May, 1985] © 1985 The Chemical Society of Japan NOTES Bull. Chem. Soc. Jpn., 58, 1597—1598 (1985) 1597

Biaryl Formation in the Copper(I) Mediated Arylation of Stable Enolate Anions with *o*-Halogenonitrobenzenes

Singanallore V. Thiruvikraman and Hitomi Suzuki*
Department of Chemistry, Faculty of Science, Ehime University, Bunkyo-cho, Matsuyama 790

(Received July 16, 1984)

Synopsis. *o*-Bromo- and *o*-iodonitrobenzenes react with stable enolate anions in hot DMF in the presence of copper(I) iodide, to afford not the expected arylation products but the coupling products, 2,2′-dinitrobiphenyls.

When heated in aprotic dipolar solvents such as DMF and HMPA in the presence of copper(I) iodide, nonactivated aromatic halides are activated to such an extent as to react with a variety of heteronucleophiles[1—7)] and enolate anions,[8—11)] giving the corresponding arylation products in good to moderate yields. However, moderately activated aryl halides such as halogenonitrobenzenes (**1**) behave differently from nonactivated ones to afford, in addition to the normal substitution product (**2**), significant amounts of *N,N*-dimethylanilines (**3**) and/or nitrobenzenes (**4**). Aryl-aryl coupling to form dinitrobiphenyls (**6**) is yet another unexpected pathway in the reaction of halogenonitrobenzenes, and is described herein.

Our attempts to prepare 2-(2-nitrophenyl)-3-oxobutanoate esters (**7**) as intermediates for the synthesis of heterocycles, by reacting *o*-bromo- or *o*-iodonitrobenzenes (**5**) with 3-oxobutanoate (acetoacetate) anion in the presence of copper(I) iodide in DMF at 100—120 °C, gave instead 2,2′-dinitrobiphenyls (**6a—6h**) as products. Table 1 lists several biphenyls obtained; in majority of cases their formation was achieved in good yields. The structures of all biphenyls were established by their elemental analyses, IR and ^{1}H NMR spectra, and agreement of their mps with those reported in literature. The effect of various enolate anions on the formation of dinitrobiphenyls is shown in Table 2. Also the role of enolate anion and copper(I) iodide is illustrated in Table 3.

Unlike the above cases, *m*-iodo- and *o*-chloronitrobenzenes suffered extensive reductive dehalogenation under similar conditions to give nitrobenzene as major product. Also *p*-iodonitrobenzene gave a mixture of ethyl 2-(4-nitrophenyl)-3-oxobutanoate and nitrobenzene accompained by a small amount of 4,4′-dinitrobiphenyl. Highly activated aromatic halides such as 2,4-dinitrochlorobenzene and 2,6- dinitroiodobenzene underwent normal S_NAr reaction without yielding any biphenyls.

As regards the mechanism which operates in the biphenyl formation, we withhold any comment at present, although it bears many features suggesting the involvement of electron transfer process.[12)]

Experimental

Reaction of o-Iodonitrobenzene (5a). Sodium hydride (0.04 g, 1 mmol; 60% suspension in paraffin oil) was placed in a 25 ml flask and triturated with dry hexane. The oil-free grey solid was then covered with DMF (0.73 g, 10 mmol), and ethyl 3-oxobutanoate (0.065 g, 0.5 mmol) was added with stirring. After several minutes when hydrogen evolution ceased, copper(I) iodide (0.18 g, 1 mmol) was added to the resultant yellow solution. The solution

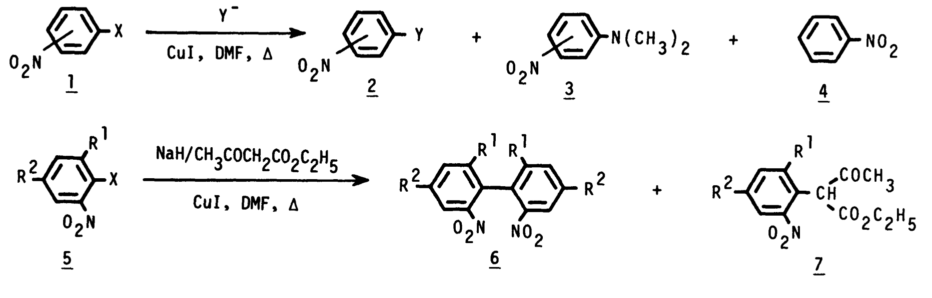

Table 1. 2,2′-Dinitrobiphenyls **6** from the copper(I) mediated reaction of *o*-halogenonitrobenzenes **5** with 3-oxobutanoate anion

	Starting halide **5**			Reaction time t/h	Temperature θ_m/°C	Dinitrobiphenyl **6**[a)]	
	R[1]	R[2]	X			Mp θ_m/°C	Yield/%
a [18)]	H	H	I	4	100	123—124[13)]	75
b [18)]	H	H	Br	6	140	123—124	55
c [19)]	CH_3	H	I	5	100	108[25)]	55
d [20)]	H	CH_3	I	5	100	140[26)]	65
e [21)]	H	CH_3	Br	7	140	140	40
f [22)]	H	CH_3O	I	4	100	131[b)]	70
g [23)]	H	CH_3O	Br	7	140	131[27)]	52
h [24)]	CO_2H	H	I	5	120	263—266[28)]	74

a) Melting points were uncorrected. Yields refer to the isolated compounds. b) Found: C, 55.53; H, 3.85; N, 9.09%. Calcd for $C_{14}H_{12}N_2O_6$: C, 55.27; H, 3.98; N, 9.21%.

Table 2. Influence of enolate nucleophiles on the yield of 2,2′-dinitrobiphenyl **6a**[a)]

Enolate nucleophile	Reaction time t/h	Temperature θ_m/°C	Product yield/%
Ethyl 3-oxobutanoate	4	100	75
2,4-Pentadione	3	80	71
1-Phenyl-1,3-butadione	3	60	83
Diethyl 3-oxopentadioate	3	70	74
Ethyl 3-phenyl-3-oxopropanoate	3	60	78
Diethyl malonate	5	110	50
Acetone	6	80	10
Ethyl 2-cyanoethanoate	6	80	—

a) Reaction conditions: Substrate **5a** 1.0 mmol, NaH 1.0 mmol, enolate 0.5 mmol, CuI 1 mmol, and DMF 10 mmol. Yields refer to the isolated ones.

Table 3. Influence of the amounts of enolate and catalyst, and temperature on the yield of 2,2′-dinitrobiphenyl **6a**[a)]

3-Oxobutanoate enolate/mmol	CuI/mmol	Temperature θ_m/°C	Product yield/%
0	1.0	100	~5
0.1			55
0.3			67
0.5			75
1.0			73
2.0			75
0.5	0	100	0
	0.15		54
	0.3		60
	0.5		65
	1.0		75
	2.0		74
0.5	1.0	140—150	60
		120	70
		100	75
		80	63
		30	—

a) Reaction conditions: Substrate **5a** 1.0 mmol, NaH 1.0 mmol, and DMF 10 mmol; reaction time 5—6 h. Yields refer to the isolated ones.

changed to orange color, and later to brown when *o*-iodonitrobenzene (0.249 g, 1 mmol) was added. The mixture was heated gradually to 100 °C and the progress of reaction was monitored by TLC. After 4 h the mixture was allowed to cool, poured into water (10 ml), and acidified to pH 5—6, and extracted twice with ether (2X15 ml). The combined extracts were washed with water, dried, and evaporated to yield crude 2,2′-dinitrobiphenyl (**6a**) as a pasty solid. It was purified by column chromatography over silica gel, followed by recrystallization from benzene/hexane to give yellow crystals of the product. Yield, 0.09 g (75%). Mp 123—124 °C (lit,[13] mp 123.5—124.5 °C).

Reaction of p-*Iodonitrobenzene.* The reaction was carried out at 140 °C using the same ratio of substrate, nucleophile, catalyst and solvent, as described above. After 4 h, when the reaction was over, the mixture was worked up as usual. The oily product obtained after removal of solvent consisted of three components as revealed by TLC. They were separated by column chromatography over silica gel to give nitrobenzene (0.037 g, 30%); 4,4′-dinitrobiphenyl (0.005 g, 4%), white solid melting at 238 °C (lit,[14] 237 °C); and ethyl 2-(4-nitrophenyl)-3-oxobutanoate[15] (0.10 g, 40%), yellow oil.

Reaction of 2, 4-Dinitrochlorobenzene. The reaction was carried out by stirring a mixture of halide (0.20 g, 1 mmol), sodium hydride (0.04 g, 1 mmol), keto ester (0.13 g, 1 mmol), copper(I) iodide (0.19 g, 1 mmol), and DMF (0.73 g, 10 mmol) at 60 °C for 3 h, and the reaction mixture was worked up as usual. The crude product obtained was further purified by column chromatography over silica gel to give ethyl 2-(2,4-dinitrophenyl)-3-oxobutanoate as pale yellow crystals. Yield, 0.266 g (90%). Mp 93—94 °C (lit,[16] mp 93—94 °C).

References

1) H. Suzuki, H. Abe, and A. Osuka, *Chem. Lett.*, **1980**, 1365.

2) H. Suzuki, H. Abe, N. Ohmasa, and A. Osuka, *Nippon Kagaku Kaishi*, **1980**, 445.

3) H. Suzuki, H. Abe, and A. Osuka, *Chem. Lett.*, **1981**, 151.

4) H. Suzuki, H. Abe, N. Ohmasa, and A. Osuka, *Chem. Lett.*, **1981**, 1115.

5) H. Suzuki and M. Shinoda, *Synthesis*, **1977**, 640.

6) H. Suzuki, K. Miyoshi, and M. Shinoda, *Bull. Chem. Soc. Jpn.*, **53**, 1765 (1980).

7) A. Osuka, N. Ohmasa, Y. Yoshida, and H. Suzuki, *Synthesis*, **1983**, 69.

8) A. Osuka, Y. Mori, and H. Suzuki, *Chem. Lett.*, **1982**, 2031.

9) H. Suzuki, T. Kobayashi, Y. Yoshida, and A. Osuka, *Chem. Lett.*, **1983**, 193.

10) A. Osuka, T. Kobayashi, and H. Suzuki, *Synthesis*, **1983**, 67.

11) H. Suzuki, S. V. Thiruvikraman, and A. Osuka, *Synthesis*, **1984**, 616.

12) R. A. Rossi and R. H. de Rossi, "Aromatic Substitution by the $S_{RN}1$ Mechanism," ACS Monograph 178 (1983).

13) R. C. Fuson and E. A. Cleveland, *Org. Synth.*, Coll. Vol. **III**, 339 (1965).

14) F. Ullmann and K. Fernaro, *Chem. Ber.*, **34**, 2177 (1901).

15) Z. Bankowska, D. Stopa, and I. Zadrozna, *Pol. J. Chem.*, **53**, 1563 (1979).

16) G. E. Hall, D. Hughes, D. Roe, and A. P. Rhodes, *Tetrahedron Lett.*, **1967**, 241.

17) M. A. F. Holleman, *Recl. Trav. Chim. Pays-Bas*, **32**, 136 (1913).

18) M. Schopft, *Chem. Ber.*, **23**, 1840 (1890).

19) M. T. Bogert and R. W. Allen, *J. Am. Chem. Soc.*, **49**, 1318 (1927).

20) St. von Niementowski, *Chem. Ber.*, **34**, 3325 (1901).

21) C. S. Gibson and J. D. A. Johnson, *J. Chem. Soc.*, **1929**, 1229.

22) H. Hahle, *J. Prakt. Chem.*, **43**, 62 (1891).

23) R. V. Henley and E. E. Turner, *J. Chem. Soc.*, **1930**, 928.

24) P. J. Culhane, *Org. Synth.*, Coll. Vol. 1, 125 (1967).

25) F. Ullmann and L. Frentzel, *Chem. Ber.*, **38**, 725 (1905).

26) F. Ullmann and W. R. Forgan, *Chem. Ber.*, **34**, 3802 (1901); R. B. Carlin and G. E. Flotz, *J. Am. Chem. Soc.*, **78**, 1997 (1956).

27) J. Gerald, Ger. Offen., 2939259 (1980); *Chem. Abstr.*, **94**, 22884j (1981).

28) R. Kuhn and O. Albrecht, *Justus Liebigs Ann. Chem.*, **455**, 272 (1927).