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NOTES ON NATURAL HISTORY

Synthesis, Characterization and Biological Evaluation of New N, N'-Disubstituted Malonamide Derivatives

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Key words: Malonamide, Spectral elucidation, Antimicrobial evaluation

Introduction

Malonamide derivatives are one of the most important synthetic substrates because they have a wide range of properties that are useful in a variety of applications (Pavia & Costa, 2005; Broudic et al., 1999; Ansari et al., 2007). Multi-component reactions are one-pot chemical transformations that include the reaction of three or more different starting components to produce a final complex product (Zhu & Bienayme, 2005). In these reactions, the majority of the atom in the starting components are involved in the final product. As the number of atoms in the starting components is involved in the final product. As the number of atoms in the final product increases, so too does the atom economy of the reactions. In MCRS this is essential (Toure & Hall, 2009; Litvinov, 2003; Hulme & Gore, 2003). Furthermore, when compared to traditional stepwise procedures, reducing the number of synthetic stages reduces the number of used solvents, energy and reaction time. (Zhu & Bienayme, 2005; Toure & Hall, 2009; Litvinov, 2003; Hulme & Gore, 2003). MCRs have ignited a lot of interest in modern organic synthesis because of their wide range of applications in the pharmaceutical industry for drug discovery (Ruijter, 2012), combinatorial chemistry for structural diversity (Gu, 2012), green chemistry (Isambert, 2011), and in the industry for lower process costs (Ugi. Academic Press, 1968). Isocyanides are useful synthons with intriguing chemical properties that have been widely employed in MCRS. (Dömling, 2000). As a result, novel MCRs must be developed and discovered to deal with the range of scaffolds found in compound collection (Ruijter, 2011).

We studied

All of the reagents and solvents used were of the highest possible quality. Which were used without purifying further. The melting point was measured in uncorrected open capillary tubes. IR, ^1H, and ^{13}C NMR spectra were recorded with tetramethylsilane as an internal standard to determine the characterisation of the synthesised compound. On a mass spectrometer, LC-MS spectra were recorded.

Synthesis series of novel malonamide derivatives (IIA-IIC)

A mixture of substituted ethyl (4-methoxyphenyl) methyl) thioureido)-3-oxopropanoate and substituted- ((2-hydroxyphenyl) (4-methoxyphenyl) methyl) thiourea (0.25 gms) was taken in a round bottom flask and then refluxed for 1 hour in an ethanolic medium. The condensed mixture was then cooled and the crude was diluted with 50% ethanol and transferred over crushed ice which was further recrystallised from 50% ethanol to form a crystalline solid. The synthesis scheme is shown in figure 1 and the physical data is shown in Table-1.

Our findings

Compound IIA: N'-(((2,5-dihydroxyphenyl)(4-methoxyphenyl) methyl) carbamothioyl)-N3-(((2-hydroxyphenyl)(4-methoxyphenyl) methyl) carbamothioyl) malonamide-

IR (KBr) cm-1: 3645 (Ar-OH stretching), 3109 (NH stretching), 2956 (CH stretching), 1574 (C=S), 1166(C-N stretching) 1650(C=O). 1HNMR (CDCl3) d: 8.64 (d,1H,NH),9.60 (s,1H,OH), 5.19(s,1H,CH),7.02, 7.08, 6.96,6.73,(m, 4H, Ar-H) 6.32, 6.69, 6.65 (m, 3H, Ar H) 3.81(s,3H CH3). MS (Relative abundance %) m/z: 660.36

Compound IIB: N'-((2,5-dihydroxyphenyl)(4-methoxyphenyl) methyl)carbamothioyl)-N3-(((2-hydroxy-5-methylphenyl)(4-methoxyphenyl)methyl)carbamothioyl)malonamide-

IR (KBr) cm-1: 3505 (Ar-OH stretching), 3006 (NH stretching), 2950 (CH stretching), 1524 (C=S), 1166(C-N stretching) 1600(C=O). 1HNMR (CDCl3) d: 8.06 (d,1H,NH),9.65 (s,1H,OH), 5.19(s,1H,CH),7.02, 7.08,6.73,(m, 3H, Ar-H),6.32, 6.69, 6.65 (m, 3H, Ar H) 3.81(s,3H CH3). MS (Relative abundance %) m/z: 674.79

Compound IIIC: N'-((1-hydroxynaphthale-2-yl)(4-methoxyphenyl) methyl) carbamothioyl)-N3-(((2-hydroxyphenyl) (4-methoxyphenyl) methyl) carbamothioyl) malonamide-

IR (KBr) cm-1: 3485 (Ar-OH stretching), 2995 (NH stretching), 2950 (CH stretching), 1514 (C=S), 1066(C-N stretching) 1605(C=O). 1HNMR (CDCl3) d: 7.66 (d,1H,NH),9.05 (s,1H,OH), 5.19(s,1H,CH),7.02,

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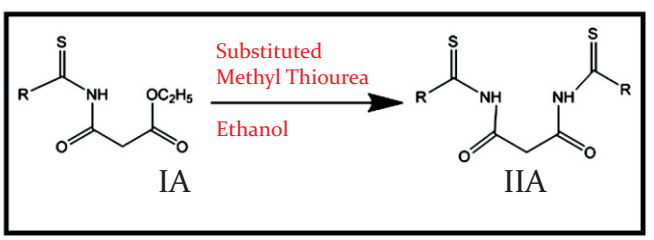

Figure- 1: Synthesis Scheme

Table 1 Physical data of novel synthesize malonamide

Comp. Code	Molecular Formula	Molecular Weight	Melting Point	Yield (%)	Color
IIA	$C_{33}H_{32}N_4O_7S_2$	660.17	160°C	34%	Brown
	Elemental Analysis- C,59.99 H,4.88 N,8.48 O,16.95 S,9.70				
IIB	$C_{34}H_{34}N_4O_7S_2$	674.79	161°C	40%	White
	Elemental Analysis- C,60.52 H,5.08 N,8.30 O,16.60 S,9.50				
IIC	$C_{37}H_{34}N_4O_6S_2$	694.19	180°C	35%	Brown
	Elemental Analysis- C,60.52 H,5.08 N,8.30 O,16.60 S,9.50				

Table-2: Antimicrobial activity of compound code II (A-C) against Bacterial (a) and Fungal (b) pathogens

a	Bacterial Pathogens	Culture zone of inhibition con. in %(mm)			
		25	50	75	100
IIA	*Escherichia coli*	9	14	20	21
IIB	*Escherichia coli*	7	13	18	19
IIC	*Escherichia coli*	8	15	20	21
b	Fungal Pathogens	Culture zone of inhibition con. in %(mm)			
		25	50	75	100
IIA	*Aspergillus niger*	18	20	21	21
IIB	*Aspergillus niger*	19	21	21	23
IIC	*Aspergillus niger*	17	19	20	20

7.08,6.73,6.83(m, 4H, Ar-H), 7.52,8.10,7.32,7.69, 6.95,7.62(m, 6H, Ar H) 3.81(s,3H CH_3). MS (Relative abundance %) m/z: 694.19.

Antimicrobial Properties

Results of antimicrobial activity (MIC) of given "Novel derivatives of malonamide" against E. coli (MTCC-1687) A. niger (MTCC) is shown in table 2. The test bacterial and fungal species used in this investigation were E.coli and A.niger. The samples were prepared at a concentration of 100 mg/ml in sterile water and sterilised using a dissociable syringe filter with a pore size of 0.22m, followed by serial dilution. In the case of all microbiological species testing, 20 µl of substance from each dilution was poured into each well for the well diffusion antimicrobial assay. During the current investigation, it was discovered that the provided samples identified as "Novel malonamide derivative" effectively controlled test bacterial and fungal species in vitro (refer to Table 2 of this report). Various concentrations of the produced chemical were tested (25,50,75,100).

Conclusion

We synthesized novel propanediamide derivatives in this study, and these compounds were investigated using FT-IR, NMR, and mass spectroscopy, which showed good results. These compounds' antimicrobial screening reveals that inhibition is depending on strain and structure. The newly synthesized compounds' antibacterial activity was successfully evaluated against *Escherichia Coli*, bacterial strains, and *Aspergillus niger* fungal strains. Compounds IIA and IIC have excellent antibacterial action against *E.coli*, while compound IIB has moderate antibacterial activity. Compound IIB has an excellent antifungal effect against IIA and IIC.

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