SYNTHESIS OF NOVEL 4-(4-METHOXYBENZENE SULPHONYL)-3, 5-DIMETHYL/3-METHYL-5-PHENYL/3, 5-DIPHENYL/3, 5-DIMETHYL-1-PHENYL/3- METHYL -1, 5-DIPHENYL /1, 3, 5-TRIPHENYL PYRAZOLE

Sandhya Chhakra and S. S. Chauhan*

Chemistry Research Lab ABB GF 07, Department of Chemistry, School of Sciences,
Mody University of Science and Technology, Lakshmangarh-332311, Sikar, (Raj.), India
E-mail : sureshsingh2288@gmail.com

ABSTRACT

An efficient synthesis of novel 3, 4, 5-trisubstituted pyrazole (2a-c) and 1, 3, 4, 5-tetrasubstituted pyrazole (2d-f) by the reaction of (1a-c) with $\text{NH}_2\text{-NH}_2$ /phenyl hydrazine in absolute $\text{C}_2\text{H}_5\text{OH}$. The structure of the various pyrazole derivatives (2a-f) has been elucidated from elemental analysis and spectral studies viz. IR, NMR.

Keywords: β -diketone, hydrazine hydrate, phenyl hydrazine, sulphonyl group, and spectral studies.

© RASĀYAN. All rights reserved

INTRODUCTION

The five-membered heterocycles containing two adjacent nitrogen heteroatoms represent a class of important compounds. The pyrazole ring has pulled in much consideration as it has turned out to be genuinely available and indicates diverse biological activity.^{1,2} The significance of pyrazole lies in the way that they can be viably utilized as antiinflammatory³, anticonvulsant⁴, antibacterial agents^{5,6}, antitumor⁷, antiviral⁸ and CNS depressant⁹.

The compound contains sulphonyl group which has been a focus of attention for their diversified biological activities¹⁰. Sulfones involve one of a kind position in the medication business with their bactericidal^{11, 12} and antimalarial¹³ activity.

The marketed drugs of pyrazole, such as *Ampyrone*, *Antipyrine*, *Dipyrone*, *Isofezolac*, *Lonazolac*, and *Pyrolan*[®] have incredible therapeutic esteem, prompted the scan for fresher bioactive compounds of this class with 4-methoxybenzene sulphonyl, as one of the substituents in the ring.

EXPERIMENTAL

Melting points are uncorrected (open capillary tubes method). The IR spectra were recorded on a Nicolet-Magna FT-IR 550 spectrophotometer in KBr pellets. The ¹H-NMR spectra were run on a BRUKER AVANCE II 400 NMR Spectrometer at 400.13 in CDCl_3 using TMS as an internal standard. Impurity checked by thin layer chromatography. Satisfactory elemental analyses were obtained.

Generalized Preparation

Preparation of Substituted Pyrazole(2a-c)¹⁴⁻¹⁸

A mixture of 1a-c (β -diketone¹⁹⁻²⁰, 2.70 g., 0.01M) and $\text{NH}_2\text{-NH}_2$ (0.5 g., 0.01 M) was placed in a flask and refluxed in absolute $\text{C}_2\text{H}_5\text{OH}$ (8 ml) for about eight hours on a warming mantle. The resultant reaction mixture was cooled and filtered. The crude product so obtained was recrystallized from $\text{C}_2\text{H}_5\text{OH}$. Impurity in the compound was checked by thin layer chromatography using chloroform: methanol (9: 1), as the mobile phase.

Preparation of Substituted Pyrazole(2d-f)

In a round-bottomed flask placed a mixture of 1a-c (β -diketone, 2.70 g., 0.01M) and phenyl hydrazine (1.08g, 0.01M) and refluxed it in absolute ethanol (10 ml) for approximately eight hours on a warming mantle. The resultant mixture was cooled and filtered. The crude product was recrystallized from ethanol. Impurity of the novel pyrazole derivative was confirmed through thin layer chromatography using ethyl acetate: n-hexane (8:2) as the mobile phase.

RESULTS AND DISCUSSION

Pyrazole derivatives (2a-f) were synthesized by the cyclocondensation of 1a-c with $\text{NH}_2\text{-NH}_2/\text{NH}_2\text{NH-Ph}$ in the presence of absolute ethanol (Scheme-1). The pyrazole (2a-f) obtained were purified by column chromatography.

Scheme-1

Hydrazine hydrate/phenyl hydrazine other than being reactant make the media essential, to propel the enol kind of determined propane-1,3-dione(1a-c).The structure of all the recently combine pyrazolesubsidaries (2a-f) was affirmed by the basic investigation, IR and ^1H NMR spectral studies(Table-1, 2 and 3).

Spectral Studies

In IR spectra, stretching vibration for NH observed at $3165\text{-}3260\text{ cm}^{-1}$ confirming NH group in the compound (2a-c). The C=N stretching mode appeared as an intense band at $1590\text{-}1620\text{ cm}^{-1}$ in five-membered heterocyclic rings. A band at $1138\text{-}1150$ and $1305\text{-}1340\text{ cm}^{-1}$ were attributed to symmetric and asymmetric -SO_2 stretching vibration respectively. Absorption band also appeared at $1035\text{-}1060$ and $1235\text{-}1265\text{ cm}^{-1}$, which was attributed to symmetric and asymmetric -OCH_3 stretching vibrations (Table-1).

In the ^1H NMR spectrum, a sharp singlet at δ 3.30-3.84 accounted for three proton of -OCH_3 group (2a-f).The methyl group at position-3 and 5 of the pyrazole ring was affirmed by a singlet at δ 2.04-2.05 for

six protons (2a & 2d). Another singlet at δ 1.98-2.01 accounted for three protons of the methyl group attached to position 3 of pyrazole ring (2b & 2e).

Table-1: IR Spectral Data (cm^{-1}) of New Pyrazole Derivative (2a-f)

Compound	Ar-H	C-H	O-CH ₃	C=N	N-H	-SO ₂
2a	3045	2910	1060 1250	1590	3245	1150 1300
2b	3010	2940	1045 1240	1610	3165	1140 1340
2c	3040	-	1050 1235	1580	3260	1150 1320
2d	3035	2890	1058 1248	1620	-	1140 1310
2e	3050	2915	1035 1265	1600	-	1145 1305
2f	3055	-	1040 1255	1620	-	1138 1308

A signal at δ 7.21-7.33 showed the presence of one proton of -NH group in the pyrazole ring. A double doublet in the region δ 6.90-7.98 accounted for the four aromatic protons (2a). A complicated pattern was observed at δ 6.88-8.04, which accounted for three phenyl groups (2f) attached to the 1, 3 and 5-position of the pyrazole ring and also other aromatic protons (Table-2). Satisfactory elemental analyses were obtained for all the compounds (Table-3).

Table-2: ¹H NMR Data (δ ppm) of Pyrazole Derivatives (2a-f)

Compound	Ar-H	O-CH ₃		-NH
2a	6.90-7.98 (4H,dd)	3.84 (3H,s)	2.05 (6H,s)	7.30 (1H,b)
2b	6.93-7.83 (9H,m)	3.61 (3H,s)	2.01 (3H,s)	7.21 (1H,b)
2c	6.85-7.86 (14H,m)	3.71 (3H,s)	-	7.33 (1H,b)
2d	6.91-7.98 (9H,m)	3.65 (3H,s)	2.04 (6H,s)	-
2e	6.85-8.05 (14H,m)	3.81 (3H,s)	1.98 (3H,s)	-
2f	6.88-8.04 (19H,m)	3.30 (3H,s)	-	-

Table-3: Physical Data of Pyrazole Derivatives (2a-f)

Compound	Molecular Formula	M.P. (°C)	Yield (%)	Elemental analysis Calculated (Found) %		
				C	H	N
2a	C ₁₂ H ₁₄ N ₂ O ₃ S	143	41	54.13	5.26	10.52
				53.68	4.92	10.06
2b	C ₁₇ H ₁₆ N ₂ O ₃ S	182	39	62.19	4.87	8.53
				61.81	4.33	8.13
2c	C ₂₂ H ₁₈ N ₂ O ₃ S	190	43	67.69	4.61	7.18
				67.11	4.19	6.83
2d	C ₁₈ H ₁₈ N ₂ O ₃ S	168	38	63.15	5.26	8.18
				62.78	4.89	7.73
2e	C ₂₃ H ₂₀ N ₂ O ₃ S	188	46	68.31	4.95	6.93
				67.91	4.53	6.51
2f	C ₂₈ H ₂₂ N ₂ O ₃ S	185	42	72.10	4.72	6.00
				71.68	4.35	5.49

CONCLUSION

Compound (2a-f), have been effectively synthesized and characterized. A higher yield of compound (2a-f) was accomplished when refluxed approximately eight hours on a warming mantle at 120⁰-125⁰C. Elemental analysis and spectral (IR and ¹H NMR) results were good agreement with predicted formulae.

ACKNOWLEDGMENT

Authors are thankful to the Dean (SOS), Mody University of Science and Technology, Lakshmangarh for providing necessary facilities to carry out present research work. Authors are also thankful to SAIF, Punjab University Chandigarh for giving spectral data.

REFERENCES

1. A. Gursoy, S. Demirayak, G. Capan, K. Erol, K. Vural, *Euro. Jour. Med. Chem.*, **35**(3), 359 (2000), DOI:10.1016/S0223-5234(00)00117-3
2. A. Mohammed, S. A. Khan, S. Srabu, *J. India Chem. Soc.*, **79**, 280 (2002)
3. A. K. Tiwari, V. P. Singh, P. Yadav, G. Gupta, A. Singh, R. K. Goel, P. Shinde, C. G. Mohan, *Bioorganic Chemistry*, **56**, 8 (2014), DOI:10.1016/j.bioorg.2014.05.004
4. P. O. Patil, S. B. Bari, *Arabian Journal of Chemistry*, **9**(4), 588 (2016), DOI:10.1016/j.arabjc.2013.08.027
5. A. Mohammed, S. M. Hasan, A. Wadoo, *Oriental Journal of Chemistry*, **18**(2), 351(2002)
6. H.B'Bhatt, S.Sharma, *Arabian Journal of Chemistry*, **10**(2), 1590(2017), DOI:10.1016/j.arabjc.2013.05.029
7. G. M. Nitulescu, C. Draghici, O. T. Olaru, *Int. J. Mol. Sci.*, **14**(11), 21805 (2013), DOI:10.3390/ijms141121805
8. B. K. Bhattacharya, R. K. Robins, G. R. Revankar, *J. Heterocyclic Chemistry*, **27**(3), 795 (1990), DOI:10.1002/jhet.5570270358
9. P. V. Taberner, J. W. Unwin, *J. Pharmacy and Pharmacology*, **39**(8), 658(1987), DOI:10.1111/j.2042-7158.1987.tb03449.x
10. I. Ahmed, Shagufta, *International Jour.of Pharmacy and Pharmaceutical Science*, **7**(3), 19 (2015)
11. M. Moise, V. Sunel, L. Profire, M. Popa, C. Lionte, *Farmacia*, **56**(3), 283 (2008)
12. E. A. Mohammad, M. Y. Mohammad, E. A. El-Bordany, *Molecules*, **18**, 832(2013), DOI:10.3390/molecules18010832
13. P. E. Thompson, B. Olszewski, J. A. Waitz, *Am. J. Tropical Medicine Hyg.*, **14**(3), 343 (1965), DOI:10.4269/ajtmh.1965.14.343
14. V. V. Dabholkar, F. Y. Ansari, *J. Serb. Chem. Soc.*, **74**(11), 1219 (2009), DOI:10.2298/JSC0911219D
15. Y. C. Joshi, P. Joshi, S. S. Chauhan, S. Nigam, *Heterocyclic Communications*, **10**, 249 (2004).
16. R. Fekry, N. A. Ismail, S. Raslan, *European Chemical Bulletin*, **5**(5), 157 (2016), DOI:10.17628/ecb.2016.5.157-162
17. R. Unny, P. Joshi, M. P. Dobhal, Y. C. Joshi, *Heterocyclic Communications*, **2**, 171 (2003)
18. S. S. Chauhan, A. Sharma, S. Saingar, Y. C. Joshi, *J. Indian Chem. Soc.*, **82**(11), 1016 (2005)
19. J. Bhagwan, Y. C. Joshi, R. P. Tyagi, B. C. Joshi, H. N. Mangal, *J. Institution of Chemistry*, **55**, 58(1983)
20. S. S. Chauhan, Y. C. Joshi, *An Indian J. Organic Chemistry*, **5**(4), 424(2009)

[RJC-5030/2018]