Dedicated to Dr. P.P. Wadgaonkar, National Chemical Laboratory, Pune, 411008 India Microwave-assisted Sinthesis of Thymyl Ethers and Esters

in Aqueous Medium¹

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Abstract—Various thymyl ethers and esters have been synthesized by reactions of thymol with alkyl halides and acid chlorides, respectively, in aqueous medium under environmentally benign conditions using microwave irradiation. The products are important as potent pest managing agents.

Terpenoids constitute an abundant and potent group of natural products, which plays an important role in the enzyme system of plants and reflects conspicuous biological activity against various pests. Monoterpenoids are secondary metabolites of plants and are self-defence tactics against plant enemies. Their better pest management efficiency have been noted. Higher terpenoids exhibit medicinal properties [1, 2]. The biological activity of monoterpenoids is believed to be related to the nature and position of functional groups or substituents. Chemical modification of natural forms of monoterpenoids may lead to improved biological activity [3, 4].

Microwave (MW) irradiation technique has opened new prospects in synthetic organic chemistry not only from the viewpoint of high reaction rates and ease of experimental procedures but also due to high yields of the products, their purity, and reaction selectivity and cleanliness. It has been commonly employed as thermal energy source in organic synthesis under Microwave-induced Organic Reaction Enhancement (MORE) chemistry [5, 6]. In continuation of our work on structural modifications of monoterpenoids [7-9], the merits of the title methodology and importance of the products prompted us to undertake the present study. Here we report on the synthesis of thymyl ethers and esters (see table) by reactions of thymol with alkyl halides and acid chlorides, respectively, in aqueous medium under conditions of microwave irradiation (Scheme 1). All the products have already been prepared via conventional [7, 9] and polymersupported reactions [8]. The use of microwave irradiation technique considerably reduced the reaction time

EXPERIMENTAL

Analytically pure thymol, alkyl halides, and some acid chlorides were commercial products. Cinnamoyl chloride and malonyl, succinyl, glutaryl, and adipyl dichlorides were prepared by the procedures described in [10, 11]. The progress of reactions and the purity of products were monitored by TLC on silica gel

Synthesis of thymyl ethers and esters in aqueous medium under microwave irradiation

Comp. no.	R or n	bp, ^a ∘C	Reaction time, min	Yield, ^b %
I	CH ₃	216–218	5	98
Π	CH ₃ CH ₂	224-225	4.5	98
III	CH ₃ CH ₂ CH ₂ CH ₂	226-228	4.5	98
IV	(CH ₃) ₂ ČH	216-218	4.5	98
V	CH ₃ (CH ₂) ₂ CH ₂	236-238	4	99
VI	$CH_2 = CH\tilde{C}H_2$	238-240	5	99
VII	C ₆ H ₅ CH ₂	253-254	5	99
VIII	HO ₂ CCH ₂	210-212	5	98
IX	n = 1	224-226	4	97
Х	n = 2	227-229	5	98
XI	CH ₃ CO	241-242	2.5	98
XII	C ₆ H ₅ CO	284-286	2	99
XIII	C ₆ H ₅ CH=CHCO	220-222	2.5	99
XIV	n = 1	219-221	2	99
XV	n = 2	235-236	3	99
XVI	n = 3	222-224	3	99
XVII	n = 4	236–238	3	99

^a Data of [8, 9]. ^b Yield of the isolated product.

and improved the yield and purity of the products which showed a high pest management potency [7, 9].

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using authentic samples [7–9]. The boiling points were determined by the open capilary technique and were not corrected. The reactions were carried out in a Kenstar OM 9918 C micriwave oven at 2450 MHz.

Thymyl ethers I–VIII (general procedure). A mixture of 2.5 mmol of thymol, 10 ml of a 1% solution of NaOH, and 2.5 mmol of the corresponding alkyl halide was placed in a 100-ml beaker and irradiated for 4–5 min at a power level of 3. Volatile alkyl halides were added in small portions after irradiation for every 1 min. The product was extracted into benzene or ether (2×20 ml), and the extract was washed with water and dried over sodium sulfate. Removal of the solvent afforded thymyl ethers **I–VIII** (see table).

Diethers **IX** and **X** were prepared in a similar way using 0.05 mol of thymol and 0.025 mol of dihaloalkane (n = 1, 2) in 20 ml of 1% aqueous NaOH.

Thymyl esters XI–XIII were synthesized as described above for ethers **I–VIII** using equimolar amounts (0.025 mol) of thymol and the corresponding acid chloride. Volatile acid chlorides were added in small portions after irradiation for every 1 min. The organic extract was washed first with a solution of sodium hydrogen carbonate and then with water and

dried over sodium sulfate. Removal of the solvent afforded products **XI-XIII** (see table).

Diesters **XIV**–**XVII** were synthesized as described above for compounds **IX** and **X** using 0.05 mol of thymol, 0.025 mol of the corresponding acid dihalide, and 20 ml of 1% aqueous NaOH (see table).

REFERENCES

- 1. Agarwal, O.P., *Chemistry of Organic Natural Products*, Meerut (India): GOEL, 1987, vol. 1, p. 408.
- Banthorpe, D.V. and Charlwood, B.V., Chemistry of Terpenes and Terpenoids, New York, 1972, pp. 337– 411.
- Coats, J.R., Karr, L.L., and Drewas, C.D., *Naturally* Occurring Pest Bioregulators, Hedin, P.H., Ed., Washington: Am. Chem. Soc., 1991, ACS Symposium Series, vol. 449, p. 305.
- Tsao, R., Lee, S., Rice, P.J., Jensen, C., and Coats, J.R., Synthesis and Chemistry of Agrochemicals. Vol. IV, Baker, D.R., Fenyes, J.G., and Basarab, G.S., Eds., Washington: Am. Chem. Soc., 1995, ACS Symposium Series, vol. 584, p. 312.
- 5. Caddick, S., Tetrahedron, 1995, vol. 38, p. 10403.
- 6. Bose, A., Banik, B., Lavlinskaia, N., and Jayaraman, M., *Chemtech*, 1997, vol. 27, pp. 9, 18–24.
- 7. Kumbhar, P.P. and Dewang, P.M., *Pestology*, 1999, vol. 23, p. 27.
- 8. Kumbhar, P.P., Kapadi, U.R., Hundiwale, D.G., Attarde, S.B., Dewang, P.M., and Pawar, N.S., *Org. Prep. Proced. Int.*, 2000, vol. 32, no. 6, p. 600.
- 9. Kumbhar, P.P. and Dewang, P.M., J. Sci. Ind. Res., 2001, vol. 60, p. 645.
- 10. Vogel, A.I., Vogel's Textbook of Practical Organic Chemistry, London: Longman Scientific and Technical, 1989, 5th ed.
- 11. Kumbhar, P.P., Cand. Sci. Dissertation, Kolhapur, 1993.