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Tetrahedron
Tetrahedron 62 (2006) 4685–4689

The Newman–Kwart rearrangement re-evaluated by microwave synthesis

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Received 1 November 2005; revised 22 December 2005; accepted 22 December 2005
Available online 29 March 2006

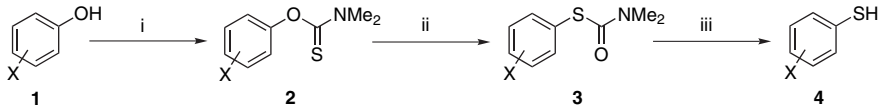
Abstract—The Newman–Kwart rearrangement (NKR) has been re-evaluated by microwave heating. Microwave technology has proven to be ideal for investigating this high temperature rearrangement and facilitated the confirmation of many aspects of this valuable reaction. Comparisons between thermal and microwave results indicate no evidence of a significant microwave effect.

1. Introduction

The Newman–Kwart rearrangement (NKR)[1,2] is a valuable synthetic technique for converting phenols **1** to thiophenols **4** via their *O*- (**2**) and *S*-thiocarbamates (**3**) (Scheme 1). Indeed, such is the utility that other sulfur-containing functional groups have been readily accessed through this methodology, including thioethers, (homo-chiral) sulfoxides, sulfones and sulfonic acids.[3] Alternatively, this approach can be used to access particular aromatic substitution patterns without the phenol/sulfur function, starting from the many widely available phenols, and de-sulfurizing the hydrolysed thiol once the desired transformations are complete. Consequently, the NKR has seen wide application in synthesis,[4] medicinal chemistry,[5] materials and supramolecular chemistry,[6] agrochemicals[7] and dyes.[8]

The NKR proceeds via an *O*- to *S*-aryl migration, which has a high activation energy. Many synthetically useful examples of the NKR require temperatures of 200–300 °C. Electron withdrawing group (EWG) substituents are known to aid the rearrangement, either reducing the reaction time or lowering the required temperature, whilst electron-donating group (EDG) substituents slow the reaction. *Ortho*-substituents can enhance the reaction rate,[9] but doubly *ortho* or very sterically hindered substituents slow the reaction or stop it altogether.[1,9] The rearrangement is proposed to proceed via a four-centre transition state **5** (Fig. 1), which is consistent with these observations. Furthermore, comprehensive kinetic and linear free energy relationships have been conducted,[9,10] which are also in agreement with this model. This should give a first-order reaction, which Newman,[1] Relles[9] and Miyazaki[10a] have shown to be the case. Lastly, this reactive intermediate (**5**) should be stabilised by polar solvents, lowering the activation energy, and thus increasing the reaction rate, but this does not appear to have been studied in detail.[10b]

We were interested in investigating the NKR under microwave irradiation[11] for a number of reasons. It was a reaction with which we had previous experience on scale-up[12] and knew was a sufficiently common motif in the pharmaceutical industry to justify in-depth study.[5] It also held wider synthetic utility.[4,6] Microwave technology provided convenient access to the high temperatures generally required for this reaction. Furthermore, a simple, first-order, unimolecular



Scheme 1. (i) DMTCC (1.1 equiv), DABCO (1.3 equiv), NMP, 50 °C, then water; (ii) solvent, heat or MW; (iii) NaOH or KOH.

Supplementary data associated with this article can be found in the online version, at doi: 10.1016/j.tet.2005.12.063.
Keywords: Microwave; Newman–Kwart; Rearrangement.
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0040–4020/$ - see front matter © 2006 Published by Elsevier Ltd.
doi:10.1016/j.tet.2005.12.063

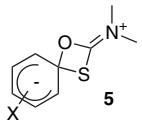


Figure 1. Proposed four-centre transition state intermediate.

model reaction would allow for a thorough and robust investigation of microwave heating. We were also hopeful that the proposed polar transition state intermediate **5** might interact favourably with microwaves,[11d] potentially giving rise to an observable microwave effect, if there was one.

From a practical point, the starting *O*-thiocarbamates **2** could be readily prepared from cheap phenols **1** in a single step. A wide variety of substitution patterns was accessible for **2**, which meant that the reaction parameters could be 'tuned' as desired. All intermediates had good UV chromophores and the NKR is ideal for analytical purposes in that it proceeds cleanly from starting material **2** to product **3** without degradation or impurity formation in most cases. The NKR can thus be readily followed by IR, LC, NMR or TLC as preferred. It was also useful for our purposes that all of substrates **2** and **3** were known; that thorough studies of kinetics with Hammett plots had been conducted;[9,10] and that all these kinetic studies had been conducted with conventional thermal heating;[13] this would provide a secure comparison for our own results.

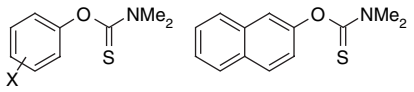
2. Results and discussion

For our initial investigations, we chose phenols **1a–o** covering a range of EWG and EDG substituents from nitro- to methoxyphenyl groups, including the electron neutral unsubstituted phenol (**1j**). To gauge the effect of aromatic substitution, we also included the *ortho* and *meta* nitro- and methoxy-substituted compounds. The starting *O*-thiocarbamates **2a–o** were readily prepared from phenols **1a–o** and dimethylthiocarbamoyl chloride (DMTCC) in fair-to-excellent yields as predominantly crystalline compounds of excellent quality (>98% by LC) (Table 1). We used our previous method[12] adapted from Sebok,[7] which had the advantage of direct isolation of **2** from the quenched aqueous reaction mixtures, thus avoiding tedious chromatography in the majority of cases. With quantities of substrates **2a–o** available, we conducted an initial screening in a focused microwave reactor.

We decided to conduct a coarse survey of reaction conversion after 20 min for all compounds **2a–o**, at 220 °C for EWG substituents and 280 °C for EDG substituents, with the relatively electron neutral compounds (**2g–j**) assayed at both temperatures. The fast reacting nitro substituents had to be reassessed at 180 °C due to over-reaction, so the other EWG compounds were also assayed at this temperature (Table 2).

As can be seen, the trend is as expected when moving from strong EWG to strong EDG substituents, with the latter requiring higher temperatures for equivalent conversions. The substituent effects for the nitro and methoxy compounds were also largely as expected. The *ortho*-substituents

Table 1. Preparation of *O*-thiocarbamates **2a–o**



	X=	Yield (%)	Quality (% LC)[a]	RRF[b] (**2** vs **3**)
2a	2-NO_2	92	100.0	3.20
2b	3-NO_2	93	100.0	1.63
2c	4-NO_2	79	100.0	3.04
2d	4-CN	93	100.0	2.66
2e	4-CO_2Me	92	100.0	2.45
2f	4-CF_3	91	99.9	1.27
2g	2-Naph	72	99.8	1.13
2h	4-Br	84	99.7	1.28
2i	4-Cl	84	99.8	1.39
2j	4-H	56[c]	99.9	3.61
2k	4-Me	66	100.0	2.41
2l	4-F	80	99.7	4.94
2m	4-MeO	49[d]	99.7	1.65
2n	3-MeO	68[c]	98.0	3.78
2o	2-MeO	75[d]	100.0	4.88

[a] Determined at 254 nm.
[b] Relative response factor (RRF) at 254 nm.
[c] Low melting solid purified by chromatography.
[d] Recrystallised from MeOH/water.

appeared to show an additional steric rate acceleration compared to the purely electronic effect of the *para*-substituents, as reported by Relles.[9] The *meta*-substituents **2b** and **2n** also showed the trend expected relative to their *ortho* and *para* regioisomers, given their respective electron withdrawing and donating properties.

From this coarse screen, we were then quickly able to pinpoint the optimum temperature for a convenient 20 min microwave reaction that would give >95% conversion, in the comparable manner reported by Newman.[1] Reaction temperatures and LC conversions for all substrates are collected in Table 3, with Newman's data alongside where available. Generally the results are in good agreement, but some minor differences will be noted, for which we offer the following explanations.

Table 2. Conversion of **2** to **3** after 20 min in microwave at given temperature (20 min in 10 vol NMP)

	X=	Conversion at 180 °C (%)[a]	Conversion at 220 °C (%)[a]	Conversion at 280 °C (%)[a]
2a	2-NO_2	98	>100[b]	—
2b	3-NO_2	4	45	—
2c	4-NO_2	68	>100[b]	—
2d	4-CN	19	99	—
2e	4-CO_2Me	4	75	—
2f	4-CF_3	2	51	—
2g	2-Naph	—	10	97
2h	4-Br	—	7	98
2i	4-Cl	—	7	95
2j	4-H	—	4	78
2k	4-Me	—	—	53
2l	4-F	—	—	51
2m	4-MeO	—	—	27
2n	3-MeO	—	—	92
2o	2-MeO	—	—	76

[a] Determined by LC at 254 nm (RRF corrected).
[b] Indicates all starting material converted and some product degradation had occurred.

Table 3. Temperature required for >95% conversion of **2** to **3** in 20 min by microwave (or conventionally)

	X=	Temp[a] (°C)	Conversion[b] (%)	Temp[c] (°C)	Yield[d] (%)
2a	2-NO_2	180	98	170	90
2b	3-NO_2	240	77[e]	235	>95
2c	4-NO_2	200	98	180	>95
2d	4-CN	220	99 (86)	—	—
2e	4-CO_2Me	240	99 (82)	220	>95
2f	4-CF_3	260	98	—	—
2g	2-Naph	280	97	285	80
2h	4-Br	280	98 (83)	—	—
2i	4-Cl	280	95 (82)	—	—
2j	4-H	290	97 (82)	—	—
2k	4-Me	295[f]	82 (83)	—	—
2l	4-F	295[f]	82	—	—
2m	4-MeO	295[f]	72	290	83
2n	3-MeO	295[f]	85 (86)	—	—
2o	2-MeO	295	95 (80)	280	90

[a] MW, 20 min in 10 vol NMP.
[b] Conversion determined by LC at 254 nm, RRF corrected with isolated yields noted in brackets.
[c] Thermal heating, 20–30 min neat.
[d] Isolated yields except where >95% quoted (from TLC response at 254 nm).
[e] Some decomposition seen above this temperature.
[f] Higher temperatures could not be accessed to achieve >95% conversion in 20 min.

Newman's reactions were conducted neat whereas ours were conducted in 10 vol of NMP (Relles and Kaji used 0.3 M solutions in phenylether). For a first-order, unimolecular reaction, rate should be independent of concentration. However, we know from our other results that there is a subtle effect related to concentration, which we believe accounts for the slight differences in the observed rate. Secondly, the exact end-point of these reactions is difficult to ascertain at 254 nm due to the generally stronger UV responses of *O*-thiocarbamates **2** over their analogous *S*-thiocarbamates **3**. Newman used IR but found this unreliable and reverted to TLC, necessitating an additional 10 min heating time in unspecified cases. We have determined the relative response factors (RRFs) to give accurate LC results (see Table 1 for data and Section 4 for method determination).

Finally, we have briefly surveyed the solvent effect for one substrate (**2a**) at one temperature (140 °C) under both microwave and thermal reaction conditions. The thermal tube reactions were sealed with caps easily removed for sampling purposes, except for the lower boiling solvents formic acid and trifluorotoluene, where crimp caps were used; hence only one time point was taken from these tubes. However, being a rearrangement, no pressure is generated in this reaction below the boiling point of the solvent used, and even at the higher end of the temperature range (250–300 °C), pressures are still relatively modest. Data are shown for both 30 and 60 min time points in Table 4. As can be seen, there is an excellent correlation between microwave and thermal results in all cases (the thermal figures are slightly higher for two low polarity solvents, diphenylether and xylene, the reasons for which are still being investigated). Our studies with other substituted *O*-thiocarbamates (**2**) and various solvents show this agreement between microwave and thermal results to be general. The reaction rate also fits the relative order of solvent polarity, supporting the hypothesis that polar solvents can stabilise polar transition state intermediate **5**. To our knowledge this is the first time such an effect has been confirmed experimentally.

Table 4. Conversion of **2a** at 140 °C in 10 vol of solvent under microwave and thermal heating

Solvent	Time (min)	Conversion (%)[a]	
		Microwave	Thermal
Dichlorobenzene	30	15	15
	60	28	27
Diphenylether	30	12	15
	60	23	27
Formic acid[b]	30	79	78
NMP	30	23	23
	60	39	40
Trifluorotoluene[b]	30	11	11
Xylene	30	8	10
	60	15	19

[a] Conversion determined by LC at 254 nm (RRF corrected).
[b] Conventional heating was conducted above the boiling point of the solvent in a sealed tube in an oil bath.

3. Conclusions

In conclusion, we have shown that the NKR is a well-behaved first-order reaction under microwave heating. We have confirmed several known aspects of the reaction mechanism and provided the first experimental support for a solvent rate effect. Furthermore, we find the reaction rate is essentially unchanged compared to thermal heating under all conditions. In short, we find no evidence for a significant microwave effect in this case, although there may be a subtle effect related to the reaction itself which we are currently investigating.

In addition, microwave technology has proven to be exceptionally convenient in a laboratory setting for accessing the high temperatures required (200–300 °C), both for the personal safety of the chemist and for rapid reactions. Furthermore, we found the IR temperature sensor to be very reliable in our hands, confirmed by comparison to our thermal heating results. Opportunities for further exploitation of the NKR as a probe to investigate microwave heating are ongoing and results will be reported shortly.

4. Experimental

4.1. General

Reaction mixtures and products were analysed by reverse phase HPLC on an Agilent 1100 series instrument according to the following conditions: column, Genesis C18 100×3.0 mm i.d.; eluent A, 95% purified water, 5% acetonitrile, 0.1% v/v formic acid; eluent B, 95% acetonitrile, 5% purified water, 0.1% v/v formic acid; flow rate 0.75 ml/min; wavelength 254 nm; temperature 35 °C; injection volume 10 μl; at t=0 min, 40% eluent B; at t=5 min, 70% eluent B; at t=7 min, 70% eluent B; 3 min post time. Typical retention times (RT) are noted in each case. Melting points were determined using a Griffin melting point apparatus (aluminium heating block) and are uncorrected. ^{1}H and

^{13}C NMR spectra were recorded on a Varian Inova 400 spectrometer at 400 and 100.6 MHz, respectively, with chemical shifts given in parts per million relative to TMS at δ=0. Electrospray (ES^+) mass spectra were performed on a Micromass ZQ (*O*-thiocarbamates, **2a–o** and *S*-thiocarbamates, **3d** and **3f**) or a Micromass Platform LC (all other *S*-thiocarbamates) mass spectrometer. Analytical TLC was carried out on commercially prepared plates coated with 0.25 mm of self-indicating Merck Kieselgel 60 F_{254} and visualised by UV light at 254 nm. Preparative scale silica gel flash chromatography was carried out by standard procedures using Merck Kieselgel 60 (230–400 mesh). Otherwise wherever not stated, assume standard practices have been applied.

4.2. Typical microwave procedure

Microwave reactions were performed in 10 ml sealed tubes in a regularly calibrated CEM *Discover* focused 300 W microwave reactor with IR temperature monitoring and non-invasive pressure transducer. In a typical procedure, 200 mg of *O*-thiocarbamate (**2**) was dissolved in NMP (2.0 ml) and heated to the required temperature with stirring for a fixed time. The heating time to reach the set temperature was typically 45–90 s, depending on the scale, the maximum wattage supplied (100–300 W) and the temperature required (140–295 °C) (typically 100 W to heat a 2 ml sample to 140 °C in ~45 s, or 300 W to heat to 295 °C in ~90 s). The heating time is not included in the quoted hold time for any given procedure; control studies show that the heating time is negligible for a 20 min reaction time. The *S*-thiocarbamate (**3**) products were isolated either directly by aqueous drown-out from NMP solutions, or by extraction into MTBE followed by flash silica gel chromatography and/or recrystallisation from methanol if required. Data only on *S*-thiocarbamates (**3a–o**) can be found in the Supplementary data. Yields are given only for preparative procedures, typically performed on 1.0 g of substrate **2** in 4.0 ml NMP (all other parameters were kept constant).

4.3. Typical oil bath procedure

For conventional (thermal) heating comparisons, identical scales, temperatures and heating times were used. Procedures were conducted in microwave test-tubes in oil baths pre-heated to the set temperature. Heating times were determined on several control samples, being typically 60–120 s depending on the exact conditions required. The heating time is not included in the quoted hold time for any given procedure; control studies show that the heating time is negligible for a 20 min reaction time. Tubes were generally sealed with CEM's *Intellivent* caps, except when working close to or above the boiling point of a given solvent, when crimp caps were used instead. However, control studies show that for high boiling solvents operating at modest temperatures (e.g., 140 °C), sealing tubes is not necessary to mimic microwave reaction conditions, since no pressure is developed. Work-up and isolation (if required) were performed as for the microwave procedures as above.

4.4. Determination of relative response factors (RRF)

RRFs were determined as follows: an accurately weighed sample of each analytically pure *O*-thiocarbamate **2** was dissolved in $CDCl_3$ with an accurately weighed sample of its respective analytically pure *S*-thiocarbamate analogue **3** in typically ~1:1 ratio. The ^{1}H NMR spectra were obtained using a method with lengthened relaxation delay (for more accurate integration) and the integration of the respective NMe_2 peaks in the ^{1}H NMR spectra compared to the relative responses in the LC spectra at 254 nm. Taking the ^{1}H NMR integration values as the correct ones allowed a correction factor to be determined for the relative response of the *O*-thiocarbamates compared to the *S*-thiocarbamates when using the LC according to the following equation:

$$\text{Relative response factor } (O\text{-thiocarbamate}) = (\text{NMR ratio} \times O\text{-thiocarbamate LC}) / \{S\text{-thiocarbamate LC} \times (1 - \text{NMR ratio})\}$$

So to determine the actual conversion to *S*-thiocarbamate using the LC spectra, the following equation is used:

$$\text{Actual } S\text{-thiocarbamate conversion} = (S\text{-thiocarbamate LC} \times \text{RRF}) / \{(S\text{-thiocarbamate LC} \times \text{RRF}) + O\text{-thiocarbamate LC}\}$$

Several samples had RRFs determined at several ratios (other than 1:1) to validate the consistency of this method.

4.5. Typical laboratory preparations

All the compounds (**2a–o** and **3a–o**) were fully characterised by LC/TLC, ^{1}H and ^{13}C NMR spectroscopy, MS, and mp where applicable. The data are not reproduced here since all compounds are known in the literature (see Supplementary data for full experimental conditions and characterisations in each case). A typical procedure is given below.

4.5.1. Preparation of an *O*-thiocarbamate (2-nitrophenyl-*O*-thiocarbamate, 2a). 2-Nitrophenol (10.43 g, 75 mmol) and DABCO (10.5 g, 93.8 mmol, 1.25 equiv) were heated in NMP (52 ml) to 50 °C with mechanical stirring to give a dark yellow solution. Dimethylthiocarbamoyl chloride (9.73 g, 78.8 mmol, 1.05 equiv) was dissolved in NMP (8 ml) and added dropwise to the previous solution over 3–4 min. (N.B. A 6–8 K exotherm was typically seen on this scale.) Some solid formed in the dark orange solution during this addition. The reaction was monitored by LC and was complete within 2–3 h at 50 °C. Water (120 ml) was added over 10–15 min at 50 °C. The original solid dissolved readily, but then a copious precipitate formed about halfway through the addition, which persisted to the end. The reaction mixture was cooled smoothly to 20 °C and the precipitate isolated by filtration. The product cake was displacement washed twice with water (20 ml each) and dried in vacuo at 50 °C to yield the title compound as an off-white to pale cream coloured crystalline solid (15.6 g, 92%). HPLC (RT 2.1 min, 99.96%); mp 120–121 °C (lit.[1] 112–113 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (1H, d, J=8.4 Hz), 7.67 (1H, t, J=7.8 Hz), 7.41 (1H, t, J=7.8 Hz), 7.26 (1H, d, J=8.0 Hz), 3.46 (3H, s), 3.41 (3H, s); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 185.90, 147.21, 142.01, 134.42, 126.55, 126.49, 125.68, 43.50, 39.09; MS (ZQ) (ES^+) 227 (M+1, 100%).

4.5.2. Preparation of an *S*-thiocarbamate (2-nitrophenyl-*S*-thiocarbamate, 3a). (See Section 4.2, Typical Microwave Procedure, for general method). The concentrated MTBE extract was purified by flash silica gel chromatography eluting with 2:1 *iso*-hexane/ethyl acetate (R_f 0.25) to give the title compound as a bright yellow oil; HPLC (RT 2.46 min, 99.1%); mp oil (lit.[1] 30–32 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (1H, dd, J=7.6, 1.2 Hz), 7.70 (1H, d, J=7.6 Hz), 7.50–7.60 (2H, m), 3.12 (3H, br s), 3.03 (3H, br s); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 164.35, 152.34, 138.16, 132.18, 129.84, 124.76, 124.30, 37.09, 29.65; MS (ES^+) 227 (M+1, 100%).

Acknowledgments

We thank CEM for technical advice and Simon Linke (AstraZeneca, Avlon) for mass spectra.

References and notes

1. Newman, M. S.; Karnes, H. A. *J. Org. Chem.* **1966**, *31*, 3980–3984.
2. Kwart, H.; Evans, E. R. *J. Org. Chem.* **1966**, *31*, 410–412.
3. See entry for dimethylthiocarbamoyl chloride: Ponaras, A. A.; Zaim, O. *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; Wiley: Chichester, West Sussex, England, 1995; Vol. 3, pp 2174–2176.
4. (a) Traxler, J. T. *J. Org. Chem.* **1979**, *44*, 4971–4973; (b) Rahman, L. K. A.; Scrowston, R. M. *J. Chem. Soc., Perkin Trans. 1* **1983**, 2973–2977; (c) Lau, C. K.; Belanger, P. C.; Dufresne, C.; Scheigetz, J. *J. Org. Chem.* **1987**, *52*, 1670–1673; (d) Asao, T.; Ito, S.; Morita, N. *Tetrahedron Lett.* **1989**, *30*, 6345–6348; (e) Beaulieu, F.; Snieckus, V. *Synthesis* **1992**, 112–118; (f) Levai, A.; Sebok, P. *Synth. Commun.* **1992**, *22*, 1735–1750.
5. (a) Hori, M.; Ban, M.; Imai, E.; Iwata, N.; Suzuki, Y.; Baba, Y.; Morita, T.; Fujimura, H.; Nozaki, M.; Niwa, M. *J. Med. Chem.* **1985**, *28*, 1656–1661; (b) Hori, M.; Iwamura, T.; Imai, E.; Shimuzu, H.; Kataoka, T.; Nozaki, M.; Niwa, M.; Fujimura, H. *Chem. Pharm. Bull.* **1989**, *37*, 1245–1248; (c) Kajino, M.; Mizuno, K.; Tawada, H.; Shibouta, Y.; Nishikawa, K.; Meguro, K. *Chem. Pharm. Bull.* **1991**, *39*, 2888–2895; (d) Springer, D. M.; Luh, B.-Y.; Goodrich, J.; Bronson, J. J. *Bioorg. Med. Chem.* **2003**, *11*, 265–279.
6. (a) Cram, D. J.; Helgeson, R. C.; Koga, K.; Kyba, E. P.; Madan, K.; Sousa, L. R.; Siegel, M. G.; Moreau, P.; Gokel, G. W.; Timko, J. M.; Sogah, G. D. Y. *J. Org. Chem.* **1978**, *43*, 2758–2772; (b) Ting, Y.; Verboom, W.; Groenen, L. C.; van Loon, J.-D.; Reinhoudt, D. N. *J. Chem. Soc., Chem. Commun.* **1990**, 1432–1433; (c) Fabbri, D.; Delogu, G.; De Lucchi, O. *J. Org. Chem.* **1993**, *58*, 1748–1750; (d) Cossu, S.; De Lucchi, O.; Fabbri, D.; Cossu, S.; De Lucchi, O.; Fabbri, D.; Valle, G.; Painter, G. F.; Smith, R. A. J. *Tetrahedron* **1997**, *53*, 6073–6084; (e) Rao, P.; Hosseini, M. W.; De Cian, A.; Fischer, J. *Chem. Commun.* **1999**, 2169–2170; (f) Kane, V. V.; Gerdes, A.; Grahn, W.; Ernst, L.; Dix, I.; Jones, P. G.; Hopf, H. *Tetrahedron Lett.* **2001**, *42*, 373–376.
7. Sebok, P.; Timar, T.; Eszenyi, T.; Patonay, T. *Synthesis* **1994**, 837–840.
8. (a) Hirano, M.; Miyashita, A.; Nohira, H. *Chem. Lett.* **1991**, 209–212; (b) Tao, Z.-F.; Qian, X. *Phosphorus, Sulfur Silicon Relat. Elem.* **1996**, *114*, 109–113; (c) Tao, Z.-F.; Qian, X.; Zhang, Y.; Fan, M. *Dyes Pigments* **1998**, *37*, 113–119.
9. Relles, H. M.; Pizzolato, G. *J. Org. Chem.* **1968**, *33*, 2249–2253.
10. (a) Miyazaki, K. *Tetrahedron Lett.* **1968**, 2793–2798; (b) Kaji, A.; Araki, Y.; Miyazaki, K. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 1393–1399.
11. For a limited selection of recent general reviews see: (a) Kappe, C. O. *Angew. Chem., Int. Ed.* **2004**, *43*, 6250–6284; (b) Hayes, B. L. *Aldrichimica Acta* **2004**, *37*, 66–76; (c) Lidström, P.; Tierney, J.; Wathey, B.; Westman, J. *Tetrahedron* **2001**, *57*, 9225–9283; (d) Perreux, L.; Loupy, A. *Tetrahedron* **2001**, *57*, 9199–9223.
12. Bowden, S. A.; Burke, J. N.; Gray, F.; McKown, S.; Moseley, J. D.; Moss, W. O.; Murray, P. M.; Welham, M. J.; Young, M. J. *Org. Process Res. Dev.* **2004**, *8*, 33–44.
13. But for an initial report on the NKR using solid supported catalysis under microwave irradiation see: Villemin, D.; Hachemi, M.; Lalaoui, M. *Synth. Commun.* **1996**, *26*, 2461–2471.