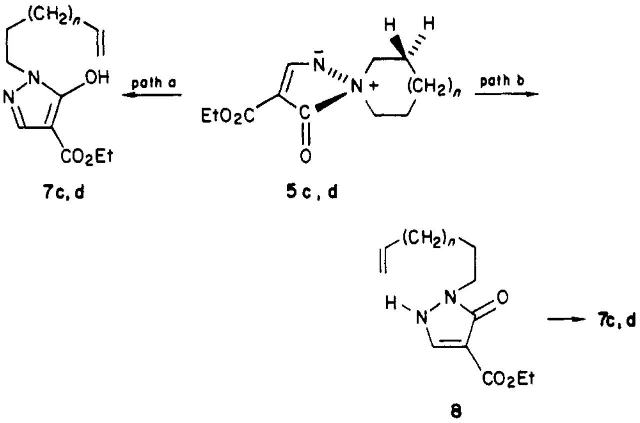
Scheme III[a]



[a] c, $n = 1$; d, $n = 2$.

to pyrazolinones **6a,b** together with ylides **5a,b** as minor products. Bridged 2-pyrazolin-5-ones **6a,b**, whose structures are supported by ^1H and ^{13}C NMR spectroscopy, show two strong infrared absorption bands in the 1700–1800-cm^{-1} range. The first band (1740 cm^{-1}) is assigned to the ester carbonyl while we attribute the second one (1765 cm^{-1} for **6a** and 1760 cm^{-1} for **6b**) to the amide carbonyl. These abnormal high values for an amide band reveal, in accordance with Bredt's rule, an important inhibition of the N—C═O resonance in these N-bridgehead lactams.[11]

On the other hand, ^1H NMR spectra of the crude materials obtained from diesters **4c,d** at 390–400 °C showed the characteristic signals of a terminal vinyl group suggesting that an elimination reaction follows or competes with the [1,4] migration. Flash column chromatography of the mixture resulting from the thermolysis of the piperidine derivative **4c** afforded besides the pyrazolinone **6c**[12] an isomeric *N*-alkenyl compound whose spectroscopic data[13] support the hydroxy-5-pyrazole structure **7c**. The analogous elimination product **7d** formed in lower yield (15% estimation on the basis of ^1H NMR spectra) could not be isolated.

Pyrazolinone **6c** submitted to flow pyrolysis at 400 °C was recovered unchanged. Thus hydroxy-5-pyrazoles **7c,d** result from an intramolecular elimination reaction of ylides **5c,d** (Scheme III), either by a six-center mechanism involving the negative charge delocalized on the carbonyl oxygen (path a) or by a Cope-type elimination[14] (path b) and subsequent isomerization (**8** → **7**) to the stable tautomer in aprotic media.[15] We believe that the elimination takes place according to the latter pathway since crystallographic analyses of analogous ylidic compounds reveal a very short C═O bond distance.[16]

As observed, the limited ring deformations of the five-membered pyrrolidinium ylide **5a** do not permit an intramolecular elimination reaction. The unexpected behavior of the six-membered morpholinium ylide **5b**, unreactive toward elimination in contrast with the isosteric piperidinium derivative **5c**, should be rationalized in terms of stereoelectronic effects which need further investigation.

We have demonstrated that the flow pyrolysis of the readily available hydrazinopropenoates **4** offers a convenient method for the preparation in one experimental step of a new class of diazabicyclo compounds **6**. Studies are now underway toward the extension to other systems of this novel ring enlargement methodology.

Registry No. **4a**, 94621-01-9; **4b**, 94621-02-0; **4c**, 94621-03-1; **4d**, 94621-04-2; **5a**, 94621-05-3; **5b**, 94621-06-4; **5c**, 94621-07-5; **5d**, 94621-08-6; **6a**, 94621-09-7; **6b**, 94621-10-0; **6c**, 94621-11-1; **6d**, 94621-12-2; **7c**, 94621-13-3; **7d**, 94621-14-4; 1-aminopyrrolidine, 16596-41-1; 4-aminomorpholine, 4319-49-7; 1-aminopiperidine, 2213-43-6; 1-aminohexahydro-1*H*-azepine, 5906-35-4; diethyl(ethoxymethylene)malonate, 87-13-8.

Supplementary Material Available: ^1H and ^{13}C NMR spectral data for pyrazolinones **6a–d** (1 page). Ordering information is given on any current masthead page.

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[11] Hall, H. K.; El-Shekeil, A. *Chem. Rev.* **1983**, *83*, 549. Pracejus, H.; Kehlen, M.; Kehlen, K.; Matschiner, H. *Tetrahedron* **1965**, *21*, 2257.

[12] Selected IR data (cm^{-1}): **6c** ($CHCl_3$) ν(COOEt) 1750, ν(NC═O) 1725; **6d** ($CHCl_3$) ν(COOEt) 1750, ν(NC═O) 1715.

[13] Compound **7c**: IR ($CHCl_3$) two strong absorptions at ν 1580 and 1670 cm^{-7}, ^1H NMR ($CDCl_3$–Me_4Si) δ 1.35 (3 H, t, *J* = 7 Hz), 2.05 (4 H, m), 3.95 (3 H, t, *J* = 7 Hz), 4.30 (3 H, t, *J* = 7 Hz), 5.05 (2 H, m), 6.75 (1 H, m), 7.20 (1 H, br s), 7.55 (1 H, s); ^{13}C NMR ($CDCl_3$–Me_4Si) δ 14.4 (q), 27.8 (t), 30.0 (t), 45.1 (t), 58.9 (t), 95.1 (s), 115.4 (t), 137.6 (d), 138.7 (d), 154.0 (s), 162.6 (s).

[14] Bach, R. D.; Andrzejewski, D.; Bair, K. W. *J. Chem. Soc., Chem. Commun.* **1974**, 820. Cope, A. C.; Le Bel, N. A. *J. Am. Chem. Soc.* **1960**, *82*, 4656.

[15] Jensen, B. S. *Acta Chem. Scand.* **1959**, *13*, 1668. For a recent investigation of the tautomerism of pyrazolin-5-ones, see: Gelin, S.; Chantegrel, B.; Nadi, A. I. *J. Org. Chem.* **1983**, *48*, 4078.

[16] The C(5)═O bond distance in 1,1-dimethyl-4-(methoxycarbonyl)-5-oxo-3-pyrazolinium ylide and in 4-cyano-1,1-dimethyl-5-oxo-3-pyrazolinium ylide is found to be 1.198 Å and 1.204 Å, respectively (crystallographic data are available from the Cambridge Crystallographic Data Center, see ref 4). The cyclic carbonyl bond length in ylides **5** which is therefore about 1.20 Å is consistent with a low contribution of the pyrazolium-5-olate resonance structure which would have favored the six-center Hofmann-type elimination mechanism. For a related discussion on C–O bond distance in betaines, see: Neugebauer, F. A.; Fischer, H.; Krieger, C. *Tetrahedron Lett.* **1984**, *25*, 629.

Allylzinc Reagent Additions in Aqueous Media

Summary: Homoallylic alcohols are obtained when allylic halides, zinc, and aldehydes or ketones in aqueous media are subjected to ultrasonic waves.

Sir: Organometallic compounds, among the most useful reagents in organic chemistry, usually must be prepared in anhydrous solvents due to the rapidity of protonolysis. The presence of water is also known in some cases, e.g., reactions involving magnesium and zinc, to inhibit the formation of the reagent.[1]

We reported some years ago that ultrasonic waves are able to promote the formation of Grignard reagents even in the presence of unusually high concentrations of water.[2] We now report that allylation of aldehydes and ketones can be easily effected in aqueous media in a Barbier-type reaction using zinc as the metal.

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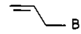
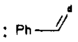
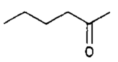
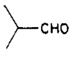
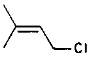
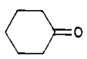
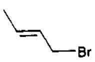
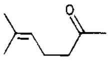
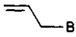
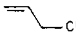
[1] Kharasch, H. S.; Reinmuth, O. "Grignard Reactions of Non-Metallic Substances"; Prentice Hall: New York, 1954; pp 14–15. Nutzel, K. "Methoden der organischer Chemie", Houben Weyl; 4th ed., Muller, E., Ed.; Georg Thieme Verlag: Stuttgart, 1973; Vol 13/2a; pp 553–858.

[2] Luche, J. L.; Damiano, J. C. *J. Am. Chem. Soc.* **1980**, *102*, 7926–7927. See also: Sprich, J. D.; Lewandos, G. S. *Inorg. Chim. Acta* **1983**, *76*, L241–242.

0022-3263/85/1950-0910$01.50/0

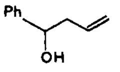
Table I

run	carbonyl compound	allylic halide[a]		reaction conditions (time, h)[b]		homoallylic alcohol yield,[c] %
1	Ph CHO		(1.2)	H_2O:THF	(4) ST	**1** 48
2			(1.2)	H_2O:THF	(0.75) US	23
3			(1.2)	NH_4Cl	(0.75) ST	61
4			(1.2)	NH_4Cl:THF	(0.75) ST	100 (95)*
5			(1.2)	aq. NaCl:THF	(0.75) ST	0
6			(1.2)	NH_4Cl:THF: 	(0.75) ST	84
7			(1.2)	NH_4Cl:BTMA[e]	(0.75) ST	72
8			(1.2)	NH_4Cl:THF	(1) ST	**2** 53
9			(2)	NH_4Cl:THF	(1) ST	70 (68)*
10			(2)	H_2O:THF	(0.75) US	36
11			(2)	H_2O:THF:CCl_4[f]	(0.75) US	31
12			(2)	NH_4Cl:THF	(1) ST	**3** 95 (84)*
13			(2)	H_2O:THF	(0.75) US	90
14			(2)	NH_4Cl:THF	(0.75) ST	**4** 100 (98)*
15			(2)	H_2O:THF	(0.5) US	89
16			(2)	NH_4Cl:THF	(1.25) ST	**5** 74 (60)*
17			(2)	H_2O:THF	(0.75) US	traces
18			(2)	NH_4Cl:THF	(2) ST	58

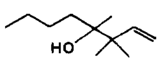
[a] Figures in parentheses indicate the halide:carbonyl compound ratio. Zinc:halide ratio is always 1.
[b] NH_4Cl stands for saturated aqueous NH_4Cl. Ratios of H_2O:THF and NH_4Cl:THF were both 5:1. ST stands for stirring, and US for sonication.
[c] VPC yields (Carbowax 20M, 10%). Isolated yields (silica gel column chromatography) are indicated by an asterisk.
[d] 5 mmol (1 equiv).
[e] 1 mmol (0.2 equiv) of benzyltrimethylammonium chloride.
[f] Traces.

Stirring a suspension of benzaldehyde (5 mmol), allyl bromide, (6 mmol), and zinc powder[3] (6 mmol) in 5 mL of distilled water and 1 mL of tetrahydrofuran (THF) for 4 h at room temperature produced 1-phenyl-3-buten-1-ol (**1**) in 48% yield. The yield was essentially the same after a 20-h stirring. Activation of the metal was attempted by chemical and sonochemical methods in order to determine if faster reactions and higher yields were possible. Thus, the above reaction was run with saturated aqueous ammonium chloride[4] instead of water. Soon after stirring was started, gas and heat were evolved. After 30–45 min, the resulting light grey mixture, containing in most cases no residual zinc, was processed as usual to give a quantitative yield of compound **1**, as shown by VPC analysis. Sonication[5] of the same reaction mixture in water:THF (5 mL:1 mL) for 45 min in an ice–water bath led to a much lower yield (23%). Due to the potential interest of these results, the reaction was run with different reactants under various conditions. The experimental data are listed in Table I.

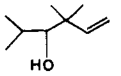
All of the reactions were carried out under an air atmosphere with a stoichiometric amount of zinc with respect to the halide. The final product mixture was in all cases clean, consisting of the untransformed carbonyl compound and the addition product.[6] That this method has a potential in synthesis is illustrated by the satisfactory yields obtained in 5 mM preparative runs (nos. 4, 9, 12, 14, and 16) and by a half-mole scale preparation of compound **1** (70% nonoptimized yield after distillation). While an attempted Reformatsky reaction using benzaldehyde and ethyl bromoacetate failed, a 30% isolated yield of compound **6** (1:1.5 diastereomer mixture) was obtained from benzaldehyde and methyl 4-bromocrotonate.[7]



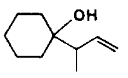
1



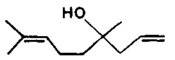
2



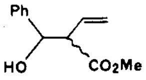
3



4



5



6

Experiments effected in the presence of a radical scavenger (styrene) or promoter (CCl_4 for sonochemical reactions[8]) revealed no decisive yield modification. Comparison of run 3 with run 4 demonstrates the effect of an organic cosolvent (THF). As the system consists of three phases, two nonmiscible liquids and a solid, its role may be to facilitate the contact of all reacting species, in that benzyltrimethylammonium chloride is also beneficial (run 7). The same interpretation can be given for the effectiveness of sonic waves, due to their well-known emulsifying properties. Ultrasonic erosion[9] should also contribute to promote the reaction by a continuous activation of the metal surface. Nevertheless, the reactions described here raise several intriguing questions. A reasonable mechanism cannot be proposed presently, but a classical organometallic process is quite improbable. Organozincs react violently with water and ammonium chloride is frequently used to quench organometallic reactions. To our knowledge, the only published organozinc reaction occurring in

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(3) Zinc dust (Merck) was used as received. The use of zinc–copper couple, prepared separately or in situ (addition of 10% $CuSO_4$ in the reaction media), had no beneficial effect.

(4) For the activation of zinc by NH_4Cl, see: Han, B. H.; Boudjouk, P. *J. Org. Chem.* **1982**, *47*, 751–752, and references cited therein.

(5) A 30-KHz Ultrason-Annemasse sonicator with a titanium probe, 120 W/cm^2. Under the same conditions, we have checked that CCl_4 in water reacts as described in ref 8.

(6) VPC analyses also revealed the presence of some volatile products, which have not yet been identified. These compounds are also detected when the allylic halide is stirred with zinc in the same solvent mixture.

(7) Rice, L. E.; Craig Boston, M.; Finklen, H. O.; Suder, B. J.; Frazier, J. O.; Hudlicky, T. *J. Org. Chem.* **1984**, *49*, 1845–1848.

(8) Weissler, A.; Cooper, H. W.; Snyder, S. *J. Am. Chem. Soc.* **1950**, *72*, 1769–1775.

(9) Howkins, S. D. *J. Acoust. Soc. Am.* **1966**, *39*, 55–61.

water is a Wurtz-type coupling of alkyl iodides.[10] As the reactions depicted here are Barbier-type reactions, the possibility of a free radical pair process occurring on the metallic surface, as suggested by Molle and Bauer[11] for the classical Barbier reaction, deserves consideration.

The positive results obtained with allylic halides could not be achieved with other halides such as benzyl and butyl bromides. However, the addition of an allylic moiety is synthetically important[12] and we expect that this simple procedure will prove quite useful.

In conclusion, the zinc-mediated addition of an allylic group to a carbonyl function can in fact occur in aqueous media. Synthetic applications and mechanistic implications of this reaction are currently being studied.

Acknowledgment. We thank Dr. A. E. Greene for fruitful discussions. Financial support by the Centre National de la Recherche Scientifique (LA 332, ATP Chimie Fine) is gratefully acknowledged.

Registry No. 1, 936-58-3; 2, 94597-04-3; 3, 28920-33-4; 4, 36971-11-6; 5, 17920-92-2; (R^*,R^*)-6, 65203-02-3; (R^*,S^*)-6, 65203-03-4; PhCHO, 100-52-7; $CH_3(CH_2)_3COCH_3$, 591-78-6; $(CH_3)_2CHCHO$, 78-84-2; $(CH_3)_2C{=}CH(CH_2)_2COCH_3$, 110-93-0; $CH_2{=}CHCH_2Br$, 106-95-6; $(CH_3)_2C{=}CHCH_2Cl$, 503-60-6; $CH_3CH{=}CHCH_2Br$, 4784-77-4; $CH_2{=}CHCH_2Cl$, 107-05-1; $BrCH_2CH{=}CHCO_2Me$, 1117-71-1; Zn, 7440-66-6; NH_4Cl, 12125-02-9; cyclohexanone, 108-94-1.

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(10) Nosek, J. *Collect. Czech. Chem. Commun.* **1964**, *29*, 597–602. For a reaction related to the presently described (allylzinc reagents in refluxing alcohols, giving lower yields), see: Killinger, T. A.; Boughton, N. A.; Runge, T. A.; Wolinski, J. *J. Organomet. Chem.* **1977**, *124*, 131–134.

(11) Molle, G.; Bauer, P. *J. Am. Chem. Soc.* **1982**, *104*, 3481–3487.

(12) For recent papers related to this reaction, see: Hiyama, T.; Sawahata, M.; Obayashi, M. *Chem. Lett.* **1984**, 1237–1238. Yamamoto, Y.; Yatagai, H.; Ishihara, Y.; Maeda, N.; Maruyama, K. *Tetrahedron* **1984**, *40*, 2239–2246. Souppe, J.; Namy, J. L.; Kagan, H. B. *Tetrahedron Lett.* **1982**, *23*, 3497–3500. Mukaiyama, T.; Harada, T. *Chem. Lett.* **1981**, 1527–1528. Augê, J.; David, S. *Tetrahedron Lett.* **1983**, *24*, 4009–4012. Nokami, J.; Otera, J.; Sudo, T.; Okawara, R. *Organometallics* **1983**, *2*, 191–193.

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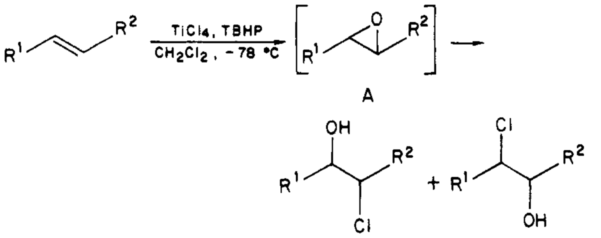
Chlorohydroxylation of Olefins with Peroxides and Titanium Tetrachloride

Summary: $TiCl_4$/TBHP (DTBP) is a powerful reagent for the direct chlorohydroxylation of olefins. Moderate diastereoselectivity has been observed in the reactions of chiral substrates bearing allylic or homoallylic substituents.

Sir: We have recently reported the asymmetric chlorohydroxylation of allylic alcohols, employing $TiCl_2(O\text{-}i\text{-}Pr)_2$ in place of $Ti(O\text{-}i\text{-}Pr)_4$ in the standard asymmetric epoxidation process.[1] We have now discovered that nonfunctionalized olefins can also be chlorohydroxylated, employing either *tert*-butyl hydroperoxide (TBHP) or di-*tert*-butyl peroxide (DTBP) in the presence of titanium tetrachloride, as depicted in eq 1.[2,3]



(1)

The intermediacy of an epoxide (A) in this reaction appears probable, and, in fact, epoxides are rapidly opened to chlorohydrins under the reaction conditions. Although the epoxide is not generally observed under standard conditions, it may be detected in many cases upon rapid workup (<5 min). The epoxides of adamantylideneadamantane[4] and methyl ricinoleate were more resistant to ring opening and were isolated in 20% and 40% yields, respectively, from standard chlorohydroxylation reactions.

The stereochemical integrity (i.e., pure anti addition) of the chlorohydroxylation process was demonstrated by ring closure (K_2CO_3/MeOH) of the chlorohydrins from *cis*- and *trans*-5-decene and (*E*)-1-methoxy-2-decene and correlation to epoxides of known geometry. The above mechanism also raises the issue of regioselectivity in the ring-opening process. Generally, the reaction gives rise to a mixture of regioisomers, although selectivity may be quite high in some cases (Table I, entry 4 (96:4) and entry 3 (only one regioisomer detected)).

Chlorohydrins are typically prepared as follows: a flame-dried flask under N_2 is charged with the olefin (1.5 mmol) and dry CH_2Cl_2 to produce a 0.05 M solution. This is cooled to −78 °C and anhydrous TBHP (1.2 equiv, CH_2Cl_2 solution)[5] is added via syringe, followed by $TiCl_4$ (1.2 equiv, CH_2Cl_2 solution). The reaction is monitored by TLC (EtOAc/hexane). If TLC shows much remaining starting material after 1 h, additional $TiCl_4$ is added. Functionalized olefins often require additional $TiCl_4$. The reaction is quenched by pouring the cold solution into a stirring mixture of Et_2O–saturated Na_2SO_4, followed by stirring at room temperature for 1 h. The ethereal layer is then washed with saturated Na_2SO_3 and saturated NaCl, dried over $MgSO_4$, and evaporated. The residual oil is purified by flash chromatography (EtOAc:hexane mixtures).

One is initially struck by the power of this reagent. Both with TBHP and with DTBP, reaction is generally complete within 15 min at −78 °C, even with simple monosubstituted olefins. The very high reactivity of DTBP under these nonradical conditions[7] is especially noteworthy. It was,

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(1) Lu, L.D.-L.; Johnson, R. A.; Finn, M. G.; Sharpless, K. B. *J. Org. Chem.* **1984**, *49*, 728.

(2) (a) Sharpless, K. B.; Johnson, R. A., U.S. Pat. 571961, Jan 1984. (b) A number of other Lewis acids were tried, including $TiCl(O\text{-}i\text{-}Pr)_3$, $TiCl_2(O\text{-}i\text{-}Pr)_2$, $BF_3{\cdot}OEt_2$, $AlCl_3$, $SnCl_4$, $TaCl_5$, $ZrCl_4$, $VOCl_3$, and HCl, but results with $TiCl_4$ were far superior.

(3) The oxidation of aromatics with peroxides in the presence of a Lewis acid has been reported previously. See, for example: (a) Apatu, J. O.; Chapman, D. C.; Heaney, H. *J. Chem. Soc., Chem. Commun.* **1981**, 1079. (b) Kurz, M. E.; Johnson, G. J. *J. Org. Chem.* **1971**, *36*, 3184. (c) Hashimoto, K. *Bull. Chem. Soc. Jpn.* **1970**, 293. (d) Chip, G. K.; Grossert, J. S. *Can. J. Chem.* **1971**, *50*, 1233. These last authors also report the chlorohydroxylation, in low yield (37%), of cyclohexene with mCPBA/$TiCl_4$.

(4) Wynberg, H.; Boelema, E.; Wieringa, J. H.; Strating, J. *Tetrahedron Lett.* **1970**, 3613. These authors report the resistance of this epoxide toward normal ring-opening reactions.

(5) The use of anhydrous TBHP solutions in toluene[6] sometimes leads to byproducts resulting from competing aromatic oxidation. See ref 3.

(6) Hill, J. G.; Rossiter, B. E.; Sharpless, K. B. *J. Org. Chem.* **1983**, *48*, 3607.