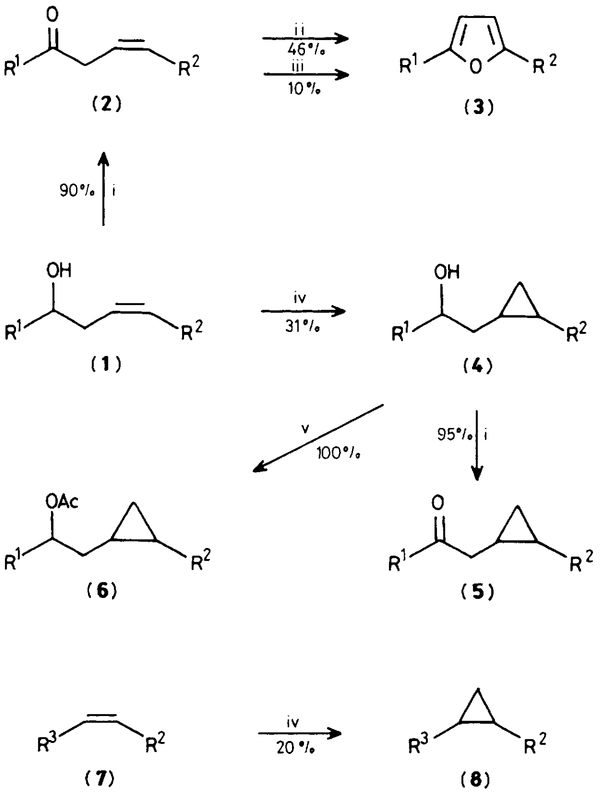
Ultrasound in Lipids. Furan Formation under Ultrasonic assisted Simmons–Smith Reaction and the Effect of Cadmium and Copper as Zinc Replacers

Marcel S. F. Lie Ken Jie* and Wilson L. K. Lam

Department of Chemistry, University of Hong Kong, Pokfulam Road, Hong Kong

Methyl 12-oxo-octadec-9-*cis*-enoate gave methyl 9,12-epoxyoctadeca-9,11-dienoate when treated with zinc or cadmium in the presence of di-iodomethane and 1,2-dimethoxyethane under concomitant ultrasonic irradiation, while under similar conditions copper caused cyclopropanation across the ethylenic bond in methyl oleate and ricinoleate.

The use of ultrasonic energy in chemical reactions has recently attracted considerable interest among organic chemists.[1,2] Under ultrasonic irradiation the solvent in a chemical reaction allows the rapid formation, growth, and implosive collapse of unstable microbubbles, generating short-lived but extremely high pressure and high temperature 'hot spots' in the system, permitting reaction rates to be considerably increased.[3] In the area of fatty acid chemistry, unsaturated long chain fatty esters and triglycerides were readily transformed to the corresponding cyclopropane derivatives, when treated with zinc in the presence of di-iodomethane and 1,2-dimethoxyethane as solvent under concomitant ultrasonic irradiation.[2,4] In the absence of ultrasound, such a reaction mixture did not undergo cyclopropanation as the zinc (not in the form of a zinc–copper couple) remained unreactive. However, when the same reaction conditions were applied to a keto-ene ester (**2**), the ultrasound-assisted reaction furnished instead a C_{18} furanoid fatty derivative (**3**) (Scheme 1) [46% yield, δ_H(90 MHz, $CDCl_3$) 0.88 (3H, t), 1.2—1.6 (18H, m), 2.30 (2H, t), 2.55 (4H, t), 3.66 (3H, s), 5.82 (2H, s); δ_C(90 MHz, $CDCl_3$) 51.41 ($-CO_2$*Me*), 104.88 (–*C*H= furan ring), 154.74 (–*C*= furan ring), 174.22 ($-CO_2Me$); g.l.c. : ECL[5] value = 18.3 (OV-101), 20.45 (3% SP2310—2% SP2300)]. Compound (**3**) has previously been obtained by the treatment of (**2**) with mercury(II) acetate or by total synthesis from furan.[6] The result of this reaction suggests that the zinc carbenoid species (generated from zinc and di-iodomethane) induced an electron withdrawing effect on the π-bond system of the ethylenic bond of the substrate causing an intramolecular cyclisation involving the strategically located keto function, yielding the stable furanoid fatty ester derivative.



Scheme 1.† $R^1 = Me(CH_2)_5$, $R^2 = (CH_2)_7CO_2Me$, $R^3 = Me(CH_2)_7$. *Reagents:* i, chromic acid, Et_2O; ii, Zn, CH_2I_2, $MeOCH_2CH_2OMe$, ultrasound, 80—90 °C, 4 h; iii, Cd, CH_2I_2, $MeOCH_2CH_2OMe$, ultrasound, 80—90 °C, 4 h; iv, Cu, CH_2I_2, $MeOCH_2CH_2OMe$, ultrasound, 80—90 °C, 4 h; v, $(AcO)_2O$, 100 °C, 1 h.

When zinc was replaced by cadmium metal, compound (**2**) in the presence of di-iodomethane with 1,2-dimethoxyethane as solvent, also gave *ca.* 10% yield of (**3**) under ultrasonic irradiation. This indicated that the cadmium (as an organocadmium species) also induced an electron withdrawing effect on the ethylenic system of the substrate promoting furan formation as did the zinc carbenoid. No furan formation was observed when the same reaction was conducted without di-iodomethane, even under ultrasonic irradiation.

The role of copper in a classical Simmons–Smith reaction had always been claimed to be limited to activation of the zinc by formation of a zinc–copper couple, playing no further part in the subsequent cyclopropanation.[7] However, Kawabata *et al.*[8] demonstrated the ease of cyclopropanation of alkenes using copper and organic *gem*-dihalides. But when copper was substituted for zinc and the reaction carried out under ultrasonic irradiation, compound (**2**) furnished high molecular weight polymeric material. The ^{1}H n.m.r. analysis of the crude product indicated the absence of furan and cyclopropane protons. However, under similar reaction conditions, compounds (**1**) and (**7**) gave the corresponding cyclopropane derivatives (**4**) and (**8**), in 31 and 20% yield respectively. The identity of compound (**4**) was confirmed by further transformation by oxidation[9] to (**5**) [δ_H (90 MHz, $CDCl_3$) −0.3 (2H, m), 0.6 (2H, m), 0.89 (3H, t), 1.2—1.6 (20H, m), 2.2—2.5 (6H, m), 3.66 (3H, s); g.l.c. : ECL value = 20.6 (OV-101)]; and acetylation to (**6**) [δ_H(90 MHz, $CDCl_3$) −0.3 (2H, m), 0.65 (2H, m), 1.2—1.6 (20H, m), 2.06 (3H, s), 2.30 (2H, t), 3.66 (3H, s), 4.87 (1H, quint.)].

---

† All reactions were carried out under nitrogen. A commercial ultrasonic laboratory cleaner (Bransonic model 321, 150 W, 55 kHz, Branson Co., Shelton, Conn., U.S.A.) was employed. A typical reaction consisted of a mixture of metal filings (zinc, cadmium, or copper, 0.5 g), di-iodomethane (0.3 g), unsaturated fatty ester (0.4 g), and 1,2-dimethoxyethane (5 ml), being irradiated for 4 h at 80—90 °C under ultrasound. Saturated ammonium chloride solution (5 ml) was then added and the organic product extracted with diethyl ether and purified by column chromatography on silicic acid.

This project was supported by the Lipid Research Fund and the Research Grants Committee of the University of Hong Kong.

Received, 13th April 1987; Com. 490

References

1 D. Bremner, *Chem. Br.*, 1986, **22**, 633; O. Repic and S. Vogt, *Tetrahedron Lett.*, 1982, **23**, 2729; E. C. Friedrich, J. M. Domek, and R. Y. Pong, *J. Org. Chem.*, 1985, **50**, 4640; C. Petrier, J. C. de Souza Barbosa, C. Dupuy, and J. L. Luche, *ibid.*, 1985, **50**, 5761; J. Einhorn and J. L. Luche, *Tetrahedron Lett.*, 1986, **27**, 1791.

2 O. Repic, P. G. Lee, and U. Giger, *Org. Prep. Proced. Int.*, 1984, **16**, 25.

3 K. S. Suslick, J. W. Goodale, P. F. Schubert, and H. H. Wang, *J. Am. Chem. Soc.*, 1983, **105**, 5781.

4 M. S. F. Lie Ken Jie and W. L. K. Lam, *J. Am. Oil Chem. Soc.*, submitted for publication.

5 T. K. Miwa, K. L. Mikolajczak, F. R. Earle, and I. A. Wolff, *Anal. Chem.*, 1960, **32**, 1739; ECL = equivalent chain length.

6 M. S. F. Lie Ken Jie and C. H. Lam, *Chem. Phys. Lipids*, 1977, **20**, 1; 1978, **21**, 275.

7 H. E. Simmons, T. L. Cairns, S. A. Vladuchick, and C. M. Hoiness, *Org. React. (N.Y.)*, 1973, **20**, 1.

8 N. Kawabata, M. Naka, and S. Yamashita, *J. Am. Chem. Soc.*, 1976, **98**, 2676.

9 H. C. Brown, C. P. Garg, and K. T. Liu, *J. Org. Chem.*, 1971, **36**, 387.