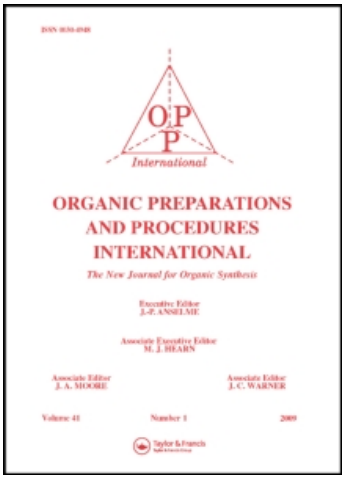

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RAPID N-ALKYLATION OF BENZOXAZINONES AND BENZOTHIAZINONES UNDER MICROWAVE IRRADIATION

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RAPID N-ALKYLATION OF BENZOXAZINONES AND BENZOTHIAZINONES UNDER MICROWAVE IRRADIATION

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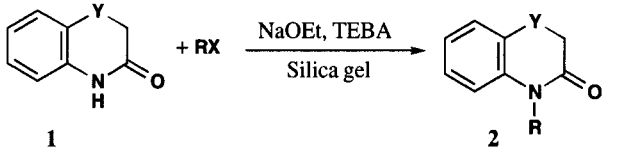
The application of microwave energy in organic synthesis was sparked by the pioneering papers of Gedye[1] and Majetich[2] and their co-workers in 1986. Recent work has demonstrated that organic reactions can be conducted safely in commercial microwave ovens with remarkable rate enhancements and dramatic reductions of reaction times compared to conventional heating. This new technique has been used to promote Diels-Alder reactions,[2-4] Claisen rearrangements,[2,3,5] *Ene* reactions[3] and a variety of other organic reactions.[3,6] We first applied the microwave technique to the Wittig reaction with excellent results.[7] This paper extended the applications of microwave to other syntheses.

N-Substituted 2H-1,4-benzoxazin-3(4H)-ones and 2H-1,4-benzothiazin-3(4H)-ones are compounds of considerable interests because of their pharmacological and antimicrobial properties. We reported that, in the presence of powder sodium hydroxide and triethylbenzylammonium chloride (TEBA) as phase transfer catalyst, 2H-1,4-benzoxazin-3(4H)-one or 2H-1,4-benzothiazin-3(4H)-one undergo N-alkylation reaction with alkyl halides, which require at least 6-8 hrs.[8] In order to reduce the reaction times, we investigated this reaction under microwave irradiation.



1 2

a) Y = O, R = Me b) Y = O, R = Et c) Y = O, R = $PhCH_2$
d) Y = O, R = CH_2COOH e) Y = S, R = Me f) Y = S, R = $PhCH_2$

2H-1,4-Benzoxazin-3(4H)-one or 2H-1,4-benzothiazin-3(4H)-one (**1**), the alkyl halide, the base and the phase-transfer catalyst were supported on silica gel or alumina and then the mixture was placed in a microwave oven. In order to optimize reaction conditions, the effect of bases, supports and catalysts were studied. These experiments showed that (l) sodium ethoxide, sodium hydroxide and potassium carbonate were efficient bases with sodium ethoxide being the best; (2) silica gel and alumina are good supports and, without them, the yields were very low; (3) the presence of phase transfer catalysts was favorable to the reaction and TEBA was better than polyethylene glycol (PEG). Using sodium ethoxide as base, TEBA as phase transfer catalyst and silica gel as support, the N-alkylation reaction of 2H-1,4-benzoxazin-3(4H)-one or 2H-1,4-benzothiazin-3(4H)-one with alkyl halide can completed rapidly within 8-10 min. Remarkable rate enhancements and significant reductions of

reaction time have been achieved (see Table 1).

TABLE. 1 N-Alkylation of 2H-1,4-Benzoxazin-3(4H)-ones and 2H-1,4-Benzothiazin-3(4H)-ones under Microwave Irradiation

Cmpd	RX	Time (min.)	Yield (%)	top. (°C)	lit. mp (°C)
2a	CH_3I	8	90	51-53	51-52[10]
2b	C_2H_5Br	10	81	oil	102-106[11] (0.1-0.5 torr)
2c	$C_6H_5CH_2Br$	10	84	63-65	64-66[8]
2d	$BrCH_2COOH$	10	72	180-182	180-182[10]
2e	CH_3I	9	86	53-55	53-54[12]
2f	$C_6H_5CH_2Br$	10	80	81-83	82-83[13]

EXPERIMENTAL SECTION

Melting points are uncorrected. IR spectra were recorded as KBr disks for solid product or film for liquids on Perkin Elmer 683 spectrophotometer. ^1H NMR spectra were obtained with F 90Q spectrometer in $CDCl_3$ using TMS as internal standard. Chemical shifts are expressed in δ (ppm). The microwave oven used here was National NN-5252. 2H-1,4-Benzoxazin-3(4H)-one and 2H-1,4-benzothiazin-3(4H)-one were prepared as described.[9]

General Procedure.- To a stirred solution of 2H-1,4-benzoxazin-3(4H)-one (2.5 mmol) or 2H-1,4-benzothiazin-3(4H)-one (2.5 mmol), alkyl halide (5 mmol), TEBA (0.25 mmol) in acetonitrile (20 mL), were added powder sodium hydroxide (7 mmol) and silica gel 200-300 mesh (5g). After they were mixed thoroughly, the solvent was evaporated under reduced pressure. The mixture in a container was inserted into the domestic microwave oven and irradiation was carried out at an output of about 400w for 8-10 minutes. Then 30 mL of methylene dichloride was added into the cooled mixture, the extract was concentrated and chromatographed to give N-alkyl 2H-1,4-benzoxazin-3(4H)-one or N-alkyl 2H-1,4-benzothiazin-3(4H)-one.

TABLE 2. Spectra Data of Compound **2**

Cmpd	IR ν (cm^{-1})	^1H NMR δ (ppm)
2a	1688, 766	2.51 (s, 3H), 5.04 (s, 2H), 7.02-7.58 (m, 4H)
2b	1716, 754	0.75 (t, 3H), 2.96 (q, 2H), 5.01 (s, 2H), 7.10-7.68 (m, 4H)
2c	1704, 746, 721, 730	4.35 (s, 2H), 5.02 (s, 2H), 7.00-7.78 (m, 10H)
2d	2612-3100, 1711, 746	4.05 (s, 2H), 5.01 (s, 2H), 7.03-7.54 (m, 4H), 11.03 (s, 1H)
2e	1701, 745	2.53 (s, 3H), 3.52 (s, 2H) 7.05-8.12 (m, 4H)
2f	1795, 743, 731, 722	3.56 (s, 2H), 4.38 (s, 2H), 7.02-8.20 (m, 10H)

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REFERENCES

1. R. J. Gedye. F. Smith, K. Westaway, H. Ali, L. Baldisera, L. Laberge and J. Rousell, *Tetrahedron Lett.*, **27**, 279 (1986).

2. R. J. Giguere, T. L. Bray, S. M. Duncan and G. Majetich, *ibid.*, **27**, 4945 (1986).

3. R. A. Abramovitch, *Org. Prep. Proced. Int.*, **23**, 683 (1991).

4. R. S. Zhu. P. J. Hong and S. S. Dai, *Synth. Commun.*, **24**, 2417 (1994).

5. A. Krishna and S. Naggraju, *J. Chem. Soc. Perkin Trans. I*, **3**, 311 (1992).

6. R. J. Giguere, *"Organic Synthesis: Theory and Application"*, Vol. 1, p 103, JAI Press Inc., Greenwich, CT, 1989.

7. C. Xu, G. Chen and X. Huang, *Org. Prep. Proced. Int.*, **27**, 459 (1995).

8. X. Huang and Z. Z. Huang, *Huaxue Shigi (China)*, **9**, 193 (1987); *Chem. Abst.*. **108**, 221649u (1987).

9. X. Huang and C. C. Chen, *Synthesis*, 851 (**1984**).

10. H. H. Freedman and A. E. Frost, *J. Org. Chem.*, **23**, 1292 (1958).

11. M. Jacques, V. Micheal and P. Delaunay, *Chem. Ther.*, **4**, 80 (1969);*Chem. Abst.*, **71**, 112872 (1969).

12. F. S. Babichev, *Zh. Obshch. Khim.*, **20**, 1904 (1950).

13. P. Janina and B. D. Halina, *Acta Pol. Pharm.*, **24**, 245 (1967); *Chem. Abst.*, **69**, 19098 (1968).

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IMPROVED PREPARATION OF SOME NITROINDOLINES

Submitted by (07/05/95)

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Amides of 5,7-dinitroindoline and of 5-bromo-7-nitroindoline have been used as photolabile protective groups for carboxylic acids[1,2] as well as photochemically activatable coupling reagents in peptide synthesis[3,4] and for the derivatization of polymer surfaces.[5] 5-Bromo-7-nitroindoline has been