run. Alkali iodide or bromide was dried in vacuo for 12 h at 120-130 °C.

Substrates. Aromatic halides were purchased from commercial sources (Aldrich, Fluka, Merck, Lancaster Synthesis) and were used without further purification.

General Procedures. *t*-AmOH (20 mmol) in 10 mL of reaction solvent was added dropwise to a suspension of degreased NaH (60 mmol) and dried $Ni(OAc)_2$ (10 mmol) in refluxing reaction solvent (30 mL) containing bpy (20 mmol). Time and temperature preparation was dependent upon the nature of the solvent (see Table I). The aryl halide (10 mmol) was added 1 h after addition of alkali iodide (10 mmol) or bromide with 10 mL of reaction solvent. The reaction was monitored by GC analysis of small aliquats. The internal standard was hydrocarbon (C_8-C_{12}).

GC analyses were performed on a 10-ft SE 30 column (temperature/pressure): benzene (50 °C/1 bar), toluene (80 °C/1 bar), halogenobenzene (160 °C/1.5 bar), anisole (120 °C/1.5 bar), (trifluoromethyl)benzene (80 °C/1 bar), other products (160 °C/1.5 bar).

After completion of the reaction, the excess hydride was carefully destroyed by dropwise addition of EtOH at 25 °C until hydrogen evolution ceased. The mixture was then acidified (except for halodimethylaniline, where diluted NH_4OH was used) and the organic phase was extracted into diethyl ether and dried over $MgSO_4$. After removal of the solvents, products were separated by flash chromatography. They were characterized by their spectroscopic data (IR, ^1H, ^{13}C) and melting point.

Procedures. Method A [NaH-*t*-AmONa-Ni(OAc)$_2$-bpy in THF]. The NiCRA-bpy was prepared in THF without alkali halide. Preparation time of the reagent was 2 h.

Method B [NaH-*t*-AmONa-Ni(OAc)$_2$-bpy-KI in THF]. The NiCRA-bpy was prepared in THF following method A. Alkali (potassium) iodide (10 mmol) was then added. After 1 h of stirring at 63 °C, the reagent was ready for use.

Method C [NaH-*t*-AmONa-Ni(OAc)$_2$-bpy-KI in Benzene]. The reagent was prepared following method A but replacing THF by a mixture of 50 mL of benzene and 50 mmol of THF. In this case, the preparation time of reagent is 4 h. KI was then added as in method B.

2,2′-Bis(trifluoromethyl)biphenyl: mp 33 °C; IR (film) 1310 (CF), 1100-1200 cm^{-1} (ArC); ^1H NMR (CCl_4) δ 7.2-8.0 (m). Anal. Calcd for $C_{14}H_8F_6$: C, 57.94; H, 2.75; F, 39.28. Found: C, 57.99; H, 2.82; F, 38.36.

3,3′-Bis(trifluoromethyl)biphenyl: liquid; IR (film) 1330 (CF), 1130 cm^{-1} (ArC); ^1H NMR (CCl_4) δ 7.4-8.0 (m). Anal. Calcd for $C_{14}H_8F_6$: C, 57.94; H, 2.78; F, 39.28. Found: C, 58.15; H, 2.80; F, 38.57.

4,4′-Bis(trifluoromethyl)biphenyl: mp 89 °C; IR (KBr) 1620, 1330 (CF), 1130 cm^{-1} (ArC); ^1H NMR (CCl_4) δ 7.75 (s, Ar). Anal. Calcd for $C_{14}H_8F_6$: C, 57.94; H, 2.78; F, 39.28. Found: C, 57.78; H, 2.62; F, 38.84.

3,3′-Difluorobiphenyl: liquid; IR (film) 1260 cm^{-1} (CF); ^1H NMR ($CDCl_3$) δ 7.2-7.6 (m, Ar). Anal. Calcd for $C_{12}H_8F_2$: C, 75.78; H, 4.24; F, 19.98. Found: C, 75.79; H, 4.56; F, 19.72.

3,3′-Diformylbiphenyl: mp 90 °C; IR (KBr) 1700 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 7.6-8.2 (m, Ar, 8 H), 10.15 (s, CHO, 2 H). Anal. Calcd for $C_{14}H_{10}O_2$: C, 79.98; H, 4.79. Found: C, 79.56; H, 4.73.

3,3′-Diacetylbiphenyl: mp 120 °C; IR (KBr) 1690 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 2.55 (s, CH_3CO, 6 H), 7.4-8.2 (m, Ar, 8 H). Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.57; H, 5.86.

Acknowledgment. We are grateful to the Centre National de la Recherche Scientifique for a financial support. We thank the referees for help and comments.

Activation of Reducing Agents. Sodium Hydride Containing Complex Reducing Agents. 32. NiCRAL's as Very Efficient Agents in Promoting Cross-Coupling of Aryl Halides

Mouhsine Lourak, Régis Vanderesse, Yves Fort, and Paul Caubère*

Laboratoire de Chimie Organique I, Faculté des Sciences, Domaine Scientifique Victor Grignard, Unité Associée au CNRS No. 203, B.P. 239, 54506 Vandoeuvre-les-Nancy Cédex, France

Received March 2, 1989

Nickel-containing complex reducing agents NiCRA-bpy are shown to be the first nickel reagents able to efficiently perform cross-coupling of aryl halides. The presence of KI in the reaction medium generally improves the procedure. The mechanism and influence of the structures of the substrates are discussed.

Introduction

In the preceding paper[1] we have shown that NiCRA-bpy[2] are very useful in performing coupling of aryl halides (Ullmann-type reaction).[3] On the other hand, it is well-known that copper-promoted cross-coupling of these substrates is a difficult task.[3] An alternative mixed cross-coupling procedure using Ni or Pd catalysts leads to little or no homocoupled byproducts.[3f] However, it necessitates the previous preparation of an organometallic reagent. It must be emphasized that none of the direct nickel procedures described till now succeeded in such reactions.[3]

Short exploratory experiments performed with NiCRA-bpy and briefly reported in a preliminary communication[4] indicated that these reagents could be of interest in per-

(1) For paper 31, see: Lourak, M.; Vanderesse, R.; Fort, Y.; Caubère, P. *J. Org. Chem.*, previous paper in this issue.

(2) Caubère, P. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 599. In this paper we have adopted the following convention: a NiCRA prepared from NaH, *t*-AmONa, and nickel acetate will be abbreviated NiCRA ($x/y/z$) where the molar ratio NaH/*t*-AmONa/$Ni(OAc)_2$ (in that order) is equal to $x/y/z$. In the same way, a NiCRAL prepared from NaH, *t*-AmONa, nickel acetate, and 2,2′-bipyridine or triphenylphosphine will be abbreviated NiCRAL ($x/y/z/t$) where the molar ratio NaH/*t*-AmONa/$Ni(OAc)_2$/2,2′-bipyridine or triphenylphosphine (in that order) is equal to $x/y/z/t$.

(3) (a) Fanta, P. E. *Chem. Rev.* **1964**, *64*, 613. (b) Bacon, R. G. R.; Hill, H. A. O. *Q. Rev.* **1965**, *19*, 95. (c) Normant, J. F. *Synthesis* **1974**, 63. (d) Fanta, P. E. *Synthesis* **1974**, 9. (e) Sainsbury, M. *Tetrahedron* **1980**, *36*, 3327. (f) Negishi, E.-I.; King, A. O.; Okukado, N. *J. Org. Chem.* **1977**, *42*, 1821.

(4) (a) Lourak, M.; Vanderesse, R.; Fort, Y.; Caubère, P. *Tetrahedron Lett.* **1988**, *29*, 545. (b) Vanderesse, R.; Fort, Y.; Lourak, M.; Caubère, P. 7th IUPAC Conference, Nancy, France, 1988.

(5) Brymnar, J.; Sleight, J. P. *J. Chem. Soc.* **1954**, 1775.

(6) Cymerman, J. C.; Loder, J. W. *J. Chem. Soc.* **1956**, 100.

(7) Dovgosheya, M. I.; Millner, R. S. *Zh. Doshchkhim.* **1964**, *34*, 977.

(8) American Cyanamid Co.; Neth. Appl. 6, **1966**, *516*, 582.

(9) Khastgir, H. N.; Bhattacharyya, B. K. *Science Culture* **1948**, *14*, 40.

0022-3263/89/1954-4844$01.50/0 © 1989 American Chemical Society

Table I. Cross-Coupling Reactions of Aryl Halides by NiCRA-bpy [4/2/1/2] at 63 °C

entry	X	Z	X′	Z′	method[a]	time, h	% global yield[b]	% yield cross-coupling[b]	proportions ArAr	ArAr′	Ar′Ar′	R[c]	ref lit.
1	Br	*o*-Me	Cl	*m*-F	C	1	89	62[d]	15	69.4	15.5	1.33	
2	Br	*m*-Me	Cl	*p*-CF_3	C	1	91	55[d]	19	61	20	0.75	
3	Br	*p*-Me	Cl	*m*-F	C	1.5	85	47[d]	21.8	55.4	22.8	0.8	
4	Br	*p*-Me	Cl	*p*-CF_3	C	1.25	89	52[d]	19.6	58	22.3	0.8	
5	Br	*o*-OMe	Cl	*p*-F	C	2	79.5	43	22	54	24	0.5	
6	Br	*o*-OMe	Cl	*p*-CF_3	C	1.5	80.6	51	17.3	63.2	19.4	2	
7	Br	*m*-OMe	Cl	*p*-CF_3	A	2	91	57	22	62.7	15	0.375	
8	Br	*m*-OMe	Cl	*p*-CF_3	C	3	89.6	55	16.5	61.3	22	0.33	
9	Br	*p*-OMe	Cl	*p*-F	C	1	92	72	11	78	11	0.75	5
10	Br	*p*-OMe	Cl	*p*-$CH(OMe)_2$	C	1	88.6	67[e]	11.5	75.6	12.8	0.75	6
11	Br	*p*-OMe	Cl	*p*-$CMe(OCH_2)_2$	C	1.5	88.4	62[e]	13.7	70	16	0.5	7
12	Br	*p*-OMe	Cl	*p*-CF_3	A	1.75	83.7	63	8.1	75.3	16.5	0.7148	8
13	Br	*p*-OMe	Cl	*p*-CF_3	B	0.4	92.5	71	12	76.8	11	0.625	8
14	Br	*p*-OMe	Cl	*p*-CF_3	C	1	90	73	10	81	9	0.75	8
15	Br	*p*-SMe	Cl	*p*-CF_3	C	2.5	83.5	61	9.5	73.5	17	0.8	
16	I	*p*-OMe	Cl	*p*-CF_3	A	1	78	53	21	67.8	11.1	0.75	8
17	I	*p*-OMe	Br	*p*-CF_3	A	1	87	56.4	19	65	16	0.75	8
18	Br	*o*-OH	Cl	*p*-F	C	3	79	43	20.4	54.4	25	0.33	
19	Br	*p*-OH	Cl	*p*-F	C	1.5	83	47	19.4	56.4	24	0.66	
20	Br	*p*-OH	Cl	*p*-$CH(OMe)_2$	C	1.75	87	63[e]	12.5	72.4	15	1	
21	Br	*p*-OH	Cl	*p*-CF_3	C	0.75	86	50	22.6	58	19.4	1.5	
22	Br	*p*-OH	Cl	*p*-CN	C	4	96	70	14.2	72.5	13.3	0.70	
23	Br	*p*-NMe_2	Cl	*p*-F	C	3	93	66	13.7	71	15.3	1.5	
24	Br	*p*-NMe_2	Cl	*p*-CF_3	C	2.5	86.4	62	14	71.75	14.3	2.5	
25	Br	*p*-Me	Br	*p*-OMe	A	0.25	96	52	23.5	53.6	21.8	1	9
26	Br	*p*-OMe	Br	*p*-CF_3	A	1.5	92	63	14	68.3	17.6	2	8
27	Br	*p*-OMe	Cl	*o*-F	C	2.75	73	36	29	49	21.4	0.363	
28	Br	*p*-OMe	Cl	*m*-F	C	1.25	83	38	29	45.6	25	0.8	
29	I	*p*-OMe	Br	*p*-Me	A	1	77.8	40	23	51.4	25.4	0.5	
30	Cl	*p*-Me	Cl	*p*-OMe	A	17	94.4	47	26.6	49.7	23.6	1.13	
31	Br	*o*-OMe	Cl	*o*-F	C	2.5	65.2	20	38.6	30.6	30.6	0.4	
32	Br	*o*-OMe	Cl	*m*-$CH(OCH_2)_2$	C	2	71	22[e]	31.4	31	37.4	0.375	
33	Br	*o*-OMe	Cl	*o*-CF_3	C	4	71	21	35.7	29.7	34.6	0.25	
34	Br	*m*-OMe	Cl	*p*-F	C	4	81	25	39	30.8	30	0.375	
35	Br	*p*-OMe	Cl	*m*-$CH(OCH_2)_2$	C	2	77.5	25[e]	35	32	33	0.375	
36	Br	*p*-OMe	Cl	*o*-CF_3	C	2.5	64	19	36.7	29.7	33.6	0.4	
37	Br	*o*-OH	Cl	*o*-F	C	3	83	34	28	41	30.5	0.33	
38	Br	*o*-OH	Cl	*o*-CF_3	C	3.5	88.6	35	31	39.5	29.3	0.428	
39	Br	*o*-OH	Cl	*p*-CF_3	C	2	81	40	26.6	24	49.4	0.375	
40	Br	*p*-OH	Cl	*o*-F	C	2.75	63	25	33.8	39.5	26.6	0.545	
41	Cl	*p*-Me	Br	*p*-OMe	A	3	84.4	20	31.1	23.7	42.2	6	
42	Cl	*p*-Me	Br	*p*-OMe	C	3	83.8	28	34.4	33.4	32.2	4	
43	Cl	*p*-Me	I	*p*-OMe	A	1.5	73.4	14	53.9	19	26.8	3	
44	Cl	*p*-OMe	Br	*p*-Me	A	4.5	74.4	16	41	21	38	9	
45	Cl	*p*-OMe	I	*p*-Me	A	2.5	65.8	10	52.6	15.2	32.1	10	
46	Cl	*p*-OMe	Cl	*p*-CF_3	A	2.5	80.4	20	38.3	24.8	36.8	2.5	8
47	I	*p*-Me	Br	*p*-OMe	A	0.75	66.4	21	45.2	31.6	23.2	1	

[a] See Experimental Section. [b] Isolated yields. [c] R = time of disappearance of ArX/time of disappearance of Ar′X′. [d] Yield determined by GC analysis. The identification of the products was made by mass spectroscopy coupled to GC. [e] Isolated as deprotected product.

forming a number of such cross-couplings.

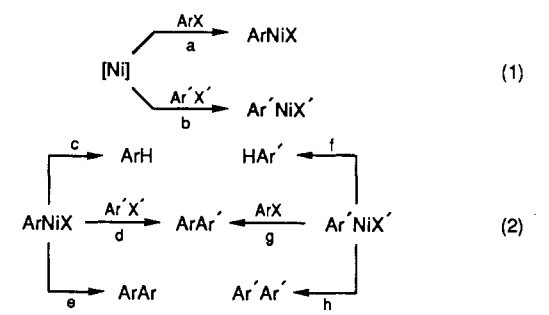
In the present paper we report full details concerning the scope and limitation of these condensations.

Results and Discussion

The short exploratory study showed that replacement of bpy by ligands such as Ph_3P, Bu_3P, $(PhO)_3P$, or *o*-phenanthroline considerably decreases either the global yield or the yield of cross-coupling product. It also appeared that the three procedures described in the preceding paper (NiCRA-bpy in THF without KI (method A), with KI (method B), in C_6H_6–small amount of THF with KI (method C)) were nearly equivalent, although method C was sometimes slightly superior.

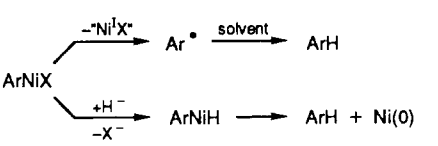
With these results in hand we performed a number of couplings; the results are gathered in Table I. Moreover, monitoring every condensation by GC analysis, we have determined the time of complete disappearance of each aryl halide. Their ratios R (also reported in the table) reflect the relative reactivity of the halides against Ni-CRA-bpy.

Scheme I[a]



[a] Ligands omitted.

Scheme II



We will first make short general comments. We have symbolized in Scheme I the main reactions occurring during the coupling of two different aryl halides.

It soon appears why obtaining acceptable yields in cross-coupling is an actual challenge. Indeed, if both substrates react identically statistical results must be expected with a ratio ArAr/ArAr′/Ar′Ar′ equal to 25/50/25, the global yield only depending on the amount of global reduction. When one of the aryl halides (for example, ArX) is reduced very rapidly, Ar′X′ will lead to Ar′Ar′ and Ar′H and yields in cross-coupling will be very low. This occurs when ArX reacts rapidly with nickel species to give an intermediate complex very unstable and/or easily reduced by hydrides of the reagent.

On the contrary the best results in cross-coupling will be obtained when (Scheme I) (a + d) or (b + g) occur as the only reactions. Note that from a synthetic point of view if the only side reactions are reductions (c + f) and if they are not the main reactions observed, the condensation may be of interest. Thus good yields in cross-coupling will be obtained if, for example, ArX reacts much more rapidly than Ar′X′ with nickel species to give a complex stable enough and very reactive against Ar′X′. Of course the reaction actually observed will be intermediate between these extreme situations.

Finally, it must be noted that when ArX and Ar′X′ are not reduced at the same rate, the amounts of each homo-coupling product differ. Of course, to the most easily reduced aryl halide will correspond the lowest yield in homo-coupling.

Coming back to the results reported in the table, it appears that a number of interesting observations emerge.

With few exceptions, overall yields of coupling vary from good to excellent; the lower were essentially due to reduction. As an illustration of the near equivalence of the different coupling procedures we have reported the condensation of two couples of substrates under different conditions (runs 7–8 and 12–14). It appeared that as far as global and cross-coupling yields were concerned, the differences observed are not very large and above all cannot be predicted. Thus methods A and C are equivalent in runs 7 and 8 while method A appears as slightly less efficient than method B and C in runs 12 to 14.

In a number of experiments (runs 1–26) the statistical ratio was overpassed in favor of the cross-coupling derivatives, which were isolated in good yields. Moreover, even when the yield ratios were not too much below the statistical one (runs 27–30) cross-coupling products were isolated in acceptable moderate yields.

It is well-known that in a copper-promoted Ullmann reaction, reactivity of aryl halides follows the classical trend I > Br ≫ Cl ≫ F. Moreover, electron-withdrawing and, to a lesser degree, electron-donating groups increase the reactivity of a given aryl halide.

If we consider run 26 concerning condensation of two aryl bromides, it appears, according to this statement as well as to our preceding results,[1] that p-$F_3CC_6H_4Br$ was more reactive than p-$MeOC_6H_4Br$ (R = 2).

Comparison of the relative yields of homo-couplings shows that an aryl halide with an electron-donating group was more prone to reduction. This is confirmed by results of runs 25 and 30 where p-methoxy-substituted aryl halides were more easily reduced than p-methyl ones. Note that aryl chlorides are more sensitive than aryl bromides to this effect.

Comparison of runs 12 and 26 shows that cross-coupling was favored by condensing a given aryl halide substituted by an electron-donating group with an aryl halide whose halogen was less reactive but substituted by an electron-withdrawing group. This conclusion was confirmed by runs 16 and 17 and by a number of experiments not reported in the present work. The condensation of a given aryl halide substituted by an electron-withdrawing group with a less reactive one substituted by an electron-donating group led to low yields of cross-coupling. Interestingly, the condensation of an aryl bromide substituted by a weak electron-withdrawing group such as m-methoxy (Hammett constant σ = 0.10) with an aryl chloride substituted by a sufficiently strong electron-withdrawing group such as p-CF_3 (σ = 0.53) still led to a good yield in cross-coupling (runs 7 or 8). However, replacement of p-CF_3 by p-F (σ = 0.15) dramatically increases the yield of the homo-coupling (run 34).

According to the polymeric nature of NiCRA's,[1] steric effects must be expected as playing an important part in this condensation. According to this statement o-MeC_6H_4Br was found to be slightly less reactive (R = 1.33) (run 1) and p-MeC_6H_4Br more reactive (R = 0.50) (run 3) than m-FC_6H_4Cl. Aryl bromides being, for a given substitution, more reactive than chlorides, this inversion of reactivity led to an increase of homo-coupling in run 3 compared to run 1. In other words, steric hindrance regulated the reactivities and favored the cross-coupling!

From the above conclusions it must be expected that an increase in the reactivity of the aryl chloride condensed on p-MeC_6H_4Br under the conditions of run 3 would lead to an increase in cross-coupling. This expectation was completely verified (run 4).

The favorable effect of strong electron-donating groups explains that o-$MeOC_6H_4Br$ was more reactive than p-FC_6H_4Cl (run 5). However, the electronic effect was not sufficient to balance the steric effect against the much more reactive p-$F_3CC_6H_4Cl$ in run 6. Again in run 5 the yield of homo-coupling was slightly higher than that in run 6.

Now, if we look at run 9, where p-$MeOC_6H_4Br$ was condensed with p-FC_6H_4Cl, it appears that coupling was faster and the yield in cross-coupling higher than that in run 5. This reflects a higher reactivity of the unhindered electron-rich intermediate complex against p-FC_6H_4Cl. An increase in the reactivity of the aryl chloride (run 14) still increased the relative amount of cross-coupling as expected from our above conclusions.

Couplings of bromophenols and p-$Me_2NC_6H_4Br$ (runs 21–24) are more difficult to explain. Indeed, in our reaction medium phenols were in phenate forms, which can give some complexes with NiCRA-bpy, and anilines may be liganded to Ni(0) species. These complexations introduced new unknown parameters.

In fact o- and p-bromophenols obey the same law as bromoanisoles as far as they are condensed with p-FC_6H_4Cl (runs 18 and 19). However, the condensation of p-HOC_6H_4Br with p-$F_3CC_6H_4Cl$, the relative reactivities were reversed. In the same way p-$Me_2NC_6H_4Br$ was found to be less reactive than p-$F_3CC_6H_4Cl$ (run 24) and even than p-FC_6H_4Cl (run 22).

Finally it is worthy of note that in a number of cases good results in cross-coupling were obtained, with aryl halides disappearing much more rapidly than their partner. This means that the intermediate nickel complex was sufficiently stable to survive until it was attacked by the other aryl halide. However, we never succeeded in a two-step condensation, the intermediates were not stable enough.

Many of the low yields in cross-coupling may be explained with the help of the above conclusions.

Thus, it must be expected that condensation of a very reactive aryl halide with an unsufficiently activated one would lead to a decrease of the relative amount of cross-coupling and, possibly, to an increase of the side reduction. Thus (run 36) when the very reactive p-$MeOC_6H_4Br$ was condensed with the very hindered o-$CF_3C_6H_4Cl$, the yield of cross-coupling was low and the yield of homo-coupling was greater than the statistical ratio. The same results were obtained when both halides were hindered (runs 31 and 33).

Finally, the low yields in cross-coupling observed in runs 43, 45, and 47 were a consequence of the marked propensity of aryl iodides to be reduced by NiCRA's.[1]

Conclusion

NiCRA-bpy is the first nickel-containing reagent that allows achievment of Ullmann-type cross-coupling in good yields and under mild conditions. The highest electronic unbalance between the substrates gives the highest yields in coupling. Work is continuing in order to make these condensations catalytic in metal.

Experimental Section

Instrumentation. GC analyses were performed on a Girdel 330 apparatus (flame-ionization detector) equipped with 10-ft SE 30 columns. IR spectra were recorded on a Perkin-Elmer spectrophotometer (Model 580B) and ^1H NMR spectra on a Perkin-Elmer R12B (60 MHz) or a Bruker AW80 (80 MHz) instrument, ^{13}C NMR spectra on a Bruker AM400 (400 MHz) instrument. GC/MS spectra were performed on a Nermag/Sidar (70 eV) apparatus. Melting points were performed on either a Koffler or a Tottoli apparatus. All reactions were carried out under nitrogen (nitrogen R, L'Air Liquide). Silica flash chromatography was performed on Kieselgel 60 (230–400 mesh) with petroleum ether/ether or EtOAc mixtures as eluant.

Materials. Fluka sodium hydride (55–60% in oil) was used after three washings with the reaction solvent under nitrogen. Each batch of sodium hydride was titrated by standard techniques. Nickel acetate (Aldrich) was dried in vacuo for 12 h at 120–130 °C. 2,2′-Bipyridine (Fluka) was recrystallized before use. Ph_3P, Bu_3P, $(PhO)_3P$, and o-phenanthroline were used without further purification. *tert*-Amyl alcohol was distilled from sodium. Alkali iodide or bromide was dried in vacuo for 12 h at 120–130 °C.

Solvents. THF was distilled from a benzophenone–sodium adduct and stored over sodium wires. Benzene was distilled from sodium adduct and stored over sodium wires. For THF, the absence of peroxides was checked before each run.

Procedures. Method A (NaH–*t*-AmONa–Ni(OAc)$_2$-bpy in THF). *t*-AmONa (20 mmol) in 10 mL of THF was added dropwise to a suspension of degreased NaH (60 mmol) and $Ni(OAc)_2$ (10 mmol) in refluxing THF (30 mL) containing bpy (20 mmol). After 2 h of stirring at 63 °C, the reagent was ready for use. The mixture of both aryl halides (5 mmol and 5 mmol) was then added along with the internal standard (hydrocarbons C_8–C_{12}) and 10 mL of THF, and the reaction was monitored by GC analysis of small aliquots (10-ft column SE 30, 160 °C/1.5 bar).

After completion of the reaction, the excess hydride was carefully destroyed by dropwise addition of EtOH at 25 °C until hydrogen evolution ceased. The mixture was then acidified (except for halodimethylaniline where diluted NH_4OH was used) with 10% HCl (150 mL) and the organic phase was extracted into diethyl ether and dried over $MgSO_4$. After removal of the solvents, products were separated by flash chromatography. They were characterized by their spectroscopic data (IR, ^1H NMR) and melting point.

Method B (NaH–*t*-AmONa–Ni(OAc)$_2$-bpy–KI in THF). The reagent was prepared in THF following method A. Potassium iodide (10 mmol) was then added. After 1 h of stirring at 63 °C, the reagent was ready for use.

Method C (NaH–*t*-AmONa–Ni(OAc)$_2$-bpy–KI in Benzene with 50 mmol of THF). The reagent was prepared following method A but replacing THF by a mixture of 50 mL of benzene and 50 mmol of THF. In this case, the preparation time of reagent is 4 h. KI was then added as in method B.

2-Fluoro-2′-methoxybiphenyl: mp 69 °C; ^1H NMR (CCl_4) δ 3.7 (s, OCH_3, 3 H), 6.8–7.4 (m, Ar, 8 H). Anal. Calcd for $C_{13}H_{11}FO$: C, 77.20; H, 5.48; F, 9.39. Found: C, 77.51; H, 5.67; F, 9.27.

4-Fluoro-2′-methoxybiphenyl: mp 58 °C; ^1H NMR ($CDCl_3$) δ 3.6 (s, OCH_3, 3 H), 6.7–7.5 (m, Ar, 8 H). Anal. Calcd for $C_{13}H_{11}FO$: C, 77.20; H, 5.48; F, 9.39. Found: C, 76.76; H, 5.63; F, 9.02.

2-Methoxy-3′-formylbiphenyl: liquid; ^1H NMR ($CDCl_3$) δ 3.8 (s, OCH_3, 3 H), 6.9–8.1 (m, Ar, 8 H), 10.1 (s, CHO, 1 H); IR (KBr) 1700 cm^{-1} (C=O). Anal. Calcd for $C_{14}H_{12}O_2$: C, 79.22; H, 5.70. Found: C, 79.67; H, 6.00.

2-Methoxy-2′-(trifluoromethyl)biphenyl: liquid; ^1H NMR ($CDCl_3$) δ 3.65 (s, OCH_3, 3 H), 6.8–7.7 (m, Ar, 8 H). Anal. Calcd for $C_{14}H_{11}F_3O$: C, 66.66; H, 4.39; F, 22.6. Found: C, 66.92; H, 4.44; F, 22.11.

2-Methoxy-4′-(trifluoromethyl)biphenyl: mp 32 °C; ^1H NMR ($CDCl_3$) δ 3.75 (s, OCH_3, 3 H), 6.8–7.6 (m, Ar, 8 H). Anal. Calcd for $C_{14}H_{11}F_3O$: C, 66.66; H, 4.39; F, 22.6. Found: C, 66.65; H, 4.45; F, 22.77.

3-Methoxy-4′-fluorobiphenyl: liquid; ^1H NMR ($CDCl_3$) δ 3.8 (s, OCH_3, 3 H), 6.7–7.6 (m, Ar, 8 H). Anal. Calcd for $C_{13}H_{11}FO$: C, 77.20; H, 5.48; F, 9.39. Found: C, 76.95; H, 5.53; F, 9.36.

3-Methoxy-4′-(trifluoromethyl)biphenyl: liquid; ^1H NMR ($CDCl_3$) δ 3.8 (s, OCH_3, 3 H), 6.9–7.9 (m, Ar, 8 H). Anal. Calcd for $C_{14}H_{11}F_3O$: C, 66.66; H, 4.39; F, 22.62. Found: C, 66.69; H, 4.68; F, 22.81.

4-Methoxy-2′-fluorobiphenyl: mp 48 °C; ^1H NMR ($CDCl_3$) δ 3.8 (s, OCH_3, 3 H), 6.8–7.4 (m, Ar, 8 H). Anal. Calcd for $C_{13}H_{11}FO$: C, 77.20; H, 5.48; F, 9.39. Found: C, 77.20; H, 5.39; F, 8.96.

4-Methoxy-3′-fluorobiphenyl: mp 68 °C; ^1H NMR ($CDCl_3$) δ 3.85 (s, OCH_3, 3 H), 6.9–7.7 (m, Ar, 8 H). Anal. Calcd for $C_{13}H_{11}FO$: C, 77.20; H, 5.48; F, 9.39. Found: C, 77.02; H, 5.59; F, 9.07.

4-Methoxy-3′-formylbiphenyl: mp 52 °C; IR (KBr) 1700 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 3.8 (s, OCH_3, 3 H), 6.9–8.0 (m, Ar, 8 H), 10.0 (s, CHO, 1 H). Anal. Calcd for $C_{14}H_{12}O_2$: C, 79.22; H, 5.70. Found: C, 78.65; H, 6.02.

4-Methoxy-2′-(trifluoromethyl)biphenyl: liquid; ^1H NMR ($CDCl_3$) δ 3.85 (s, OCH_3, 3 H), 6.8–7.6 (m, Ar, 8 H). Anal. Calcd for $C_{14}H_{11}F_3O$: C, 66.66; H, 4.39; F, 22.6. Found: C, 66.73; H, 4.32; F, 22.2.

2-Fluoro-2′-hydroxybiphenyl: mp 103 °C; IR (film) 3580 cm^{-1} (OH); ^1H NMR ($CDCl_3$) δ 4.7–4.9 (br, OH, 1 H), 6.6–7.5 (m, Ar, 8 H). Anal. Calcd for $C_{12}H_9FO$: C, 76.58; H, 4.82; F, 10.10. Found: C, 76.52; H, 4.87; F, 10.06.

4-Fluoro-2′-hydroxybiphenyl: mp 45 °C; IR (KBr) 3200–3500 cm^{-1} (OH); ^1H NMR ($CDCl_3$) δ 4.95 (br, OH, 1 H), 6.8–7.5 (m, Ar, 8 H). Anal. Calcd for $C_{12}H_9FO$: C, 76.58; H, 4.82; F, 10.10. Found: C, 76.04; H, 4.81; F, 9.65.

2-(Trifluoromethyl)-2′-hydroxybiphenyl: mp 54 °C; IR (film) 3200–3500 cm^{-1} (OH); ^1H NMR (CCl_4) δ 4.6–5.1 (br, OH, 1 H), 6.6–7.8 (m, Ar, 8 H). Anal. Calcd for $C_{13}H_9F_3O$: C, 65.54; H, 3.80; F, 23.93. Found: C, 65.40; H, 3.87; F, 23.74.

4-(Trifluoromethyl)-2′-hydroxybiphenyl: mp 115 °C; IR (KBr) 3250 cm^{-1} (OH); ^1H NMR ($CDCl_3$) δ 5.0 (br, OH, 1 H), 6.9–8.0 (m, Ar, 8 H). Anal. Calcd for $C_{13}H_9F_3O$: C, 65.54; H, 3.80; F, 23.93. Found: C, 65.61; H, 3.81; F, 23.63.

2-Fluoro-4′-hydroxybiphenyl: mp 152 °C; IR ($CHCl_3$) 3200–3600 cm^{-1} (OH); ^1H NMR ($CDCl_3$) δ 4.95 (br, OH, 1 H), 6.9–7.4 (m, Ar, 8 H). Anal. Calcd for $C_{12}H_9FO$: C, 76.58; H, 4.82; F, 10.10. Found: C, 76.03; H, 4.90; F, 9.42.

4-Fluoro-4′-hydroxybiphenyl: mp 166 °C; IR (KBr) 3200–3500 cm^{-1} (OH); ^1H NMR ($CDCl_3$) δ 4.1–4.4 (br, OH, 1 H), 6.6–7.6 (m, Ar, 8 H). Anal. Calcd for $C_{12}H_9FO$: C, 76.58; H, 4.82; F, 10.10. Found: C, 76.32; H, 4.83; F, 9.48.

4-Formyl-4′-hydroxybiphenyl: mp 178 °C; IR (CCl_4) 3200–3500 (OH), 1710 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 5.3 (br, OH, 1 H), 6.9–8.0 (m, Ar, 8 H). Anal. Calcd for $C_{13}H_{10}O_2$: C, 78.77; H, 5.08; F, 10.10. Found: C, 78.59; H, 5.36.

4-(Trifluoromethyl)-4′-hydroxybiphenyl: mp 138 °C; IR (KBr) 3200–3500 cm^{-1} (OH); ^1H NMR ($CDCl_3$) δ 5.2 (br, OH, 1 H), 6.9–7.7 (m, Ar, 8 H). Anal. Calcd for $C_{13}H_9F_3O$: C, 65.54; H, 3.80; F, 23.93. Found: C, 65.91; H, 3.93; F, 23.56.

4-Fluoro-4'-(dimethylamino)biphenyl: mp 164 °C; ^{1}H NMR ($CDCl_3$) δ 2.9 (s, NMe_2, 6 H), 6.75–7.55 (m, Ar, 8 H). Anal. Calcd for $C_{14}H_{14}FN$: C, 78.11; H, 6.55; F, 8.82; N, 6.50. Found: C, 77.68; H, 6.53; F, 8.00; N, 6.31.

4-(Trifluoromethyl)-4'-(dimethylamino)biphenyl: mp 196 °C; ^{1}H NMR ($CDCl_3$) δ 2.5 (s, NMe_2, 6 H), 7.35 (d, J = 9 Hz, 4 H), 7.85 (d, J = 9 Hz, 4 H). Anal. Calcd for $C_{15}H_{14}F_3N$: C, 67.91; H, 5.32; F, 21.48; N, 5.28. Found: C, 69.07; H, 5.60; F, 20.15; N, 5.11.

4-Methoxy-4'-methylbiphenyl: mp 107 °C; IR (CCl_4) 3100–2820 (ArOMe) 1250 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 2.35 (s, CH_3, 3 H), 3.8 (s, OCH_3, 3 H), 6.9 (d, J = 9 Hz, 2 H), 7.15 (d, J = 8 Hz, 2 H), 7.2–7.4 (m, 4 H). Anal. Calcd for $C_{14}H_{14}O$: C, 84.81; H, 7.11. Found: C, 84.78; H, 7.20.

4-(Trifluoromethyl)-4'-(methylthio)biphenyl: mp 165 °C; ^{1}H NMR ($CDCl_3$) δ 2.5 (s, SMe, 3 H), 7.2–7.65 (m, Ar, 8 H). Anal. Calcd for $C_{14}H_{11}F_3S$: C, 62.67; H, 4.13; S, 11.95; F, 21.24. Found: C, 64.94; H, 3.93; S, 10.42; F, 18.53.

Acknowledgment. We are grateful to the Centre National de la Recherche Scientifique for financial support. We thank the referees for help and comments.

Activation of Reducing Agents. Sodium Hydride Containing Complex Reducing Agents. 33. NiCRA's and NiCRAL's as New Efficient Desulfurizing Reagents

Sandrine Becker, Yves Fort, Régis Vanderesse, and Paul Caubère*

Laboratoire de Chimie Organique I, Faculté des Sciences, Domaine Scientifique Victor Grignard, Unité de Recherche Associée au CNRS No. 203, B.P. 239, 54506 Vandoeuvre-les-Nancy Cédex, France

Received March 2, 1989

It is shown that nickel-containing complex reducing agents alone or in the presence of 2,2'-bipyridine (NiCRA and NiCRA-bpy, respectively) are very efficient in the desulfurization of sulfur-containing organic compounds. A number of functional groups are resistant. Advantages of the inexpensive and nonpyrophoric CRA's are their easy preparation and handling. The mechanisms of these desulfurizations are discussed and compared to those with Ni(0) complexes.

Introduction

The desulfurization of organic compounds is an important reaction in organic chemistry. Indeed, it is a key process in the production of nonpolluting fuels.[1] On the other hand, the synthesis of organic compounds using sulfur chemistry as an auxiliary tool would not be possible without removal of the carbon–sulfur bond in the last step. A desulfurization procedure ought to be mild and chemoselective to be of use in synthesis. Considering the high diversity of the sulfurated functions to be removed and of the functional groups to be resistant, it is soon realized why many reagents have been proposed. Examination of the voluminous literature dealing with desulfurizations shows that in spite of the abundance of the procedures, numerous synthetic problems remain unsolved and that room exists for new reagents.

Among the more useful reagents, Raney nickel[2,3] and in situ generated nickel boride[4] are widely used heterogeneous reagents. Drawbacks of the former are their tedious preparation, hazardous handling,[3a] the difficulty of accurately determining the weight of Ni,[3] and the lack of chemo- and stereoselectivity. Nickel boride is more convenient. It is not pyrophoric and the amount of Ni used is easily known.[4] However, in spite of a lower reactivity, which limits its use,[4b,c] nickel boride lacks chemo- and stereoselectivity.

The desulfurization properties of Raney nickel and nickel boride have been mainly attributed to the large amount of hydrogen adsorbed on the surface of the finely divided catalyst.[2b,3a,5]

On the other hand, it is well-known that single electron transfer (SET) plays an important role in a large number of desulfurizations.[1,6] Thus, nickel reagents possessing a high SET ability might be good desulfurizing reagents in the absence of hydrogen.

The easily prepared, nonpyrophoric nickel-containing complex reducing agents (NiCRA's and NiCRAL's)[7] de-

(1) (a) Eisch, J. J.; Hallenbeck, L. E.; Han, K. I. *J. Org. Chem.* **1983**, *48*, 2963 and references cited therein. (b) Eisch, J. J.; Hallenbeck, L. E.; Lucarrelli, M. A. *Fuel* **1985**, *64*, 440 and references cited therein. (c) Aitken, J.; Heeps, T.; Steedman, W. *Fuel* **1968**, *47*, 353.

(2) (a) Pettit, G. R. In *Organic Reactions*; Cope, A. C., Ed.; John Wiley and Sons, Inc.: 1966; Vol. 12, p 356. (b) Hauptmann, H.; Water, W. F. *Chem. Rev.* **1962**, *62*, 347. (c) Bonner, W. A.; Grimm, R. A. In *The Chemistry of Organic Sulfur Compounds*; Karrash, N., Meyers, C. Y., Eds.; Pergamon Press: New York, 1966; Vol. 2, p 35. (d) Magnus, P. D. *Tetrahedron* **1977**, *33*, 2019. (e) Trost, B. M. *Chem. Rev.* **1978**, *78*, 363. (f) Field, L. *Synthesis* **1978**, 713. (g) Dieter, R. K. *Tetrahedron* **1986**, *42*, 3029. (h) De Lucchi, O.; Pasquato, L. *Tetrahedron* **1988**, *44*, 6755.

(3) (a) Mozingo, R.; Wolf, D. E.; Harris, S. A.; Folkers, K. *J. Am. Chem. Soc.* **1943**, *65*, 1013. (b) Snyder, H. R.; Cannon, G. W. *J. Am. Chem. soc.* **1944**, *66*, 155. (c) Blicke, F. F.; Sheets, D. G. *J. Am. Chem. Soc.* **1948**, *70*, 3768. (d) Latif, K. A.; Umor Ali, M. *Indian J. Chem.* **1984**, *23B*, 471. (e) Dieter, K.; Lin, Y. J. *Tetrahedron Lett.* **1985**, *26*, 39. (f) Nagai, M. *Chem. Lett.* **1987**, 1023. (g) Nakyama, J.; Yamaoka, S.; Oshino, H. *Tetrahedron Lett.* **1988**, *29*, 1161. (h) Barton, D. H. R.; Britten-Kelly, M. R.; Ferreira, D. *J. Chem. Soc. Perkin Trans. 1* **1978**, 1090.

(4) (a) Truce, W. E.; Perry, F. M. *J. Org. Chem.* **1965**, *30*, 1316. (b) Clark, J.; Grantham, R. K.; Lydiate, J. *J. Chem. Soc. C* **1968**, 1122. (c) Boar, R. B.; Hawkins, D. W.; McGhie, J. F.; Barton, D. H. R. *J. Chem. Soc. Perkin I* **1973**, 654. (d) Myrboh, B.; Singh, L. W.; Ila, H.; Junpappa, H. *Synthesis* **1982**, 307. (e) Sarma, D. N.; Sharma, R. P. *Tetrahedron Lett.* **1985**, *26*, 371. (f) Shut, j.; Engberts, J. B. F. N.; Wynberg, H. *Synth. Commun.* **1972**, *2*, 415. (g) Truce, W. E.; Perry F. M. *J. Org. Chem.* **1965**, *30*, 1316. (h) Everby, M. R.; Waigh, R. D. *Synth. Commun.* **1986**, *16*, 779.

(5) Truce, W. E.; Roberts, F. E *J. Org. Chem.* **1963**, *28*, 961.

(6) Eisch, J. J.; Im, K. R. *J. Organomet. Chem.* **1977**, *139*, C51.

(7) Caubere, P. *Angew. Chem. Int. Ed. Engl.* **1983**, *22*, 599. In this paper we have adopted the following convention: a NiCRA prepared from NaH, *t*-AmONa, and nickel acetate will be abbreviated NiCRA ($x/y/z$), where the molar ratio NaH/*t*-AmONa/Ni(OAc)$_2$ (in that order) is equal to $x/y/z$. In the same way, a NiCRAL prepared from NaH, *t*-AmONa, nickel acetate, and 2,2'-bipyridine or triphenylphosphine will be abbreviated NiCRAL ($x/y/z/t$), where the molar ratio NaH/*t*-AmONa/Ni(OAc)$_2$/2,2'-bipyridine or triphenylphosphine (in that order) is equal to $x/y/z/t$.

0022-3263/89/1954-4848$01.50/0 © 1989 American Chemical Society