Tetrahedron Letters No. 22, pp 1871 - 1874, 1977. Pergamon Press. Printed in Great Britain.

CROWN-CATION COMPLEX EFFECTS. VI.
A PHASE TRANSFER CATALYTIC SYNTHESIS OF UNSYMMETRICAL BIARYLS

Stephen H. Korzeniowski, Lorna Blum and George W. Gokel*
Department of Chemistry
The Pennsylvania State University
University Park, PA 16802 USA

(Received in USA 27 October 1976; received in UK for publication 19 April 1977)

There are numerous methods reported in the literature for the preparation both of symmetrical and unsymmetrical biaryls. The classical methods include the Gomberg-Bachmann-Hey reaction,[1] the Ullmann reaction[2] and Kharasch's coupling of Grignard derived aryl radicals.[3] In recent years, a number of new methods (especially involving organometallic reagents[4]) have become available, some of which afford impressive yields of the desired coupling products.[5]

We wish to report the preparation of a wide variety of mixed biaryls in good to excellent yield by a phase transfer catalytic Gomberg-Bachmann-Hey reaction. Potassium acetate, phase-transferred into non-polar solution by the presence of 18-crown-6,[6] reacts with aryldiazonium ion, apparently forming a diazoanhydride. Decomposition of the diazoanhydride in the presence of various arenes leads to coupling products between the aryl radicals and the arene. This variation of the G-B-H reaction affords much higher yields than are traditionally realized by this method. A representative set of results is presented in the table. The overall yields reported there are for the conversion of the aniline into the biphenyl *via* the aryldiazonium ion. The literature yield is the best yield hitherto reported for the corresponding G-B-H process.

We have found that mixed biaryls can be successfully prepared from diazonium compounds bearing either electron releasing or electron attracting substituents. In addition, the radical coupling process succeeds in benzene, mesitylene and thiophene as well as several other solvents. The reaction is successful when potassium acetate is used as initiator or when either potassium propionate, sodium hydroxide, potassium hydroxide or potassium carbonate is substituted for it, but the yields are less satisfactory. We believe that the reaction occurs according to the established mechanism[7] as shown below.

$$\text{Ar-N}_2{}^+\text{BF}_4{}^- \ + \ \enclose{circle}{\text{K}^+}\ {}^-\text{OAc} \ \rightleftarrows \ \text{KBF}_4 \ + \ \text{Ar-N=N-OAc}$$

$$\text{Ar-N=N-OAc} \ + \ \text{AcO}^- \ \rightarrow \ \text{Ar-N=N-O}^- \ + \ \text{Ac}_2\text{O}$$

$$\text{Ar-N=N-O}^- \ + \ {}^+\text{N}_2\text{-Ar} \ \rightarrow \ \text{Ar-N=N-O-N=N-Ar}$$

$$\text{Ar-N=N-O-N=N-Ar} \ \rightarrow \ \text{Ar-N=N-O}^\cdot \ + \ \text{N}_2 \ + \ \text{Ar}^\cdot$$

$$\text{Ar}^\cdot \ + \ \text{C}_6\text{H}_6 \ \rightarrow \ \text{Ar-C}_6\text{H}_5$$

An important advantage of the method is that the stable, well-behaved aryldiazonium tetrafluoroborates and hexafluorophosphates can be used as solid reagents. In the presence of potassium acetate, a metathetical gegenion exchange process takes place resulting in formation of the transient diazoacetate.[7,8] It is in this step we believe the crown plays a crucial role.[8] In the absence of crown, a much poorer yield results in a comparable time, and even if the reaction is allowed to proceed ten times longer, a poorer ultimate yield of biaryls is obtained.[9] Once the reaction is initiated in non-polar solution, it proceeds smoothly at or below room temperature in one to two hours. In most cases, a filtration chromatography removes crown, any residual salt, diazo-tars and other by-products, yielding biaryls of high purity. A detailed experimental procedure is given below.

Preparation of 4-Chlorobiphenyl

Potassium acetate (1.20 g, 0.0122 mol) is added in one portion to a stirred, colorless mixture of 4-chlorobenzenediazonium tetrafluoroborate (1.37 g, 0.061 mol) and 18-crown-6 (0.080 g, 0.0003 mol) in benzene (60 ml) at 20°C in a vessel protected from the light and purged by a nitrogen atmosphere. The mixture becomes yellow immediately and then red within a few minutes. Stirring is continued for 90 minutes, followed by filtration to remove the solid. The resulting solution is washed with brine, water, then dried over sodium sulfate and the solvent is removed *in vacuo*. The resulting red oil is chromatographed on a short column of alumina using hexane as eluant, from which is obtained 4-chlorobiphenyl (0.920 g, 80%) as white flakes, mp 76-77°C. Lit. mp 77°C.

Acknowledgment. We warmly thank the Research Corporation and the Donors of the Petroleum Research Fund, administered by the American Chemical Society, for grants which supported this work.

TABLE

Phase Transfer Catalytic Synthesis of Biaryls

$$Y\text{-}C_6H_4\text{-}N_2{}^+BF_4{}^- \xrightarrow[\text{KOAc, Ar-H}]{\text{18-crown-6}} Y\text{-}C_6H_4\text{-Ar}$$

Y	Arene	Time (hr)	m-% 18C6	Product	Yield[a]	Overall Yield[b]	Lit. Yield[c]	MP	Lit.MP
4-MeO	benzene	1.5	0.075	4-methoxybiphenyl	80	66	25[d]	89	89[d]
4-Me	benzene	1.5	0.075	4-methylbiphenyl	73	51	22[d]	46-47	46[d]
3-Me	benzene	1.5	0.050	3-methylbiphenyl	58	47	28[e]	-----	---
4-H	benzene	1.5	0.025	biphenyl	62	54	22[d]	69	70[d]
4-Br	benzene	1.5	0.100	4-bromobiphenyl	81	65	44[d]	90	90[d]
4-Br	benzene	1.0	0.025	4-bromobiphenyl	77	62	---	90	90[d]
4-Br	benzene	1.0	-----	4-bromobiphenyl	11	9	---	90	90[d]
4-Br	benzene	24.0	-----	4-bromobiphenyl	(64)[g]	51	---	--	90[d]
2-Br	benzene	1.5	0.075	2-bromobiphenyl	81	63	---	--	---
4-Cl	benzene	1.5	0.050	4-chlorobiphenyl	80	64	40[f]	76-77	77[d]
4-Cl	mesitylene	1.5	0.025	2,4,6-trimethyl-4'-chlorobiphenyl	55	44	--[h]	64-65	---
4-Cl	thiophene	1.5	0.050	4-(2-thienyl)-chlorobenzene	62[i]	49	33[j]	81-82.5	83[j]
4-F	benzene	1.5	0.075	4-fluorobiphenyl	60	46	---	73-74	74[k]
$4\text{-}NO_2$	benzene	1.5	0.075	4-nitrobiphenyl	85	76	60[d]	114	114[f]
$4\text{-}NO_2$	thiophene	1.5	0.050	4-(2-thienyl)-nitrobenzene	38	34	23[f]	136-7	137-8[f]

(a) Isolated yield of ≥99% pure material, based on diazonium salt. (b) Yield based on aniline. Neither conversion was optimized so the values reported are minimum yields. (c) These values are the best available literature values for synthesis of the biaryls by a G-B-H reaction. (d) See reference 10. (e) See reference 11. (f) See reference 12. (g) Yield determined by glpc analysis. (h) See reference 4b. (i) Product ≥95% pure by glpc analysis. (j) See reference 13. (k) See reference 14.

Notes and References

1. a) W.E. Bachmann and R.A. Hoffman, Organic Reactions, 2, 224 (1944).
   b) O.C. Dermer and M.T. Edmison, Chem. Rev., 57, 77 (1957).

2. P.E. Fanta, Synthesis, 9 (1974).

3. L.F. Elsom, J.D. Hunt and A. McKillop, Organomet. Chem. Rev., A8, 135 (1972).

4. a) A. McKillop, L.F. Elsom and E.C. Taylor, Tetrahedron, 26, 4641 (1970).
   b) H.C. Bell, J.R. Kalman, J.T. Pinhey and S. Sternhell, Tetrahedron Letters, 857 (1974).
   c) J. Bergman, Tetrahedron, 28, 3323 (1972).
   d) R.A. Kretchmer and R. Glowinski, J. Org. Chem., 41, 2661 (1976).
   e) M.F. Semmelhack, P.M. Helmquist and L.D. Jones, J. Amer. Chem. Soc., 93, 5908 (1971).

5. For photochemical methods, see:
   a) E.C. Taylor, H.W. Altland, F. Kienzle and A. McKillop, J. Org. Chem., 41, 24 (1976).
   b) W. Wolf and N. Kharasch, J. Org. Chem., 30, 2493 (1965).

   For oxidative coupling methods, see:
   c) E.C. Taylor, A.G. Turrell and A. McKillop, J. Org. Chem., 42, 764 (1977).
   d) S.M. Kupchan, A.J. Liepa, V. Kameswaran and R.F. Bryan, J. Amer. Chem. Soc., 95, 6861 (1973).
   e) R.E. Damon, R.H. Schlessinger and J.F. Blount, J. Org. Chem., 41, 3772 (1976).

   For thermal coupling methods, see:
   f) D.H. Hey, Adv. Free Radical Chem., 2, 47 (1966).

6. G.W. Gokel, D.J. Cram, C.L. Liotta, H.P. Harris and F.L. Cook, J. Org. Chem., 39, 2445 (1974).

7. a) C. Rüchardt and B. Freudenberg, Tetrahedron Letters, 3623 (1964).
   b) C. Rüchardt and E. Merz, Tetrahedron Letters, 2431 (1964).

8. S.H. Korzeniowski and G.W. Gokel, Tetrahedron Letters, 1977 (in press).

9. In the presence of the radical scavenger 1,1-diphenylethylene (1 eq.) the yield of biphenyl from 4-bromobenzenediazonium ion decreased from 81% to 12%. A similar, though not quite as dramatic decrease in yield was observed in the presence either of hydroquinone or air.

10. J. Elks, J.W. Haworth and D.H. Hey, J. Chem. Soc., 1284 (1940).

11. M. Gomberg and J.C. Pernert, J. Amer. Chem. Soc., 48, 1372 (1926).

12. M. Gomberg and W.E. Bachmann, J. Amer. Chem. Soc., 46, 2339 (1924).

13. N.P. Buu-Hoi and N. Hoan, Rec. Trav. Chim., 69, 1455 (1950).

14. G. Schiemann and W. Roselius, Chem. Ber., 62, 1805 (1929).