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Acid-Catalyzed Hydration of Alkynes in Aqueous Microemulsions

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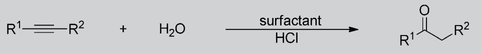
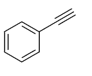
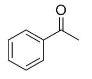
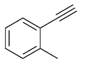
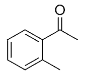
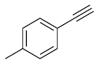
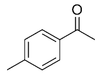
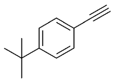
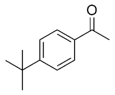
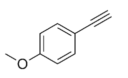
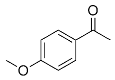
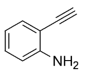
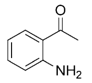
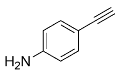
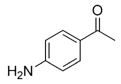
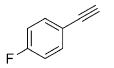
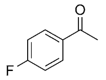
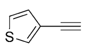
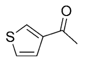
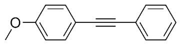
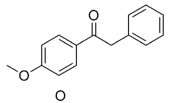
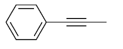
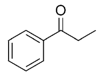
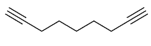
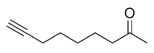
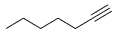
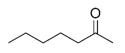
The hydration of alkynes was reported for the first time in 1860[1] and is widely applied in industrially important processes. However, the methods currently used for this hydration still suffer from substantial shortcomings.[2] The process, which relies on interactions between acetylenes and Lewis or Brønsted acids, requires high temperatures[3] and often leads to low yields and unwanted polymers.[4–6] A dramatic improvement of yields was achieved by performing the hydrations in the presence of mercury(II) compounds;[7] however, these are highly toxic.[8,9] The mercury derivatives can be replaced by several heavy-transition-metal compounds, but these themselves are usually unfavorable from an environmental point of view.[10] The mechanism of alkyne hydration by metal complexes has been studied and documented.[11] In the hydration processes water can not only serve as reagent but may also serve as solvent for water-soluble substrates. In many cases, however, the amount of water must be restricted to 15–20 % of the reaction mixture.[12]

During our recent studies on the possibilities of replacing harmful organic solvents in syntheses of industrial importance by benign media,[13] we found that aqueous microemulsions can often replace organic media, even when the reactants are hydrophobic and insoluble in water.[14] We now report that microemulsions can be applied successfully to efficient Markovnikov hydrations of acetylenes, also. Reports on the use of microemulsions with organometallic catalysts for the hydration of alkynes have, so far, been scarce,[15] whilst metal-free processes require unique protocols (e.g., a procedure by Wong et al., who used a sulfate adduct of an ionic liquid[14]). Our procedure is extremely simple. We find it imperative to announce this green alkyne hydration protocol because it can be widely applied by organic chemists.

Under the conditions described in the Experimental Section, the alkynes listed in Table 1 were selectively hydrated. No *anti*-Markovnikov products were formed in these reactions. The hydrations gave similar results regardless of whether small- or large-scale reactions (1–150 mmol) were run. No significant electronic or steric effects were observed, except when the phenylacetylene had a bulky *t*Bu substituent. Notably, in entry 10 only 1-(4-methoxyphenyl)-2-phenylethanone free of

Table 1. Hydration of some representative alkynes in aqueous microemulsions.[a]



Entry	Alkyne	Product	*t* [h]	Isolated[b–c] compounds [%]
1			7	95[d]
2			3	94
3			3	94[d]
4			6	93[d]
5			1	97
6			1	95
7			1	96
8			5	92[d]
9			3	94
10			10	96
11			48	60[d,e]
12			24	23[e]
13			24	18[e]

[a] Reaction conditions: alkyne (0.8 wt % of the microemulsion); 1-PrOH (6.6 wt %); cetyltrimethylammonium bromide (CTAB, 3.3 wt %); triply distilled water (TDW; 89.3 wt %). Hydrochloric acid to form a 0.33 M HCl microemulsion; 140 °C. [b] Average of at least two experiments that did not differ by more than ±2 %. [c] The physical data are given in the Supporting Information. [d] The given percentages refer only to the carbonyl compounds. In entries 1, 3, 4, 8, and 11 were isolated 1.0, 3.0, 2.0, 2.4, and 2.8 % of α-chlorovinylarenes as well as 0.7, 2.0, 1.8, 1.8, and 5.5 % of α-bromovinylarenes, respectively. In all other experiments either no side products were formed or their amount was < 0.3 %. [e] In entries 11, 12, and 13, the percentage of recovered unreacted alkynes was 26, 73, and 80 %, respectively.

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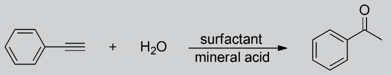
the isomeric 2-(4-methoxyphenyl)-1-phenylethanone was formed.

Replacement of cetyltrimethylammonium bromide (CTAB) by other cationic surfactants had only a small effect on the reaction efficiency (Table 2, entries 2–4 and entry 7). Some anionic and non-ionic additives (e.g., sodium dodecylsulfate, C_{12}–C_{14} alcohols–polyoxyethylene glycol ethers), however, had a more significant effect on the process. In none of the short experiments of Table 2 did the yield of vinylic side product mentioned in Table 1 exceed 0.3%. The presence of the vinyl halides could be completely eliminated by using sodium 4-dodecyl benzene sulfonate (SDBS) as surfactant and by replacing the hydrochloric acid by 0.33 м aqueous sulfuric acid. When using SDBS, however, it proved necessary to prepare the microemulsions at temperatures between 50 and 55 °C and extend the reaction times. On the other hand the SDBS surfactant, which is sparingly soluble at room temperature, could be recovered upon cooling of the reaction mixture. 1-Ethenyl-4-methylbenzene, 4-ethynyl-1-fluorobenzene, and 1-(1,1-dimethylethyl)-4-ethynylbenzene gave the corresponding ketones in quantitative yields after 16 h at 140 °C. Under these conditions the disubstituted 1-propyn-1-ylbenzene was hydrated to the extent of 60%.

Table 2. Dependence of the hydration of ethynylbenzene on the nature of the surfactants.[a]



Entry	Surfactant[b]	Isolated PhCOMe [%][d]
1	SDS	72
2	DTAB	96
3	TTAB	95
4	CTAC	88
5	CTAB	87
6	CTAB[c]	81
7	OTAB	96
8	Marlipal	83
9	SDBS	90

[a] Reaction conditions as described for Table 1, except that all experiments were performed for only 3 h. [b] SDS: Sodium dodecylsulfate; DTAB: dodecyltrimetylammonium bromide; TTAB: tetradecyltrimethylammonium bromide; CTAC: cetyltrimethylammonium chloride; CTAB: cetyltrimethylammonium bromide; OTAB: octadecyltrimethylammonium bromide; Marlipal: C_{12}–C_{14} alcohols polyoxyethyleneglycol ethers (7-EO); SDBS: sodium 4-dodecylbenzenesulfonate. [c] The hydrochloric acid was replaced by 0.33 м hydrobromic acid. [d] Average of at least two experiments that did not differ by more than ±2%.

The hydration of the alkynes in aqueous microemulsions is coupled with a selective hydrogen exchange. Therefore, the replacement of the water by D_2O can be used for an efficient preparation of terminal CD_3-substituted ketones. The use of microemulsions permits recovery of most of the D_2O in a way that the deuterium content in the fourth run is still as high as 93%, even when using non-labeled HCl and 1-PrOH. Under the conditions of Table 1 (140 °C) but replacing H_2O by D_2O, we were able to isolate 92% of $C_6H_5COCD_3$ after 7 h, 80% of 4-$FC_6H_4COCD_3$ after 5 h, 92% of 4-$CH_3C_6H_4COCD_3$ after 3 h, and 96% of 4-$MeOC_6H_4COCD_3$ after 1 h. According to NMR analysis all of these products had isotopic purities of approximately 93%. See the Supporting Information for further details on the purity of the resulting ketones and physical data of the deuteriated products.

In conclusion, the simple hydration protocol described here can be regarded as a green version of this key reaction. It can potentially be applied to a wide range of substrates, is free of toxic mercury or late-metal catalysts, and the products can be isolated just by phase separation.

Experimental Section

In a representative experiment, a microemulsion composed of 1-ethynyl-4-methoxybenzene (19.95 g, 151 mmol, 0.8 wt% of the starting reaction mixture), CTAB (82.5 g, 3.3 wt%), 1-PrOH (206 mL, 6.6 wt%), and triply distilled water (TDW, 2.23 L, 89.3 wt%) was placed either in a glass vessel or in an autoclave. Hydrochloric acid was added to form a 0.33 м microemulsion. The reaction mixture was heated to 80 °C for 24 h. After cooling, the microemulsion was broken by addition of NaCl (30 g), and the aqueous phase was extracted with ether (2×50 mL). Neutralization with aqueous $NaHCO_3$, drying ($MgSO_4$), and distillation at 2.0 Torr (1 Torr = 1.333×10^2 Pa) afforded 20.0 g (88%) of analytically pure 4-methoxyacetophenone. See the Supporting Information for different reaction conditions and physical data of some other ketones obtained by alkyne hydration.

Acknowledgements

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Keywords: alkynes · green chemistry · homogeneous catalysis · microemulsions · synthetic methods

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