and chemical shift are expressed in δ (ppm). Mass spectra were taken on Jeol SX-102/PA-6000 (EI) spectrometer. Compound **1** was prepared according to literature reported[23].

Synthesis of ethyl-1,2,3-benzotriazol-1-yl acetate (2):

To the solution of benzotriazole **(1)** (0.01 mole) in ethanol, ethyl chloroacetate (0.01 mole) and catalytic amount of K_2CO_3 was added as a base. The reaction mixture was irradiated under microwave for 8:00 – 9:00 minutes and then it was filtered hot. Solvent was allowed to evaporate to yield the product as white shining crystals. Recrystallization was carried out from absolute alcohol.

Synthesis of 2-[(1,2,3-benzotiazol-1-yl-acetate hydrazine carbothioamide (3):

An equimolar mixture of **(2)** (0.01 mole) and thiosemicarbazide (0.01 mole) in ethanol was kept under microwave irradiation for 8:00-8:30 minutes with a time interval of 10 seconds. The reaction mixture was then allowed to cool and the obtained yellow solid was recrystallized from absolute alcohol.

Synthesis of 2-[1,2,3-benzotriazol) acetohydrazido]-1,3-thiazolidin-4-one (4):

A mixture of carbothioamide **(3)** (0.01 mole), chloroacetic acid (0.01 mole) and anhydrous sodium acetate (0.01 mole) as a base in absolute alcohol was irradiated under microwave irradiation for 4:00-4:30 minutes using funnel as a loose top. The reaction mixture was cooled and poured into ice-cold water. The solid thus separated was filtered, washed with water, dried and recrystallized from ethanol.

Synthesis of 2-[(1,2,3-benzotriazolyl) acetohydrazido]-5-(4-chlorobenzylidene)-1,3-thiazolidin-4-one (5a):

Compound **(4)** (0.01 mole) was suspended in minimum quantity of ethanol. To this chlorobenzaldehyde (0.01 mole), anhydrous sodium acetate (0.02 mol) and glacial acetic acid (10 ml) were added and irradiated for 3:00-5:00 minutes under microwave irradiation. The reaction mixture was cooled at room temperature and then poured into ice-cold water. The separated solid was filtered washed with water and crystallized from glacial acetic acid.
Similarly, other compounds **(5b-d)** were also synthesized.

Compound No.	X	Molecular formula (M.W.)	Molecular weight	Melting point (°C)	Yield (%)	Calculated / Found (%)			
						C	H	N	S
2	–	$C_{10}H_{11}N_3O_2$	205	74	86	58.53 (58.50)	5.36 (5.33)	20.48 (20.42)	–
3	–	$C_9H_{10}N_6OS$	250	145	92	43.20 (43.16)	4.00 (3.97)	33.60 (33.54)	12.8 (12.5)
4	–	$C_{11}H_{10}N_6O_2S$	290	154	75	45.51 (45.50)	3.44 (3.42)	28.96 (28.89)	11.03 (10.98)
5a	Cl	$C_{18}H_{13}N_6O_2SCl$	412	282	82	52.42 (52.40)	3.15 (3.12)	20.38 (20.27)	7.76 (7.72)
5b	OCH_3	$C_{19}H_{16}N_6O_3S$	408	257	67	55.88 (55.83)	3.92 (3.89)	22.22 (22.18)	7.84 (7.79)
5c	NO_2	$C_{18}H_{15}N_7O_4S$	423	278	72	51.06 (51.02)	3.54 (3.49)	23.16 (23.10)	7.56 (7.51)
5d	H	$C_{18}H_{14}N_6O_2S$	378	248	76	57.14 (57.11)	3.70 (3.68)	20.58 (20.56)	8.46 (8.42)

Table 1 : Characterization data of synthesized compounds

Comp. No.	Spectral Data	
2	IR (cm^{-1}):	2987 (C-H str., CH_3), 2934 (C-H str., CH_2), 1743 (C=O str.), 1597 (C=N str.), 1029 (C-O str.)
	^{1}H NMR (δ):	7.6 (m, 4H, Ar-4), 4.24 (q, 2H, $COOCH_2$ CH_3), 3.70 (S, 2H, NCH_2), 1.26 (t, 3H, $COOCH_2$ CH_3)
3	IR (cm^{-1}):	3378, 3237 (N-H str.), 2290 (C-H str., CH_2), 1745 (C=O str.) 1597 (C=N str.), 1105 (C=S str.)
	^{1}H NMR (δ):	8.3 (m, 4H, NH.NHC=S.NH_2), 7.6-7.7 (m, 4H, Ar-H) 3.68 (S, 2H, NCH_2)
4	IR (cm^{-1}):	3431 (N-H str.), 2967, 2810 (C-H str., CH_2), 1712 (C=O str.), 159s4 (C=N str.), 691 (C-S-C str.)
	^{1}H NMR (δ):	8.11 (S, 1H, CONH), 7.6-7.7 (m, 4H, Ar-H), 5.6 (S, 1H, NH of thiazolidinone ring), 4.4 (3, 2H, CH_2), 3.6 (S, 2H, NCH_2)
5a	IR (cm^{-1}):	3436 (N-H str.), 2957 (C-H str., CH_2) 1695, 1686 (C=O str.), 742 (C-Cl str.), 695 (C-S-C str.)
	^{1}HNMR (δ):	8.1 (S, 1H, CONH), 7.6-7.9 (m, 8H, Ar-H), 6.3 (S, 1H, C= CH-Ar), 5.68 (S, 1H, NH of thiazolidinone ring), 3.6 (S, 2H, NCH_2)
5b	IR (cm^{-1}):	3413 (N-H str.), 2940 (C-H str., CH_2), 1702, 1685 (C=O str.), 1040 (C-O str.)
	^{1}H NMR (δ):	8.0 (S, 1H, CONH), 7.7-7.9 (m, 8H, Ar-H), 6.2 (S, 1H, C=CH-Ar), 5.5 (S, 1H, NH of thiazolidinone ring), 3.5 (S, 2H, NCH_2)
5c	IR (cm^{-1}):	3416 (N-H str.), 2940 (C-H str., -CH_2), 1705, 1685 (C=O str.), 1556 & 1340 C-NO_2 asymmetric and symmetric stretching
	^{1}H NMR (δ):	8.0 (S, 1H, -CONH), 7.7-7.9 (m, 8H, Ar-H), 6.2 (S, 1H, C=CH-Ar), 5.5 (S, 1H, NH of thiazole)
5d	IR (cm^{-1}):	3413 (N-H str.), 2967 (C-H str., -CH_2), 1712, 1694 (C=O str.), 1594 (C=N str.)
	^{1}H NMR (δ):	7.9 (S, 1H, CONH), 7.7-7.9 (m, 9H, Ar-H), 6.1 (S, 1H, C=CH-Ar), 5.9 (S, 1H, NH of thiazolidinone ring)

Table 2 : Spectral data of synthesized compounds

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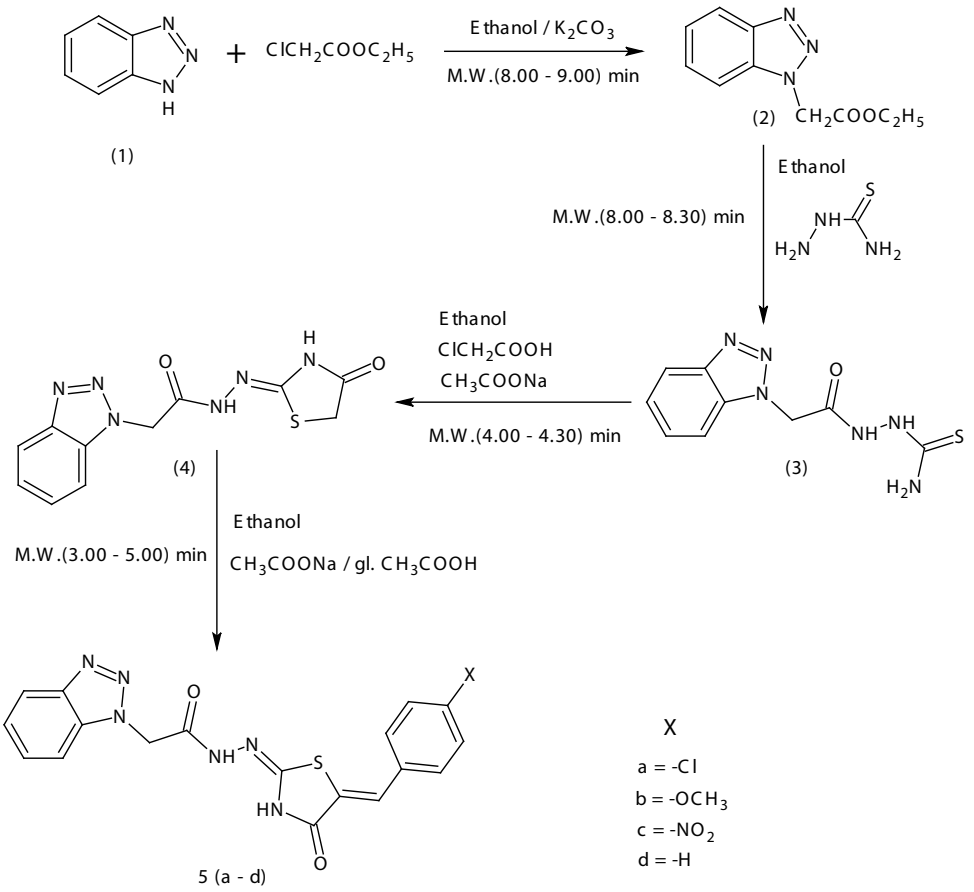

Reaction Scheme

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