Tetrahedron Letters, Vol.27, No.6, pp 687-690, 1986 0040-4039/86 $3.00 + .00
Printed in Great Britain

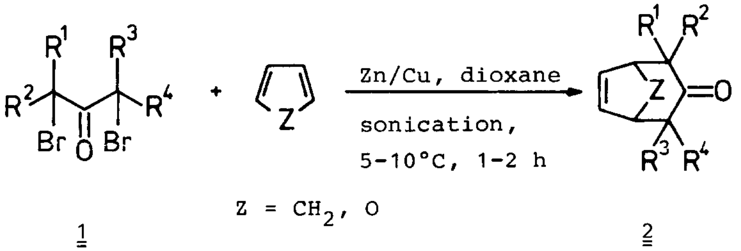
ULTRASONICS IN THE METAL PROMOTED CYCLOADDITION OF α,α'-DIBROMO KETONES TO 1,3-DIENES

Navalkishore N. Joshi and H. Martin R. Hoffmann*

Department of Organic Chemistry, University of Hannover, Schneiderberg 1 B,
D-3000 Hannover, Federal Republic of Germany

ABSTRACT: The zinc promoted cycloaddition of α,α'-dibromo ketones to 1,3-dienes is facilitated by ultrasound; highly hindered bicyclo [3.2.1]oct-6-en-3-ones including a variety of spiroannulated derivatives, are easily accessible for the first time.

During the last few years sonochemistry has rapidly gained importance in various organic reactions. It is by now well known that certain heterogeneous reactions benefit strikingly when conducted in the presence of ultrasound[1]. Advantages are greatly increased reaction rates, enhanced yields, mild conditions and simple methodology.



1

2

75 - 79%

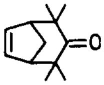
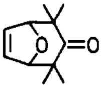
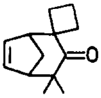
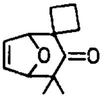
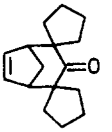
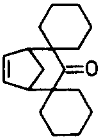
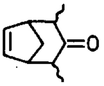
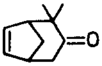
R^1/R^2 = alkyl, cycloalkyl

R^3/R^4 = alkyl, cycloalkyl, H

The reductive cyclocoupling of α,α'-dibromo ketones with 1,3-dienes has been performed under homogeneous and more often under heterogeneous conditions, i.e. with Zn-Cu couple[2] and with $Fe_2(CO)_9$[3]. Despite reaction times of 20 - 24 h, the use of Me_3SiCl[4] as a mediator and other tricks[5], Zn-Cu couple may lead to only moderate yield of cycloadducts. The application of $Fe_2(CO)_9$ appears superior from the point of view of yields, but it involves the use of toxic and expensive metal carbonyl, high reaction temperature and long reaction time (cf. Table 1, footnote c). We have now found that ultrasound aids the Zn-Cu method significantly[6].

The sonicated reaction proceeds cleanly and rapidly, even in the absence of Me_3SiCl. Using this method, it is possible to couple a wide variety of dibromo ketones with cyclopentadiene.

Table 1. Cycloadducts $\underline{\underline{2}}$ Prepared

Entry	α,α'-DIBROMO KETONE $\underline{\underline{1}}$	DIENE	CYCLOADDUCT $\underline{\underline{2}}$	ISOLATED YIELD, %
1	$R^1 = R^2 = R^3 = R^4 = CH_3$	cyclopentadiene		88^a 50^b 71^c
2	dto.	furan		91^a 60^b 89^c
3	$R^1\frown R^2 = -(CH_2)_3-$ $R^3 = R^4 = CH_3$	cyclopentadiene		84^a
4	dto.	furan		88^a
5	$R^1\frown R^2 = R^3\frown R^4 = -(CH_2)_4-$	cyclopentadiene		71^a
6	$R^1\frown R^2 = R^3\frown R^4 = -(CH_2)_5-$	dto.		78^a 26^b
7	$R^1 = R^3 = CH_3$ $R^2 = R^4 = H$	dto.		90^d 65^b 81^c
8	$R^1 = R^2 = CH_3$ $R^3 = R^4 = H$	dto.		81^d 30^b

a: Zn/Cu-method with sonication; 5 - 10°C, 1 - 2 h.

b: Zn/Cu-method without sonication; 1 eq. Me_3SiCl, room temperature, 20 - 24 h.

c: $Fe_2(CO)_9$-method (Ref. 3); 10 - 60 eq. diene, 40 - 90°C, 12 - 80 h.

d: Sonicated reaction, catalyzed with 0.01 eq. Me_3SiCl, 15 - 30 min.

In all cases consistently high yields of cycloadducts were obtained. The procedure is equally applicable to furan, as exemplified by entries 2 and 4.

Highly crowded ditertiary dibromo ketones seem to work especially well with this method. The reaction is rather sluggish with disecondary (entry 7) and primary-tertiary (entry 8) dibromo ketones. However, this problem could easily be overcome by using a catalytic amount of Me_3SiCl. The catalysed reaction proceeded exothermically and was complete in less than 30 min, regardless of the nature of reactants. The sonicated reaction could also be scaled up to batches of 0.1 mole[7]. Amongst various solvents examined, dioxane was found to be the solvent of choice. The reaction in ether or benzene gave poor yields, and proceeded erratically in tetrahydrofuran. Interestingly, this observation is parallel to the one made by Han and Boudjouk for the Reformatsky reaction[8].

In summary, the modified Zn-Cu couple method significantly improves the reductive coupling of α,α'-dibromo ketones with 1,3-dienes. Besides several obvious advantages over existing methods, the present procedure seems indispensible when dealing with highly crowded dibromo ketones (e.g. entries 3 - 6). A special structural feature of the resulting cycloadducts is the presence of extraordinarily high steric hindrance around the carbonyl group. The facile introduction of the strained cyclobutane moiety (entries 3,4) is also of interest.

General Procedure: A 50 ml 2-necked flask fitted with a condenser and rubber septum was charged with Zn-dust (30 mmol) and CuCl (3 mmol). The system was evacuated and purged with N_2. Freshly distilled cyclopentadiene (15 mmol) or furan (30 mmol) was introduced and the flask was submerged in a common laboratory cleaner (Brasonic 220). The reaction mixture was sonicated while a solution of dibromo ketone (10 mmol) in anhydrous dioxane (10 ml) was introduced over a period of 10 - 15 min. The bath temperature was maintained below 10°C for the first 1 h, and then allowed to slowly reach room temperature. The reaction was monitored by GC (while no effort was made to optimize the reaction time, most reactions with cyclopentadiene were complete within 1 h and with furan in 1.5 h). After 2 h, the reaction mixture was diluted with light petroleum (40 ml) and filtered. The filtrate was washed with water (3 x 10 ml), dried over anhydrous K_2CO_3, and concentrated. Purification of the products was accomplished by flash chromatography (silica gel, 5 % ether in light petroleum) followed by crystallization or Kugelrohr distillation.

The experimental procedure for the reactions on a larger scale[7] was similar except that the dibromo ketone solution was introduced over a period of 1 h, and a mechanical stirrer was employed together with sonication.

Acknowledgement: We thank the Alexander von Humboldt Foundation for a Research Fellowship (to N.N.J.).

References and Notes

1. H. C. Brown and U. S. Racherla, Tetrahedron Lett., 26, 4311 (1985);
G. Mehta and H. S. P. Rao, Synth.Commun., 15, 991 (1985), and references cited therein.
2. H.M.R. Hoffmann, K. E. Clemens and R. H. Smithers, J.Am.Chem.Soc., 94, 3940 (1972).
3. R. Noyori, S. Makino and H. Takaya, J.Am.Chem.Soc., 93, 1272 (1971);
H. Takaya, S. Makino, Y. Hayakawa and R. Noyori, J.Am.Chem.Soc., 100, 1765 (1978).
4. R. J. Giguere, D. I. Rawson and H.M.R. Hoffmann, Synthesis, 902 (1978);
H.M.R. Hoffmann, A. Weber and R. J. Giguere, Chem.Ber. 117, 3325 (1984).
5. Zn supported on alumina: J. G. Vinter and H.M.R. Hoffmann, J.Am.Chem.Soc., 96, 5466 (1974);
Zn activated with $(EtO)_3B$: H.M.R. Hoffmann and M. N. Iqbal, Tetrahedron Lett., 4487 (1975).
6. Ultrasonic irradiation also appears to facilitate the $Fe_2(CO)_9$-promoted reaction. For example we have found that the coupling of 2,4-dibromo-2,4-dimethyl-3-pentanone with cyclopentadiene was complete (> 90 % GC yield) within 8 h at room temperature. The mild reaction conditions made it unnecessary to use more than 3 eq. of the diene.
7. Reactions in entries 1 and 2 were also performed on a 100 mmol scale, and the respective cycloadducts were obtained in 75 % and 79 % yield.
8. B. H. Han and P. Boudjouk, J.Org.Chem., 47, 5030 (1982).

(Received in Germany 31 October 1985)