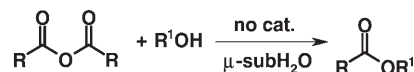


A Highly Selective, High-Speed, and Hydrolysis-Free O-Acylation in Subcritical Water in the Absence of a Catalyst**

Masahiro Sato,* Keiichiro Matsushima, Hajime Kawanami,* and Yutaka Ikuhsima

The acylation of alcohols and phenols to esters with carboxylic anhydrides is a fundamental chemical transformation in the production of important intermediates and fine chemicals.^[1] Catalytic versions of this reaction are being investigated intensively to replace the current non-stoichiometric acylation processes that generate large amounts of carboxylic acid and solvent waste.^[2–8] Lewis acids such as Sc(OTf)₃,^[4] Me₃SiOTf,^[5] and In(OTf)₃^[6] have shown promising catalytic properties although these catalysts are expensive and highly acidic, which means they cannot be used in the presence of acid-sensitive alcohols. Bi(OTf)₃ has recently been shown to catalyze the acylation of sterically hindered alcohols in aprotic organic solvents in the presence of water.^[7] The major general limitations of this approach concern rapid catalyst deactivation by deposition of char or coke on the catalyst surface, which proves troublesome and costly when it comes to regenerating the catalyst.^[9] Furthermore, large volumes of organic solvents and long reaction times are needed for depletion^[2–8] in batchwise solution-phase processes.

Herein we report a new and highly efficient acylation of alcohols without acid or base catalysts that involves a microreaction system with subcritical water (subH₂O) as both the catalyst and the substrate and product phase (Scheme 1). Chemical microprocessing is generally defined as continuous flow through regular domains in which the internal structures of fluid channels have characteristic dimensions, typically in the “sub-millimeter” range,^[10] hence the term “micro” will be used hereafter (see the Supporting Information). This methodology is based on the assumption



Scheme 1.

that H₂O becomes Lewis acidic^[11] and that the dielectric constant (ϵ) of the reaction medium can be controlled by adjusting the pressure and temperature^[12] in the subH₂O region.^[13] This subH₂O microreaction system can also provide a continuous operation that is characterized by instantaneous heating and subsequent quenching of the substrates along with vigorous mixing, which leads to high-speed acylation and therefore greatly reduced hydrolysis of the substrate and product. The results reported herein confirm the feasibility of this approach and provide an insight into the ability of water to act as a Lewis acid in the subH₂O region. This new approach compares favorably in terms of activity, scope, and selectivity with other catalytic reactions performed in volatile organic solvents or under solvent-free conditions for the selective and high-speed acylation of alcohols.

The acylation of a solution of benzyl alcohol (**1**, 0.47 mol kg^{−1}) to benzyl acetate (**1a**) in the presence of 1.1 molar equivalents of acetic anhydride was examined as a test reaction (see the Supporting Information). Benzyl acetate was formed exclusively in an excellent yield of 99.0% at around 200 °C and 5 MPa in less than 10 seconds, even in the absence of an acid catalyst and organic solvent (Figure 1). The dielectric constant ($\epsilon = 34.9$) of subH₂O at 5 MPa and 200 °C is similar to those of MeCN, DMAc (*N,N*-dimethylacetamide), and DMF ($\epsilon = 36–38$), which are frequently used as solvents in acylation reactions, hence the substrates and ester products are soluble in subH₂O.

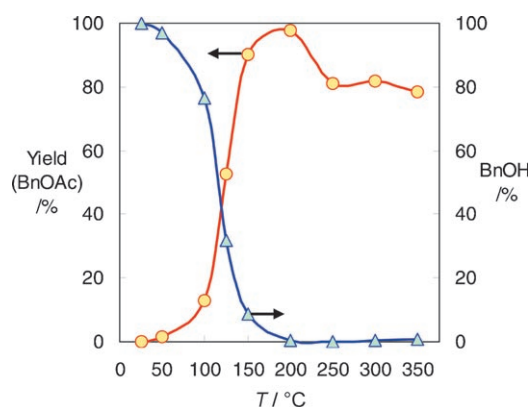


Figure 1. Temperature dependence of the acylation of BnOH by acetic anhydride in a subH₂O microreaction system at a pressure of 5 MPa and a reaction time of 9.9 seconds.

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[**] We thank Dr. M. Chatterjee for his critical reading of this manuscript and Dr. T. Yokoyama for fruitful discussions. This research was partially supported by the New Energy and Industrial Technology Development Organization (NEDO) (Development of Microspace and Nanospace Reaction Environment Technology for Functional Materials Project).

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The yield of **1a** is plotted against the dielectric constant of water in Figure 2.^[14] Benzyl acetate **1a** could only be synthesized in the limited dielectric constant range, $\epsilon < 50$, where the yield is remarkably high. The yield is essentially

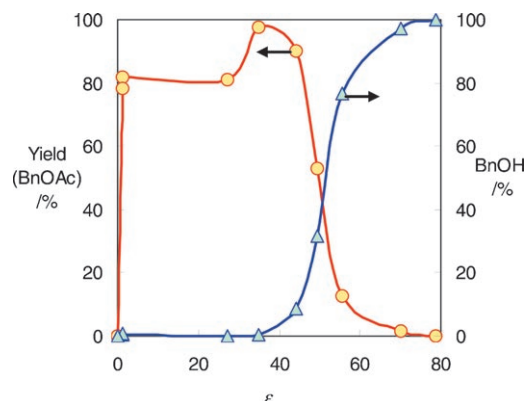


Figure 2. Dielectric constant (ϵ) dependence of the acylation of BnOH by acetic anhydride in a subH₂O microreaction system at a pressure of 5 MPa and a reaction time of 9.9 s.

quantitative at $\epsilon = 35$ and then decreases sharply with an increase of ϵ ; no ester is obtained with $\epsilon > 60$. The ϵ value that gives the maximum yield is close to that of MeCN ($\epsilon = 37$). Water molecules are likely to act as catalysts in the subH₂O region by transferring a proton along locally formed hydrogen bonds,^[15] which leads to a lowering of the energy required for bond cleavage and bond formation.^[16] The role of water in intermolecular hydrogen transfer is supported by quantum chemical calculations.^[17]

In a typical procedure, a stream containing a mixture of alcohol and anhydride is placed across a high-speed flow of subH₂O and the resulting mixture is introduced into a microreactor (μ -reactor), where the acylation proceeds rapidly as a result of the vigorous mixing caused by a turbulent flow with a Reynolds number of around 5×10^3 . Acylation occurs exclusively in the “on-water” manner^[18] which is characteristic of the subH₂O microreaction system. No significant side reactions such as hydrolysis, hydration, or pyrolysis occur, which means that the selectivity for **1a** is quantitative and the conversion is well above 99 %. A similar behavior is observed for various primary, secondary, and tertiary alcohols, phenol derivatives, and dihydroxy compounds with the same subH₂O microreaction system (see Tables 1–5 and the Supporting Information). Once conversion is complete, which occurs after around 9.9 seconds at 200 °C and 5 MPa (Figure 1), the product **1a** accumulates at the bottom of the aqueous solution and can be easily and quantitatively isolated by phase separation or filtration.

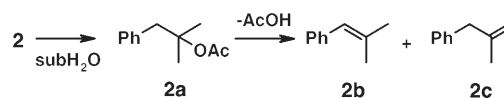
Table 1 summarizes the results obtained for the acylation of **1** and 2-methyl-1-phenylpropan-2-ol (**2**) as typical primary and tertiary alcohols under various reaction conditions. It is important to note that acylation of **1** in this microreaction system has already been shown to occur with complete selectivity and a conversion of 99 % in the absence of a catalyst (Table 1, entry 3). However, the same reaction with subH₂O in a batchwise process gives a yield of only 17 % at

Table 1: Acylation of BnOH (**1**) and 2-methyl-1-phenylpropan-2-ol (**2**) in a catalyst-free microreaction system.^[a]

Entry	Substrate	Anhydride (equiv)	Molality [mol kg ⁻¹] ^[b]	Conv. [%]	Sel. [%]	Yield [%]
1 ^[c]		Ac ₂ O (1.1)	0.47	18	95	17
2 ^[d]		Ac ₂ O (1.1)	8.90	88	100	88
3		Ac ₂ O (1.1)	0.46	99.0	100	99.0
4		(<i>i</i> BuCO) ₂ O (1.1)	0.46	99.8	100	99.8
5 ^[d]		Ac ₂ O (4.0)	2.45	39	98	38
6		Ac ₂ O (1.1)	0.37	70	72	50
7		Ac ₂ O (4.0)	0.17	89	87	77
8 ^[e]		Ac ₂ O (4.0)	0.17	96	65	63
9		Ac ₂ O (40)	0.02	80	94	75

[a] In H₂O at 200 °C, $p = 5$ MPa, $t = 9.9$ s. [b] Molality of substrate relative to total weight of Ac₂O and solvent. [c] Batch process, $t = 15$ s. [d] No solvent added. [e] Reaction temperature 225 °C.

the same temperature and pressure after approximately the same reaction time (Table 1, entry 1). This may be due to the strong hydrolytic properties of subH₂O upon prolonged heating in a batch system.^[19] Under H₂O-free conditions **1a** was obtained in a good yield of 88 % with the microreaction system (Table 1, entry 2), while acylation of the tertiary alcohol **2** gave only a 38 % yield of the desired ester (Table 1, entry 5). Alcohol **2** is labile above 225 °C and can form olefinic by-products such as **2b** and **2c** (Scheme 2), hence the yield of the desired acylated product **2a** has a tendency to decrease with an increase in temperature (Table 1, entries 7



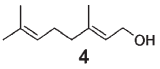
Scheme 2.

and 8). Formation of the by-products occurs by consecutive elimination of acyl groups from the ester products. The reaction temperature should therefore be kept lower to suppress such elimination reactions—the yield of acetate **2a** was found to be 77 % at 200 °C compared to 63 % at 225 °C.

Another example of the scope of the subH₂O microreaction system in acylation is summarized in Table 2, where it can be seen that the acylation activities induced in the subH₂O microreaction system are remarkably higher than those with a conventional homogeneous catalyst in an organic solvent. Thus, the acylation of **3** and **4** gives around 80 % yield of the acylated products after 4–6 hours under solvent-free conditions in a batchwise process with Bi(OTf)₃ as the Lewis acid catalyst (Table 2, entries 1 and 4).^[7]

This negative trend is also apparent when performing the reaction in organic solvents, where higher yields of 93–95 % are only obtained after reaction times of up to 8.5 hours in MeCN or THF (Table 2, entries 2 and 5).^[7] Amazingly, use of the subH₂O microreaction system in the complete absence of an acid catalyst improved the yields significantly after only

Table 2: Acylation of furfuryl alcohol (**3**) and geraniol (**4**).

Entry	Substrate	Anhydride (equiv)	Process ^[a]	Catalyst (equiv)	Solvent	Molality [mol kg ⁻¹] ^[b]	T [°C]	p [MPa]	t [s]	Conv. [%]	Sel. [%]	Yield [%]
1 ^[c]		Ac ₂ O (10)	B	Bi(OTf) ₃ (0.05)	none	9.8 × 10 ⁻⁴	25	0.1	19 800	–	–	80
2 ^[c]		Ac ₂ O (10)	B	Bi(OTf) ₃ (0.05)	THF	9.8 × 10 ⁻⁴	25	0.1	30 600	–	–	93
3		Ac ₂ O (1.1)	μ	–	H ₂ O	0.50	200	5	9.9	96	100	96
4 ^[c]		Ac ₂ O (10)	B	Bi(OTf) ₃ (0.01)	none	9.8 × 10 ⁻⁴	25	0.1	12 600	–	–	81
5 ^[c]		Ac ₂ O (10)	B	Bi(OTf) ₃ (1.0)	MeCN	9.8 × 10 ⁻⁴	25	0.1	30 600	–	–	95
6		Ac ₂ O (1.1)	μ	–	H ₂ O	0.35	200	5	9.9	98.8	100	98.8

[a] B: batch process; μ: subH₂O microreaction system. [b] Molality of substrate with respect to total weight of Ac₂O and solvent. [c] From reference [7].

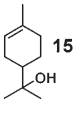
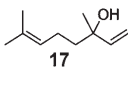
9.9 seconds (Table 2, entries 3 and 6). It is highly likely that water molecules participate in the acylation reaction, which probably passes through a six-membered ring transition state,^[20] although this postulated mechanism is still to be confirmed by kinetic methods.

The above results motivated us to turn our attention to other alcohols. Thus, primary (**5**) and secondary alcohols (**6–8**) and phenolic derivatives (**9–12**) were transformed into the acylated products in excellent yields of more than 95 % and with 100 % selectivity at 200–250 °C (see the Supporting Information for **5–8** and Table 3, entries 2, 4, 5, and 6, for **9–12**). The amount of acetic anhydride used is less than in the previously reported catalytic processes^[2–8] and the yields are higher. Interestingly, α-tocopherol (**12**) gives a very high yield of the corresponding acetate with almost quantitative selectivity (99 %) after a very short reaction time even in the absence of an acid catalyst (Table 3, entry 6), and eugenol (**11**), which readily isomerizes thermally, is acylated in 95 % yield with this subH₂O microreaction system (Table 3, entry 5).

Even tertiary alcohols such as *tert*-butyl alcohol (**13**), 1-ethynyl-1-cyclohexanol (**14**), and α-terpineol (**15**) are rapidly acylated, with yields of 90 % or above in the presence of

1.1 molar equivalents of acetic anhydride at 200 °C (Table 4, entries 1, 3, and 5, respectively). This result suggests that acylation is much faster than dehydration when the amount of acetic anhydride used is increased. The only exceptions so far

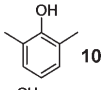
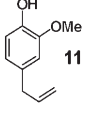
Table 4: Acylation of tertiary alcohols by acetic anhydride in a subH₂O microreaction system.^[a]

Entry	Substrate	Anhydride (equiv)	Molality [mol kg ⁻¹]	Conv. [%]	Sel. [%]	Yield [%]
1		Ac ₂ O (1.1)	0.37	100	94	94
2		Ac ₂ O (4.0)	0.16	100	92	92
3		Ac ₂ O (1.1)	0.33	100	86	86
4		Ac ₂ O (4.0)	0.15	79	99	79
5		Ac ₂ O (1.1)	0.29	100	97	97
6		Ac ₂ O (4.0)	0.15	92	97	90
7	2	Ac ₂ O (1.1)	0.37	70	72	50
8		Ac ₂ O (4.0)	0.17	89	87	77
9		Ac ₂ O (1.1)/AcOH (2.0)	0.36	100	70	70
10		Ac ₂ O (4.0)/AcOH (2.0)	0.17	100	82	82
11		Ac ₂ O (1.1)	0.28	18	31	6
12		Ac ₂ O (4.0)	0.15	53	63	33
13		Ac ₂ O (10)	0.08	66	83	55
14		Ac ₂ O (30)	0.02	77	98	75

[a] T = 200 °C, p = 5 MPa, t = 9.9 s.

are the tertiary alcohols 1-hydroxyisobutyric acid (**16**) and linalool (**17**), which are transformed rapidly but form large amounts of olefinic by-products as a result of dehydration in the presence of 1.1 molar equivalents of acetic anhydride (Table 4, entries 9 and 11, respectively). Addition of a large excess of acetic anhydride, however, improves the activity and selectivity at the same pressure, temperature, and reaction time. For example, the acylation of **17** gives a selectivity of only 63 % in the presence of four molar equivalents of acetic anhydride, whereas higher selectivities of up to 98 % are obtained upon increasing the amount of acetic anhydride (Table 4, entries 11–14). This reaction therefore seems to

Table 3: Acylation of phenolic derivatives with acetic anhydride in a subH₂O microreaction system.^[a]

Entry	Substrate	Molality [mol kg ⁻¹]	Conv. [%]	Yield [%]
1 ^[b]		0.38	82	82
2		0.38	97	97
3 ^[b]		0.29	47	47
4		0.29	97	97
5		0.25	95	95
6 ^[c]	α-tocopherol (12)	0.16	99.0	99.0

[a] 1.1 equiv Ac₂O, p = 5 MPa, t = 9.9 s, T = 250 °C; all reactions proceeded with 100 % selectivity. [b] T = 200 °C. [c] 1.1 equiv Ac₂O/1 equiv AcOH as the acylating agent.

Table 5: Selective acylation of diols by acetic anhydride in a subH₂O microreaction system.

Entry	Substrate	Products	Anhydride (equiv)	Molality [mol kg ⁻¹]	T [°C]	p [MPa]	t [s]	Conv. [%]	Sel. [%] a b
1			Ac ₂ O (1.1)/ AcOH (0.5)	0.39	225	5	9.9	85	65 35
2			Ac ₂ O (1.1)/ AcOH (0.5)	1.17	225	5	5.5	95	97 3
3			Ac ₂ O (2.2)/ AcOH (1.0)	0.25	225	5	9.9	100	7 93
4			Ac ₂ O (1.1)/ AcOH (0.3)	0.49	200	5	9.9	94	61 39
5			Ac ₂ O (1.1)/ AcOH (0.3)	1.47	200	5	5.5	89	90 10
6			Ac ₂ O (2.2)/ AcOH (0.5)	0.30	200	5	9.9	99.9	0 99.9
7 ^[a]			Ac ₂ O (1.0)	—	80	0.1	2 h	—	— (23) ^[b,c]
8			Ac ₂ O (1.1)	0.49	200	5	9.9	99	67 33
9			Ac ₂ O (1.1)	1.47	200	5	5.5	93	91 9
10 ^[a]			Ac ₂ O (2.5)	—	80	0.1	2.5 h	—	— (76) ^[b]
11			Ac ₂ O (2.2)	0.31	225	5	9.9	99.9	0.1 99.9
12			Ac ₂ O (1.1)	0.41	200	5	9.9	99.8	86 14
13			Ac ₂ O (1.1)	1.23	200	5	5.5	95	95 5
14			Ac ₂ O (2.2)	0.28	200	5	9.9	99.4	36 64
15			Ac ₂ O (2.2)	0.28	225	5	9.9	94.2	26 74
16			Ac ₂ O (5.1)	0.15	200	5	9.9	99.1	0.3 99.7

[a] CoCl₂ (5 mol%) in MeCN was added as a catalyst.^[2c] [b] The value in parentheses is the yield of acylated products. [c] 21% of **20c**.

depend more on the nature of the substituent R¹ of the alcohol than the R group of the anhydride (Scheme 1, Table 1, entries 3 and 4).

Few studies have been reported to date on the regioselective acylation of dihydroxy compounds in the presence of a Lewis acid in organic solvents, and of these hardly any have provided satisfactory yields of the desired products.^[2c,5,21] As shown in Table 5, the subH₂O microreaction system makes it possible to regioselectively acylate either or both hydroxy groups of various dihydroxy compounds without the need for a catalyst by controlling the molar ratio of acetic anhydride to dihydroxy compound. In the presence of a large excess of acetic anhydride (2.2–5.1 molar equivalents), both hydroxy groups of catechol (**18**), 1,3-propanediol (**19**), 1,3-butanediol (**20**), and 3-methyl-1,3-butanediol (**21**) are acylated to form the corresponding diacetates (**18b**, **19b**, **20b**, and **21b**) in nearly quantitative yields (Table 5, entries 3, 6, 11, and 16), whereas the usual conditions of 1.1 molar equivalents of acetic anhydride only one (primary) hydroxy moiety of these compounds is regioselectively transformed into the corresponding monoacetate (**18a**, **19a**, **20a**, and **21a**) with excellent selectivities of 90–97% (Table 5, entries 2, 5, 9, 13). The resulting esters are insoluble in water and either float on the surface or accumulate at the bottom, which means that they can easily be recovered from the reaction mixture by decantation.

In summary, we have developed a high-speed, highly selective, and hydrolysis-free acylation of various alcohols by acetic anhydride in the absence of catalyst that makes use of a subH₂O flow-type microreaction system. The desired esters are obtained in excellent yields (> 93%) with 100% selectivity at temperatures between 200 and 250 °C. Tertiary alcohols can also be transformed into the corresponding esters in the presence of a large excess of anhydride below 200 °C. Varying the amount of acetic anhydride added relative to the alcohols allows the regioselective acylation of one or both hydroxy groups of various dihydroxy compounds. This system nicely demonstrates the potential benefits that can result from combining the properties of subH₂O with microprocesses. Finally, it is worth noting that this approach is an environmentally benign process that could find applications in industrial-scale acylations, thus making this approach of general interest for the field of “green” organic synthesis.

Received: January 15, 2007

Revised: March 30, 2007

Published online: July 19, 2007

Keywords: acylation · green chemistry · subcritical water · synthetic methods

- [1] W. Green, P. G. M. Wuts, *Protective Groups in Organic Synthesis*, 3rd ed., Wiley, New York, **1999**, p. 150.
- [2] a) TsOH: A. C. Cope, E. C. Herrick, *Org. Synth. Coll. Vol. 4*, **1963**, p. 304; b) ZnCl_2 : R. H. Baker, F. G. Bordwell, *Org. Synth. Coll. Vol. 3*, **1955**, p. 141; c) CoCl_2 : S. Ahmad, J. Iqbal, *J. Chem. Soc. Chem. Commun.* **1987**, 114; d) NaOAc: The Miner Laboratories, *Org. Synth. Coll. Vol. 1*, **1941**, p. 285; e) pyridine: J. B. Lambert, G.-T. Wang, R. B. Finzel, D. H. Teramura, *J. Am. Chem. Soc.* **1987**, 109, 7838; f) Me_3SiCl : N. C. Barua, R. P. Sharma, J. N. Baruah, *Tetrahedron Lett.* **1983**, 24, 1189; D. S. Matteson, E. C. Beedle, A. A. Kandil, *J. Org. Chem.* **1987**, 52, 5034; g) PBU_3 : E. Vedejs, N. S. Bannet, L. M. Conn, S. T. Diver, M. Gingras, S. Lin, P. A. Oliver, M. J. Person, *J. Org. Chem.* **1993**, 58, 7286; h) Me_3SiOTf : P. A. Procopiou, S. P. D. Baugh, S. S. Flack, G. G. A. Inglis, *J. Org. Chem.* **1998**, 63, 2342.
- [3] a) G. Höfle, W. Steglich, H. Vorbrüggen, *Angew. Chem.* **1978**, 90, 602; *Angew. Chem. Int. Ed. Engl.* **1978**, 17, 569; b) A. Hassner, L. R. Krepski, V. Alexanian, *Tetrahedron* **1978**, 34, 2069.
- [4] a) K. Ishihara, M. Kubota, H. Kurihara, H. Yamamoto, *J. Org. Chem.* **1996**, 61, 4560; b) K. Ishihara, M. Kubota, H. Kurihara, H. Yamamoto, *J. Am. Chem. Soc.* **1995**, 117, 4413.
- [5] P. A. Procopiou, S. P. D. Baugh, S. S. Flack, G. G. A. Inglis, *J. Org. Chem.* **1998**, 63, 2342.
- [6] K. K. Chauhan, C. G. Frost, I. Love, D. Waite, *Synlett* **1999**, 1743.
- [7] a) A. Orita, C. Tanahashi, A. Kakuda, J. Otera, *Angew. Chem.* **2000**, 112, 2999; *Angew. Chem. Int. Ed.* **2000**, 39, 2877; b) A. Orita, C. Tanahashi, A. Kakuda, J. Otera, *J. Org. Chem.* **2001**, 66, 8926.
- [8] C.-T. Chen, J.-H. Kuo, C.-H. Li, N. B. Barhate, S.-W. Hon, T.-W. Li, S.-D. Chao, C.-C. Liu, Y.-C. Li, I.-H. Chang, J.-S. Lin, C.-J. Liu, Y.-C. Chou, *Org. Lett.* **2001**, 3, 3729.
- [9] a) M. H. Valkenberg, C. deCastro, W. F. Hölderich, *Appl. Catal. A* **2001**, 215, 185; b) P. Marécot, H. Martinez, J. Barbier, *J. Catal.* **1992**, 138, 474; c) R. A. van Santen, J. W. Niemantsverdriet, *Fundamental And Applied Catalysis: Chemical Kinetics and Catalysis* (Eds.: M. V. Twigg, N. S. Spencer), Plenum, New York, **1995**; d) A. Corma, H. García, *Chem. Rev.* **2003**, 103, 4307; e) H. Yamamoto, *Lewis Acids in Organic Synthesis*, Wiley-VCH, Weinheim, **2000**.
- [10] V. Hessel, S. Hardt, H. Löwe, *Chemical Microprocess Engineering: Fundamentals, Modelling and Reactions*, Wiley-VCH, Weinheim, **2004**.
- [11] Y. Ikushima, K. Hatakeda, M. Sato, O. Sato, M. Arai, *Chem. Commun.* **2002**, 2208.
- [12] W. L. Marshall, E. U. Franck, *J. Phys. Chem. Ref. Data* **1981**, 10, 295.
- [13] a) C. A. Eckert, C. L. Liotta, D. Bush, J. S. Brown, J. P. Hallett, *J. Phys. Chem. B* **2004**, 108, 18108; b) N. Akiya, P. E. Savage, *Chem. Rev.* **2002**, 102, 2725; c) R. van Eldik, F.-G. Kläener, *High Pressure Chemistry*, Wiley-VCH, Weinheim, **2002**, pp. 422–425; d) D. Bröll, C. Kaul, A. Krämer, P. Krammer, T. Richter, M. Jung, H. Vogel, P. Zehner, *Angew. Chem.* **1999**, 111, 3180; *Angew. Chem. Int. Ed.* **1999**, 38, 2998.
- [14] A. H. Harvey, A. P. Peskin, S. A. Klein, *NIST Standard Reference Database 10, NIST/ASME Steam properties*, ver 2.2, **2000**.
- [15] A. J. Belsky, P. G. Maiella, T. B. Brill, *J. Phys. Chem. A* **1999**, 103, 4253.
- [16] H. Takahashi, S. Hisaoka, T. Nitta, *Chem. Phys. Lett.* **2002**, 363, 80.
- [17] M. Boero, T. Ikeshoji, C. C. Liew, K. Terakurra, M. Parrinello, *J. Am. Chem. Soc.* **2004**, 126, 6280.
- [18] a) S. Narayan, J. Muldoon, M. G. Finn, V. V. Fokin, H. C. Kolb, K. B. Sharpless, *Angew. Chem.* **2005**, 117, 3339; *Angew. Chem. Int. Ed.* **2005**, 44, 3275; b) J. E. Klijn, J. B. F. N. Engberts, *Nature* **2005**, 435, 746.
- [19] a) J. An, L. Bagnell, T. Cablewski, C. R. Strauss, R. W. Trainer, *J. Org. Chem.* **1997**, 62, 2505; b) A. R. Katritzky, D. A. Nichols, M. Siskin, R. Murugan, M. Balasubramanian, *Chem. Rev.* **2001**, 101, 837; c) M. Siskin, A. R. Katritzky, *Chem. Rev.* **2001**, 101, 825; d) A. R. Katritzky, M. Balasubramanian, M. Siskin, *Energy Fuels* **1990**, 4, 499; e) A. R. Katritzky, F. J. Luxem, M. Siskin, *Energy Fuels* **1990**, 4, 514.
- [20] a) H. G. Kruger, *J. Mol. Struct. (Theochem)* **2002**, 577, 281; b) K. R. Davis, J. L. Hogg, *J. Org. Chem.* **1983**, 48, 1041.
- [21] R. T. LaLonde, C. Wong, A. I.-M. Tsai, *J. Am. Chem. Soc.* **1976**, 98, 3007.