Improved Simmons-Smith Reactions

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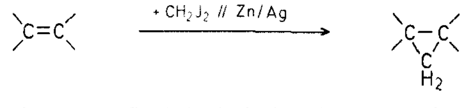
The Simmons-Smith reaction[1] provides a convenient synthesis of cyclopropane derivatives. Various methods for the preparation of the zinc-copper couple used and for its reaction with diiodomethane have been reported[2]. However, the reaction seems to be not always reproducible: the yields markedly depend on the procedure employed and on the structure of the starting olefin.

While the reaction with simple olefins leads to cyclopropanes in acceptable yields, the reaction with conjugated olefins such as α,β-unsaturated ketones[3], esters[1,4], or aldehydes[3b], and olefins derived from ketones such as enamines[5], enol ethers[1], or enol esters[1] is often complicated and the yields are generally rather low.

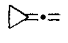
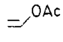
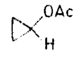
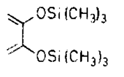
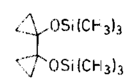
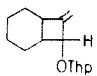
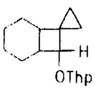
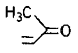
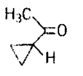
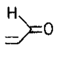
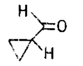
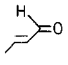
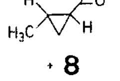
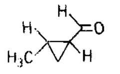
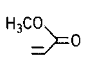
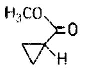
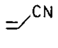
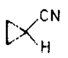
We now report two modifications of the reaction which give improved yields, particularly with functionally substituted olefins:

- a zinc-silver couple is used in place of the zinc-copper couple,



- the usual final hydrolysis of the reaction mixture is replaced by the addition of an amine (e.g. pyridine) in order to remove zinc salts.

Table 1. Examples of Improved Simmons-Smith Reactions using Zinc-Silver Couple and Pyridine Work-up

Olefin	Method[a]	Reaction time hr	Products	Yield[b] %	The corresponding reactions using Zn/Cu couple[c]			
					Equivalents of CH_2J_2	Time hr	Yield %	References
 **1**	A[d]	2		95	1.3	24	92	2[c]
			+ **1**	5	1.4	36	50	3
 **2**	A[d,e]	24		36	6	24	38	9
				15			5	
			+ **2**	47			57	
 **3**	A	18		30	0.5	20	31	1
			+ **3**	70				
 **4**	A	3		78	1.3	3	72[c]	
 **5**	A[f]	15		85				
 **6**	A	2		60	1.4	48	48	3
 **7**	B[i]	18		5	1.4	20	0	3[h]
			+ **7**	95				
 **8**	A	24		15	1.4	20	0	3[h]
			+ **8**	85				
	B	18		88			80[c]	
			+ **8**	12				
 **9**	B[i]	18		80	0.7	48	9[h]	1
			+ **9**	20				
 **10**	A or B			0				

[a] In both methods, 1.3 equivalents of diiodomethane were used for 1.0 equivalent of olefin, except in the case of allene. All reactions were conducted in boiling ether. The products were isolated by distillation.

[b] The yields were determined by analytical and preparative G. L. C. of the distillate. Practically no resinification occured. From **4**, **5**, and **6**, only one product was isolated by distillation.

[c] The reaction mixtures were worked up by acidic hydrolysis, except for the cyclopropanation of **4** and **8** (pyridine work-up).

[d] The same yield is obtained when the cyclopropane derivative is extracted from the mixture by acidic hydrolysis.

[e] P. Le Perchec, J. M. Conia, to be published.

[f] G. Rousseau, J. M. Conia, to be published.

[g] New compound;
I. R.: $\nu = 3060, 2815, 2720, 1715\ cm^{-1}$.
^1H-N.M.R. (CCl_4): $\delta = 1.21$ (m, 6H), 0.85 (m, 1H), 9.10 (d, 2H) ppm.
Mass spectrum: M^+ 84; other peaks, $m/e = 83$, 70, 69, 55.
Actually, a Simmons-Smith reaction carried out with methyl crotonate[1].

[i] With method A, complete resinification occurs.

Use of Zinc-Silver Couple

Various experiments have been performed, in our laboratory, in order to repeat or to improve the yields of some capricious Simmons-Smith reactions. In this work, a direct relation has been noticed between the yields and the origin of the diiodomethane (the best results were obtained with crude diiodomethane) stabilized by silver wool. Further experiments revealed that the presence of silver metal is the main factor for the improvement.

Zinc-silver couple has been reported to be unsufficiently reactive[2b]; its use in the Simmons-Smith reaction has hitherto not been investigated. In our hands, the use of zinc-silver couple in the Simmons-Smith reaction proved to be advantageous over the use of zinc-copper couple:

- it is more reactive toward diiodomethane;
- it gives better yields with olefins;
- only a slight excess is necessary to complete the reaction;
- the reaction time is considerably reduced.

Complexation of the Zinc Salts by Pyridine

The work-up of the reaction mixture by acid hydrolysis is not in all cases convenient. For instance in the cyclopropanation of α,β-unsaturated silyl ethers[6,7] employing the usual work-up conditions, the readily formed cyclopropanols can undergo ring opening[8]. Furthermore, the coordination complexes formed from functionally substituted compounds and JCH_2ZnJ and/or ZnJ_2 (strong Lewis acid) are not always completely hydrolyzed; the remaining complexes, even when present only in traces, may effect polymerization of the cyclopropane products.

These undesired side reactions can be avoided by adding an amine (e.g. pyridine) to the ethereal reaction solution instead of hydrolyzing the mixture. Under these conditions, the cyclopropane products are set free from their zinc complexes, e.g. $>Zn\cdots{:}O$, complexes of the type $>Zn\cdots{:}N\leqq$ being formed which are easily separated by filtration. The filtrate may then be directly distilled in vacuo. In this mode of work-up, washing with sodium thiosulfate is not necessary because no free iodine is formed.

Employing the above modifications of the Simmons-Smith reaction, esters, aldehydes, ketones, and ethers containing cyclopropane rings may be easily synthesized from the corresponding olefinic compounds.

Preparation of Zinc-Silver Couple:

To a stirred hot solution of silver acetate (100 mg) in acetic acid (100 ml), granular zinc (17 g, 0.26 g-atom) is added all at once. The mixture is stirred for 30 sec, the zinc-silver couple formed is isolated by decantation, and washed with acetic acid (1 × 100 ml) and ether (5 × 100 ml). Anhydrous ether (150 ml) is then poured onto the product and silver wool (2 or 3 small batches) is added.

Cyclopropanation of Olefins:

Method A: To an ethereal suspension of the zinc-silver couple, prepared as described above, diiodomethane (34 g, 0.13 mol) is added dropwise, with stirring, at such a rate as to maintain gentle reflux. Stirring is continued for 1 hr at room temperature. Then, the olefin (0.10 mol) is added dropwise over a period of 15 min and the mixture is refluxed for the period indicated in Table 1. The mixture is then cooled to 0° (ice bath), ether (150 ml) is added, and pyridine (12.6 g, 0.16 mol) is added, dropwise and with vigorous stirring, over a 1 hr period. The resultant precipitate is removed by filtration and washed with ether (3 × 30 ml). Filtrate and washings are combined and a little pyridine is added dropwise until no more precipitate is formed. After filtration, ether is evaporated in vacuo, the residual solution filtered, and the filtrate rectified in vacuo.

Method B: The olefin is rapidly poured into an ethereal suspension of the zinc-silver couple, prepared as described above. Diiodomethane (34 g, 0.13 mol) is then added dropwise, with stirring, at such a rate as to maintain gentle reflux. After the addition is completed, refluxing is continued for the period indicated in Table 1. Work-up of the reaction mixture is carried out as described under Method A.

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[1] H. E. Simmons, R. D. Smith, J. Amer. Chem. Soc. **80**, 5323 (1958); **81**, 4256 (1959).

[2] The zinc-copper couple has been prepared from:
(a) an aqueous solution of copper(II) sulfate and activated (HCl) zinc: R. S. Shank, H. Shechter, J. Org. Chem. **24**, 1825 (1959).
(b) a solution of copper(II) acetate in acetic acid: E. Le Goff, J. Org. Chem. **29**, 2048 (1964).
(c) copper(I) halide and zinc dust: R. J. Rawson, I. T. Harrison, J. Org. Chem. **35**, 2057 (1970).

[3] (a) J. M. Conia, J. C. Limasset, Tetrahedron Lett. **1965**, 3151.
(b) J. C. Limasset, P. Amice, J. M. Conia, Bull. Soc. Chim. France **1969**, 3981.

[4] S. Sawada, K. Takekana, Y. Inouye, J. Org. Chem. **33**, 1767 (1968).

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[6] M. Audibrand, R. Le Goaller, P. Arnaud, C. R. Acad. Sci. [C] **268**, 2322 (1969).

[7] J. M. Denis, J. M. Conia, Tetrahedron Lett., submitted for publication.

[8] C. H. De Puy, F. W. Breitbeil, K. R. Debruin, J. Amer. Chem. Soc. **88**, 3347 (1966).

[9] P. Le Perchec, J. M. Conia, Tetrahedron Lett. **1970**, 1587.