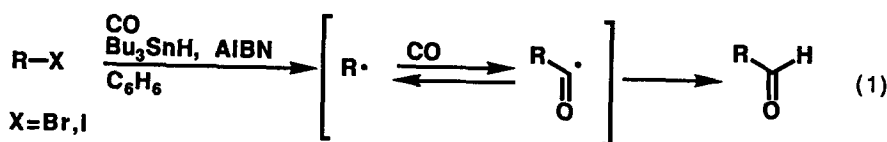


FREE-RADICAL CARBONYLATION. CONVERSION OF AROMATIC HALIDES TO ALDEHYDES

Iihyong Ryu,* Kazuya Kusano, Norio Masumi, Hiroshi Yamazaki,
Akiya Ogawa, and Noboru Sonoda*
*Department of Applied Chemistry, Faculty of Engineering,
Osaka University, Suita, Osaka 565, Japan*

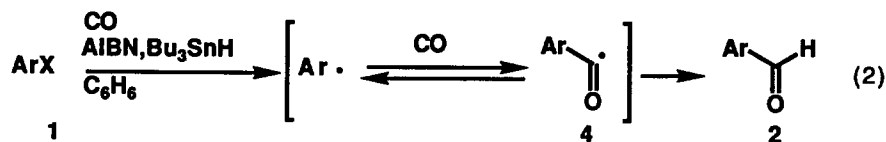
Summary: The free-radical carbonylation of aromatic iodides 1 with carbon monoxide to aromatic aldehydes 2 was successfully achieved under highly diluted conditions ($[Bu_3SnH]=ca. 0.02M$).

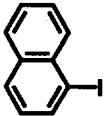
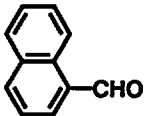
Carbonylation of organic compounds with carbon monoxide is one of basic and important reaction processes in organic synthesis and, for this purpose, the methodology involving acyltransition-metals as the key species is most commonly used.¹ In contrast, carbonylation involving acyl radicals has long been neglected due to rather fruitless results by the initial work.² Recent publication from this laboratory has described that organic halides can be successfully carbonylated by free-radical reaction under tin hydride conditions, yielding the corresponding aldehydes (eq 1).³ The process employing low concentrations ($[Bu_3SnH]=ca. 0.06M$) worked well for the carbonylation of adequate aliphatic bromides and iodides. However, later we have noticed that the employed conditions for *aliphatic* carbonylation are not uniformly applied to *aromatic* carbonylation, since competitive reduction process in the latter case often became more serious.⁴ We report herein that free-radical carbonylation of aryl halides leading to aldehydes was effected by the use of highly diluted conditions ($[Bu_3SnH]=ca. 0.02M$).⁵



When a mixture of p-iodoanisole 1c (0.75 mmol), Bu_3SnH (0.98 mmol, [0.02 M]), AIBN (0.01mmol), and benzene (45 mL) was heated with stirring at 110°C for 2 h under the pressure of carbon monoxide (70 atm), carbonylation of 1c took place to give 78% yield of p-anisaldehyde (2c) (Table I, run 3). In accordance with our previous observation,³ higher CO pressure resulted in a more predominant CO trapping process over the competitive reduction to aromatic hydrocarbon. In an effort to secure better yields of formylated products 2, highly diluted conditions ($[Bu_3SnH]=ca. 0.02M$) under 70~90 atm of CO were chosen.⁶ Results of aromatic formylation by free-radical process are summarized in Table I.

Table I. Free-Radical Carbonylation of Aromatic Halides under Highly Diluted Conditions^a



run	ArX, 1	[Bu ₃ SnH] (M), CO (atm)	ArCHO, 2	yield (%) ^b
1	C ₆ H ₅ I (1a)	0.02, 90	C ₆ H ₅ CHO (2a)	63
2	p-MeOC ₆ H ₄ Br (1b)	0.02, 70	p-MeOC ₆ H ₄ CHO (2b=2c)	44 ^c
3	p-MeOC ₆ H ₄ I (1c)	0.02, 70	p-MeOC ₆ H ₄ CHO (2c)	78
4		0.06, 70		70
5		0.15, 70		51
6		0.02, 50		49
7	m-MeOC ₆ H ₄ I (1d)	0.02, 90	m-MeOC ₆ H ₄ CHO (2d)	68
8	o-MeOC ₆ H ₄ I (1e)	0.02, 90	o-MeOC ₆ H ₄ CHO (2e)	50
9	p-MeC ₆ H ₄ I (1f)	0.02, 90	p-MeC ₆ H ₄ CHO (2f)	63
10		0.02, 70		57
11	m-MeC ₆ H ₄ I (1g)	0.02, 90	m-MeC ₆ H ₄ CHO (2g)	68
12	o-MeC ₆ H ₄ I (1h)	0.02, 90	o-MeC ₆ H ₄ CHO (2h)	(85)
13	p-ClC ₆ H ₄ I (1i)	0.02, 90	p-ClC ₆ H ₄ CHO (2i)	52 ^d
14	m-ClC ₆ H ₄ I (1j)	0.02, 90	m-ClC ₆ H ₄ CHO (2j)	39 ^e
15	o-ClC ₆ H ₄ I (1k)	0.02, 90	o-ClC ₆ H ₄ CHO (2k)	19 ^f
16	 (1l)	0.02, 90	 (2l)	(68)

^aIn general, reactions were carried out using a 50-mL stainless steel autoclave with a glass tube inserted: 1 (0.75 mmol), Bu₃SnH (0.98 mmol), AIBN (0.1 mmol), benzene (45 mL; [Bu₃SnH]=ca. 0.02M), 110°C, 2 h. ^bGC yields. Isolated yields are in parentheses. ^cUnreacted 1b: 37%. ^dUnreacted 1i: 16%. ^eUnreacted 1j: 16%. ^fUnreacted 1k: 26%.

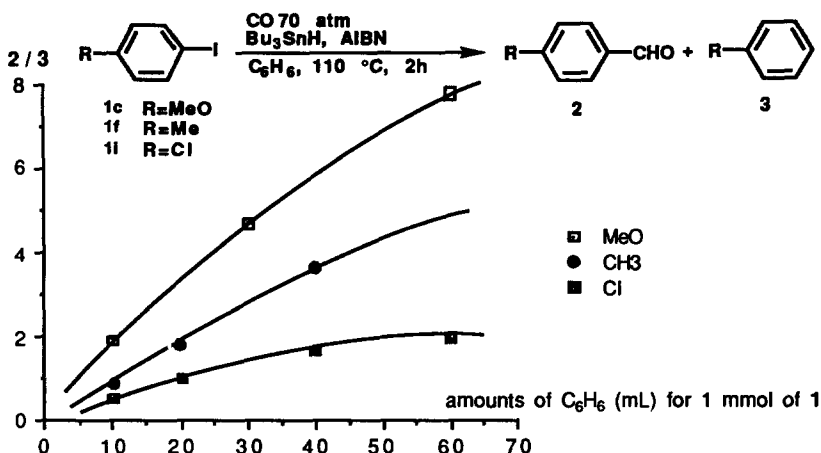
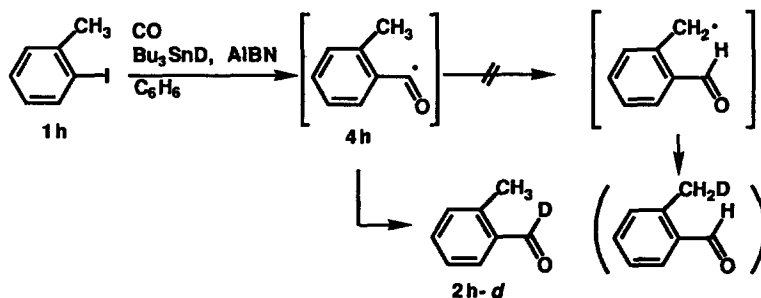


Figure I. Effects of Dilution on Ratios of 2/3

Aromatic iodide **1c** gave a better result than the corresponding aromatic bromide **1b** due to relatively smooth consumption of the former (runs 2 and 3). In general, electron-donating substituents such as methoxy and methyl merit for this carbonylation. The higher diluted conditions brought about the improvement of carbonylation/reduction ratios, while the extent of the effect appeared to be highly dependent on the electronic nature of the substituents, as shown in Figure I (p-MeO > p-Me > p-Cl). The dismal yields in the examples of m-Cl- and o-Cl-iodobenzenes are largely a consequence of low conversions (runs 14 and 15). From o-Me-iodobenzene (**1h**) high yield of **2h** was obtained (run 10). The possibility of a 1,5-hydrogen transfer from o-Me group led us to examine the radical carbonylation of **1h** using tin deuteride. The result of sole formation of **2h-d** clearly precluded such an intramolecular process⁷ (Scheme I). We speculate that simple reduction of **1h** may be sterically hampered by o-Me group, allowing carbonylation to predominate.

Scheme I



It should be noted that highly diluted conditions employed for this carbonylation were not effective for free-radical tin hydride reduction.⁸ For example, attempted reduction of **1c** in a low concentration ($[\text{Bu}_3\text{SnH}] = \text{ca. } 0.02 \text{ M}$) gave only 40 % yield of anisole (**3c**) along with 48 % yield of unreacted **1c**. The fact that the consumption of **1c** is more smooth in carbonylation rather than reduction may be attributed to the difference in the efficiency of aryl radical and aroyl radical to abstract hydrogen.⁹

In summary, this paper describes a new methodology for the carbonylation of aromatic halides by a free-radical process under highly diluted conditions. Further investigations are now in progress.

References and Notes

- (1) For recent reviews, see: (a) C. Narayama and M. Periasamy, *Synthesis*, 253 (1985). (b) T. A. Weil, L. Casser, M. Foa, In *Organic Synthesis via Metal Carbonyls*; I. Wender and P. Pino, Eds.; Wiley: New York; Vol. 2, p 517 (1977). (c) H. Bahrman, B. Cornils, C. D. Frohling, and A. Mullen, In *New Syntheses with Carbon Monoxide*, J. Falbe, Ed.; Springer: Berlin (1980).
- (2) (a) D. D. Coffman, P. S. Pinkney, F. T. Wall, W. H. Wood, and H. S. Young, *J. Am. Chem. Soc.* **74**, 3391 (1952). (b) M. M. Brubaker, D. D. Coffman, and H. H. Hoehn, *Ibid.*, **74**, 1509 (1952). (c) R. E. Foster, A. W. Larchar, R. D. Lipscomb, and B. C. McKusik, *Ibid.*, **78**, 5606 (1956). (d) J. C. Sauer, *Ibid.*, **79**, 5314 (1957).
- (3) I. Ryu, K. Kusano, A. Ogawa, N. Kambe, and N. Sonoda, *J. Am. Chem. Soc.*, **112**, 452 (1990)
- (4) It has been known that phenyl radical abstracts hydrogen from Bu_3SnH ca. 200 times faster than butyl radical. See: L. J. Johnston, J. Luszyk, D. D. M. Wayner, A. N. Abeywickreyma, A. L. Beckwith, J. L. Scaiano, and K. U. Ingold, *J. Am. Chem. Soc.*, **107**, 4594 (1985)
- (5) Cf. Pd(0)-catalyzed carbonylation using tin hydride, see: V. P. Baillargeon and J. K. Stille, *J. Am. Chem. Soc.*, **108**, 452 (1986).
- (6) A typical procedure: *o*-Me-iodobenzene (**1h**; 156 mg, 0.72 mmol), Bu_3SnH (272 mg, 0.936 mmol), AIBN (16mg), and benzene (45 mL) were placed in a 100-mL stainless steel autoclave with an inserted glass tube. The reaction mixture was stirred under carbon monoxide pressure (80 atm) at 110°C for 2 h. After the evacuation of excess carbon monoxide at room temperature, benzene was removed under reduced pressure. The residue was stirred for 1 h with diethyl ether (10 mL) and saturated aqueous potassium fluoride solution (10 mL). Filtration, extraction with ether, drying (sodium sulfate), and concentration, followed by purification by flash chromatography (SiO_2 , *n*-pentane/ether=9/1) gave *o*-methylbenzaldehyde (**2h**) (73.3 mg, 85 %).
- (7) G. Brunton, D. Griller, C. R. C. Barclay, and K. U. Ingold, *J. Am. Chem. Soc.*, **98**, 6803 (1976).
- (8) Free-radical reduction of aromatic bromides and iodides with tin hydrides is not always a smooth reaction. The initial work employed forcing reaction conditions (excess amounts of tin hydride, high concentrations (often without solvent), and excessive heating). (a) A. L. J. Beckwith and W. B. Gara, *J. Chem. Soc. Perkin II*, 795 (1975). (b) D. H. Lorenz, P. Shapiro, A. Stern, and E. I. Becker, *J. Org. Chem.*, **26**, 2332, (1963). Becker's observation of the substituent effect that electron-withdrawing substituents are favorable for reduction is conflicting with our data.
- (9) Kinetic data for hydrogen abstraction from tin hydride by aroyl radical are not yet available.

(Received in Japan 30 July 1990)