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Solvent-Free Synthesis of Substituted Phenoxyacetic Acids under Microwave Irradiation

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ABSTRACT

A comparison of microwave-activated vs. classical organic synthesis is presented for a variety of growth-regulator compounds with a phenoxyacetic acid structure. Microwave-assisted nucleophilic substitutions are safely and conveniently carried out in an open vessel, without any solvent. Yields are very good, and reaction times are extremely short.

Microwave-assisted heating treatment of liquid and solid samples has become a very helpful method for organic and inorganic synthesis as well as for extraction of organic compounds or trace metals from soils, sediments, oils and biological samples [1-4]. The early experiments were carried out using domestic microwave ovens and rudimentary vessels. Now is possible to use the specially designed equipment that allows adequate control and monitoring of temperature and pressure for reactions performed in liquid media [5-7].

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The microwave activation of organic reactions has attracted much attention. It is well known that a specific effect of microwaves takes place only in non-polar solvent media or in 'dry media' [3].

The compounds presented here have an old history. They have been used since 1930 as growth regulators for plants or as weed killers [8-11]. The phenoxyalkylcarboxylic acids are synthetic auxins. The classical synthesis of these compounds involves the reaction of a phenol with monohalogenoacetic acid in alkaline media. The solution is refluxed for a few hours (see Table 2) and then it is acidulated. The phenoxyacetic acids result in good yields (45-70%). This method is sometimes tedious. We tried to change it by sorbing the reagents on an inorganic solid support and by replacing conventional heating with microwave irradiating as an activation procedure. The same treatment was done without the solid support, only for the mixture of reagents. The results are presented below.

EXPERIMENTAL

Our treatment precinct is an original one, consist in a parallelipipedic microwave-cavity, H101 resonance mode. The reactions were performed in a quartz made open vessel and carried out in the NaOH/Al₂O₃ system, on K-zeolite, and without any inorganic support. The K-zeolite is original from Mârşid(Romania) and it has the following composition (mass percentage): SiO₂ - 69.86, Al₂O₃-11.45, Fe₂O₃-1.16, CaO-0.58, MgO-0.31, K₂O-8.70, Na₂O-0.72. The products were identified by TLC on "MERCK" silicagel 60 F 254 plates

eluting with toluene: acetone mixture. The visualization was done using a 254 nm UV lamp. Melting points for the isolated products are presented in Table 2.

General procedure for sample preparation:

The NaOH/Al₂O₃ support was prepared by mixing a NaOH aqueous solution with solid alumina (Merck activ. II-III 70-230 mesh) and drying at $80\div100$ °C. Both the substituted phenol (0.0125 mole) and the monochloroacetic acid (0.013 mole) were solved in acetone and sorbed on the inorganic support (0.013 mole/10 g). The solvent was then evaporated at room temperature.

In order to substitute the catalytic effect of sodium hydroxide we used a K-zeolite support, with the above mentioned composition. The sample was prepared by absorbing the acetonic solution of the reagents (molar ratio phenol: monochloroacetic acid = 1:1.1) in the zeolite and drying at room temperature overnight.

When the reactions were performed in 'dry media', without any support or solvent, the reagents were well mixed in the molar ratio phenol: monochloroacetic acid: NaOH = 1: 1.1:1.2.

In all these cases, after the microwave treatment (700 W power input and 2.45 Ghz, see Table 2), the reaction mixture was dissolved in water, the inorganic support (in case we used it) was separated by filtration. The aqueous solution was acidulated to $pII = 1.5 \div 2$ in order to precipitate the main product and thus was isolated by filtration, washed with water, dried and purified by recrystalisation.

RESULTS AND DISCUSSIONS

The preparation of microwave-assisted substituted phenoxyacetic acids was achieved according to the following scheme (see also Table 1):



When we used NaOH/Al₂O₃ as solid support the products were isolated in very poor yields (2-4%), because of the strong and irreversible adsorption of the products on the inorganic support after microwave treatment. When zeolite support was used, no product was obtained.

The best yields were found for reactions performed in 'dry media', without any inorganic solid support or solvent.

In the case of phenols 1c and 1d, both hydroxyl groups were active, thus we obtained 1,3- and 1,4-phenylen-dioxy-diacetic acids. The results of our experiments are shown in Table 2.

Our data show that solvent-free preparation of phenoxyacetic acids under microwaves is very convenient from the practical viewpoint. The absence of

Reagent	<u>R1</u>	R ₂	R ₃	R ₄	<u>R5</u>
1.5				TT	TT
12	п	н	н	H	H
1b	t-Bu	Н	t-Bu	Н	H H H H H
lc	Н	Н	OH	Н	
1d	Н	OH	Н	Н	
le	t-Bu	Н	Н	Н	
1f	NO_2	Н	Н	H i-Pr	
lg	CH3	Н	Н		
1h	CH3	Н	Н	Н	CH ₃
1i	CH3	CH ₃	Н	Н	Н
Product	R ₁	R ₂	R ₃	R ₄	R ₅
3a	Н	Н	Н	Н	н
3b	t-Bu	Н	t-Bu	Н	Н
3c	Н	Н	O-CH2-COOH	Н	н
3d	Н	O-CH2-COOHH	Ĥ	Н	Н
3e	t-Bu	H	Н	н	Н
3f	NO_2	Н	Н	Н	Н
3g	CH ₃	Н	Н	i-Pr	Н
3h	CH ₃	Н	Н	Н	CH1
3i	CH	CH ₂	Н	н	н

TABLE 1. Phenols (1) and phenoxyacetic acids (3)

solvents coupled with the high yields and very short reaction times make this procedure for phenoxyacetic acids preparation very attractive and environmentally benign. Waste water problems are 'ab ovo' eliminated.

CONCLUSION

Microwave-assisted synthesis of the above biological-active compounds demonstrate once more that a great simplification of procedure can be achieved

(2.45 Ghz).											
Phenol	Microwaves			Conventional							
	acid	Time	Yield	М.р.	Time	Yield	М.р.	Lit.			
	·····	(min)	(%)	(°C)	(min)	(%)	(°C)				
Phenol	Phenoxyacetic	0.5	70	94-	240	73	99-	12			
<u>1a</u>	3a			96			100				
2,4-di-tert-	2,4-di-tertButyl-										
Butyl-phenol	phenoxyacetic	0.66	64	166-	-	-	-	13			
1b	3b			167							
Hydroquinone	1,4-Phenylen-	0.66	58	251-	180	68-	251	14			
lc	dioxy-acetic 3c			253		72					
Resorcinol	1,3-Phenylen-	0.4	60	190	180	62	194	15			
1d	dioxy-acetic 3d										
2-tert-Butyl-	2-tert-Butyl-										
phenol le	phenoxyacetic	2.25	76	139-	-	-	145-	16			
	3e			141			146				
2-Nitro-Phenol	2-Nitro-										
lf	Phenoxyacetic	4	70	157-	660	46	156	17			
	3f			159							
2-Methyl-	2-Methyl-5-iso-										
5-isopropyl-	propyl-phenoxy-	1	62	140-	-	53.8	149	18			
phenol 1g	acetic 3g			142							
2,6-Dimethyl-	2,6-Dimethyl-										
phenol	phenoxyacetic	0.3	70	133-	-	-	-	-			
1h	3h			134							
2,3-Dimethyl-	2,6-Dimethyl-										
phenol	phenoxyacetic	0.4	55	162-	-	60	160	18			
li	3i			163							

 TABLE 2.
 Phenoxyacetic acids prepared by microwave irradiation at 700W

and, generally, the organic reactions take place more rapidly on this way, safely and in higher yields. The use of an inorganic solid support is not always the best choice, due to the sorption problems that occurs.

REFERENCES

- 1. Clark D.E. and Sutton W.H., Annu. Rev. Mater. Sci., 1996, 26, 299;
- 2. Strauss C.R. and Trainor R.W., Aust. J. Chem, 1995, 48, 1665;

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- Bram G., Loupy A. and Villemin D., "Solid Supports and Catalysts in Organic Synthesis", Ed. K. Smith. Ellis Horwood and Prentice Hall, Chichester, 1992, Ch. 12, pp. 303;
- 4. Onuska F.I. and Terry K.A., Chromatographia, 1993, 36, 191;
- 5. Majetich G. and Hicks R., Radiat. Phys. Chem., 1995, 45, 567;
- Mincey D.W., Williams R.C., Giglio J.J., Graves G.A. and Pacella A.J., Analytica Chimica Acta, 1992, 264, 97;
- Suard C., Mourel R-M, Cerdan B., Bart G. and Feinberg M.H., Analytica Chimica Acta, 1996, 318, 261;
- Kögl F.A., Haagen-Smit A.J. and Erxleben H., Z. Physiol. Chem., 1934, 228, 90;
- 9. Kögl F.A. and Kostermans D.G., Z. Physiol. Chem., 1934, 228, 113;
- Moore T.C., "Biochemistry and Physiology of Plant Hormones", Springer Verlag New York, 1979, pp. 32;
- Rayle L.D. and Cleland R., "Plant Growth Substances", Springer Verlag Berlin-Heidelberg, 1972, pp. 44;
- Thadani S.B. and Das Gupta S.K., *Hindustan Antibiotics Bull.*, 1959, 2, 53; *Chem. Abstr.*. 1960, 54, 17302i;
- 13. Anderson M., Ark. Kemi., 1967, 27, 381; Chem. Abstr. 1968, 68, 21422h;
- 14. Naoya Y., Macromol. Chem., 1959, 32, 1; Chem. Abstr. 1960, 54, 1408g;
- Kawai W. and Tsutsumi S., Nippon Kagaku Zasshi, 1960, 81, 1167;
 Chem. Abstr. 1962, 56, 2594d;
- 16. Hart H., J. Am. Chem. Soc., 1949, 71, 1966; Chem. Abstr. 1949, 43,

6998g;

- Kurihora T. and Takeda H., Tohoku Yakka Daigaku Kiyo, 1962, 9, 77;
 Chem. Abstr. 1963, 59, 2808g;
- Csiba I., Krasnec L. and Stuchlik M., Cesk. Farm., 1968, 17, 28: Chem. Abstr., 1968, 69, 67041g.

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