comparison of the 400-MHz ^{1}H NMR spectrum with that of an authentic sample.

Preparation of *trans*-2-Ethyl-3-(tributylstannyl)cyclohexanone (25). To a solution of (tributylstannyl)lithium (0.33 M THF solution, 27.5 mL, 8.99 mmol) was added dropwise 2-cyclohexen-1-one (864 mg, 8.99 mmol) at −78 °C, and the reaction mixture was stirred for 20 min at −78 °C. A solution of iodoethane (0.86 mL, 11 mmol) and hexamethylphosphoric triamide (HMPA, 0.2 mL) in 2 mL of THF was added dropwise at −50 °C over 10 min, and the mixture was allowed to warm to room temperature. After 22 h at room temperature, additional iodoethane (0.43 mL, 5.4 mmol) was added, and the mixture was stirred for 18 h. The reaction mixture was quenched by the addition of an aqueous NH_4Cl solution and extracted with diethyl ether. Usual workup left an oil, which was purified by flash chromatography (18:1 hexane/ethyl acetate) to give the trans ketone **25** (2.58 g, 69%): IR (film) 1710, 1460, 1380, 1070 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.79–0.93 (18 H), 1.22–1.82 (18 H), 1.97 (1 H, m), 2.12 (1 H, m), 2.36 (2 H, m); ^{13}C NMR (25 MHz) δ 213.9 ($J(^{119}\text{Sn}-^{13}\text{C})$ = 44.0 Hz), 56.2 ($J(^{119}\text{Sn}-^{13}\text{C})$ = 14.7 Hz), 42.9, 33.9 ($J(^{119}\text{Sn}-^{13}\text{C})$ = 322 Hz), 32.4 ($J(^{119}\text{Sn}-^{13}\text{C})$ = 61.5 Hz), 30.4 ($J(^{119}\text{Sn}-^{13}\text{C})$ = 13.2 Hz), 29.3 ($J(^{119}\text{Sn}-^{13}\text{C})$ = 20.5 Hz), 27.6 ($J(^{119}\text{Sn}-^{13}\text{C})$ = 54.2 Hz), 24.6 ($J(^{119}\text{Sn}-^{13}\text{C})$ = 19.1 Hz), 13.7, 12.6, 9.2 ($J(^{119}\text{Sn}-^{13}\text{C})$ = 307 Hz); MS m/z 359 (M^+ − Bu, base peak), 291, 235, 179; HRMS calcd for $C_{16}H_{31}OSn$ (M^+ − Bu) 359.1397, found 359.1397.

Preparation of 2-Ethyl-1-methyl-3-(tributylstannyl)cyclohexanol (26). The ketone **25** (830 mg, 2.0 mmol) was treated with methyllithium (0.6 M diethyl ether solution, 6.55 mL, 4.0 mmol) as in the preparation of **5a** to give an oil. The crude product was purified by flash chromatography (11:1 hexane/ethyl acetate) to give the alcohol **26** (537 mg, 62%) as an 89:11 mixture of stereoisomers and **25** (218 mg). **26**: IR (film) 3470, 1460, 1380, 1170, 925, 735 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.84 (6 H), 0.90 (9 H, t, J = 7 Hz), 0.97 (2.67 H, t, J = 7 Hz), 1.02 (0.33 H, t, J = 7 Hz), 1.16 (0.33 H, s), 1.21 (2.67 H, s), 1.20–1.64 (22 H), 1.86 (1 H, m); MS m/z 375 (M^+ − Bu), 357, 291, 251, 235, 179, 123 (base peak), 95, 81; HRMS calcd for $C_{17}H_{35}OSn$ (M^+ − Bu) 375.1709, found 375.1681.

Grob Fragmentation of 26 under MOPMO Conditions. According to the general procedure for Grob fragmentation of **5** under MOPMO conditions, **26** (105 mg, 0.24 mmol) was treated with ISB (64 mg, 0.29 mmol), BF_3–Et_2O (42 mg, 0.29 mmol), and DCC (60 mg, 0.29 mmol) at room temperature for 3.5 h. The crude product was purified by preparative TLC (9:1 hexane/ethyl acetate) to give the known *trans*-enone **27**[24,39] (23 mg, 67%): ^{1}H NMR (400 MHz) δ 0.96 (3 H, t, J = 7 Hz), 1.64 (2 H, quint, J = 7 Hz), 1.99 (4 H), 2.13 (3 H, s), 2.41 (2 H, t, J = 7 Hz), 5.36 (1 H, dtt, J = 15, 7, 1.5 Hz), 5.46 (1 H, dtt, J = 15, 7, 1.5 Hz).

Reaction of *cis*-Benzyl Ether 36 with the MOPMO Combination. According to the general procedure for Grob fragmentation of **5** under MOPMO conditions, *cis*-benzyl ether **36**[15] (41 mg, 0.09 mmol), prepared from *cis*-**7a**, was treated with ISB (23 mg, 0.10 mmol), BF_3–Et_2O (15 mg, 0.10 mmol), and DCC (21 mg, 0.10 mmol) at room temperature for 18 h. The reaction mixture was quenched with an aqueous NH_4Cl solution and extracted with dichloromethane. Usual workup left an oil, which was purified by flash chromatography (19:1 chloroform/methanol) to give the known chlorostannane **37**[15] (36 mg, 91%).

Reaction of 37 with Butylmagnesium Chloride. A solution of butylmagnesium chloride (1.3 M THF solution, 0.05 mL, 0.07 mmol) was added to a solution of **37** (9.2 mg, 0.02 mmol) in THF (0.5 mL) at room temperature, and the mixture was stirred for 5.5 h. The reaction mixture was quenched with an aqueous NH_4Cl solution and extracted with diethyl ether. Usual workup left an oil, which was purified by preparative TLC (19:1 hexane/ethyl acetate) to give the tributylstannane **36** (8.9 mg, 93%).

Acknowledgment. We thank Professor K. Mori of University of Tokyo for the spectral data of *erythro*-6-acetoxy-5-hexadecanolide.

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Activation of Reducing Agents. Sodium Hydride Containing Complex Reducing Agents. 31. NiCRAL's as Very Efficient Agents in Promoting Homo-Coupling of Aryl Halides

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Homo-coupling of aryl bromides and chlorides is efficiently performed with nickel-containing complex reducing agents NiCRA-bpy. In a number of cases the presence of alkali iodides improves the procedure. Yields are very high and a number of functional groups are resistant. The mechanistic and catalytic aspects of these reactions are discussed.

Introduction

The classical Ullmann reaction employs a copper-promoted coupling of aryl halides. This very useful reaction, however, presents a number of drawbacks:[1] (i) need of rather high reaction temperatures, (ii) yields often moderate, (iii) aryl chlorides, with a few exceptions, are unreactive, (iv) high sensitivity to steric hindrance, and (v) cross-coupling not easily performed.

The introduction by Semmelhack and co-workers[2] of zerovalent nickel complexes in place of copper brought a revival of interest on the old Ullmann reaction. One of the limitations of Semmelhack's condensations was the use of air-sensitive reagents generally prepared by cumbersome

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[2] Semmelhack, M. F.; Helquist, P. M.; Jones, L. D. *J. Am. Chem. Soc.* **1971**, *93*, 5908. Semmelhack, M. F.; Speltz-Ryono, L. *Ibid.* **1975**, *97*, 3873. Semmelhack, M. F.; Helquist, P.; Jones, L. D.; Keller, L.; Mendelson, L.; Speltz-Ryono, L.; Gorszynski-Smith, J.; Staufer, R. D. *Ibid.* **1981**, *103*, 6460.

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Table I. Coupling of Chlorobenzene by NiCRA-bpy [4/2/1/2][a] in Various Solvents (50 mL)

entry	solvent	*T*, °C	prepn[b] time, h	reactn time, h	yield, %[c] PhPh	yield, %[c] PhH
1	Et_2O	33	4	36	60	36
2	THF	63	2	2.5	89	trace
3	DME	63	2	1.5		95
4	anisole	70	1	32	83	trace
5	benzene	63	16	18	45	
6	benzene + 50 mmol THF	63	4	3.5	90	
7	xylene	63	2	18	57	40
8	xylene + 50 mmol THF	63	2	18	68	25
9	cyclohexane	63	4	29	60	35
10	cyclohexane + 50 mmol THF	63	4	31	62	35
11	hexane + 50 mmol THF	63	4	18	51	30
12	DMF	25	4	17		97
13	NMP	63	3	2	38	42

[a] Reaction performed on a 10-mmol scale with a molar ratio Ni/ArX = 1 (see Experimental Section and ref 14). [b] See Experimental Section. [c] Determined by GC analysis.

techniques. This limitation was circumvented by Kende and co-workers,[3] who in situ generated Ni(0) species by reaction of liganded nickel salts with Zn in DMF. From these pioneering works, various nickel-using procedures were devised in order to the perform Ullmann-type reaction.[4–13] Examination of the published results leads to the following general conclusions: (i) Aryl iodides are generally coupled but limitations are found with aryl bromides and yields vary from moderate to good. With one exception,[8] coupling of aryl chlorides are scarcely successfull. (ii) The presence of hydroxy, carboxy (or salt), or nitro groups impedes the couplings. (iii) The condensation is very sensitive to ortho steric hindrance. (iv) With few exceptions, heteroaryl halides, particularly nitrogen-containing ones, are hardly coupled. (v) Cross-coupling cannot be performed.

Special mention must be made of the procedure developed by Colon and Kelsey.[8] These authors used catalytic amounts of nickel salts with an excess of Zn in the presence of ligands such as Ph_3P or 2,2′-bipyridine (bpy) in DMA or DMF. Para-substituted aryl chlorides were coupled in good to very good yields. However, hydroxy-, amino-, or nitroaryl chorides were hardly or not coupled. This procedure, like the others, was found to be inadequate for performing cross-couplings.

This brief review shows that there is still room for new reagents.

In previous short publications we showed that complex reducing agents NiCRAL [*x*/*y*/*z*/*t*][14] were very promising in promoting homo-coupling of aryl halides.[15] They did not need use of solvents such as DMA or DMF and seemed devoid of a number of the above-mentioned drawbacks. Moreover, they also appeared to be very promising in performing cross-couplings[16] as well as coupling of heteroaryl halides.[17]

Table II. Salt Effect on Coupling Reaction[a] of Halogenobenzene by NiCRA-bpy [4/2/1/2] in THF (50 mL) at 63 °C

entry	X	MX^1 (10 mmol)	time, h	yield PhPh, %[b]
1	Cl	none	2.5	89
2		LiI, NaI, KI	1–1.5	92–98
3		NaBr, KBr	1.5–2	80–83
4	Br	none	1	86
5		LiI, NaI, KI	0.5–0.75	80–85

[a] Reactions performed at 63 °C in THF on a 10-mmol scale with a molar ratio Ni/ArX = 1. [b] Determined by GC analysis.

In the present and following papers, we report full details on the scope and limitations of NiCRAL's in homo- and cross-coupling of aryl halides. Coupling of heteroaryl halides will be published later.

Results and Discussion

Solvent Effect. Since one of our goals was to replace DMA or DMF by more useful solvents, we first studied the influence of this parameter on the coupling of phenyl chloride. During this study we used *t*-AmONa-containing NiCRA-bpy [4/2/1/2] and the ratio C_6H_5Cl/NaH/*t*-AmONa/$Ni(OAc)_2$/bpy was equal to 1/4/2/1/2. *This means that at the very beginning of the preparation of the reagent, 6 molar equiv of NaH was needed, two of them being used for the in situ preparation of t-AmONa.*

Since 2 molar equiv of NaH are used to reduce Ni(II),[18] *at the end of the preparation of NiCRA-bpy, there are only 2 molar equiv of NaH remaining in the reagent.*

The results obtained are gathered in Table I. From these data a number of interesting features emerges.

While THF and anisole lead to excellent yields, DME strongly favors reduction, the classical side reaction of Ullmann condensations. In hydrocarbons such as xylene, cyclohexane, hexane, and particularly benzene, couplings took place in good to excellent yields as long as a small amount of THF was added (see Experimental Section). Without THF, erratic results were obtained as a consequence of the low reproducibility observed during the preparation of CRA's.[19] Finally, polar aprotic solvents were of no interest and it must be worthy of note that DMF not only slowed the conversion of phenyl chloride but led only to the reduced products.

It was concluded that THF and benzene (in the presence of a small amount of THF) were the best solvents.

Salt Effect. From the literature[4–8] it appears that the addition of salts such as alkali iodides to the reagent used in nickel-promoted Ullmann-type reaction often improves their efficiency. This beneficial effect was explained either by the formation of a complex favoring electron transfers[8] or by a nickel-catalyzed transformation of aryl halides

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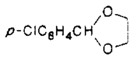
Table III. Coupling of Aryl Halides by NiCRA-bpy [4/2/1/2][a] in THF (50 mL) at 63 °C

entry	XC_6H_4Z	method[b]	time, h	yield, %[c]	lit. ref
1	bromobenzene	B	0.5	82	25a
2	chlorobenzene	B	1.5	92	25a
3	*o*-BrC_6H_4Me	B	1.15	75	25a
4	*m*-BrC_6H_4Me	A	0.75	88	25c
5	*p*-BrC_6H_4Me	B	0.25	84	25b, 26
6	*o*-BrC_6H_4OMe	A	0.5	74	25a
7	*m*-BrC_6H_4OMe	A	0.25	82	25e
8	*p*-BrC_6H_4OMe	A	0.5	70	25d, 26
9	*p*-BrC_6H_4OH	A	0.5	68	25
10	*p*-BrC_6H_4Cl	A	0.25	60[d]	
11	*p*-BrC_6H_4F	A	0.25	85	25a, 34
12	*o*-$BrC_6H_4CF_3$	A	0.25	42	31
13	*m*-$BrC_6H_4CF_3$	A	0.10	87	
14	*p*-$BrC_6H_4CF_3$	A	0.10	93	
15	*o*-ClC_6H_4Me	B	4.5	90	25a
16	*m*-ClC_6H_4Me	B	4.5	85	25c
17	*p*-ClC_6H_4Me	A	17	90	25b, 26
18	*o*-ClC_6H_4OMe	A	3	91	25a
19	*m*-ClC_6H_4OMe	A	2	82	25e
20	*p*-ClC_6H_4OMe	A	10	87	25d, 26
21		A	0.5	78[e]	28
22	*o*-$ClC_6H_4CF_3$	A	12	71	31
23	*m*-$ClC_6H_4CF_3$	B	0.70	93	
24	*p*-$ClC_6H_4CF_3$	B	0.30	88	

[a] Reaction performed on a 10-mmol scale with a molar ratio Ni/ArX = 1. [b] See Experimental Section. [c] Isolated yields. [d] The identification of the products was made by mass spectroscopy coupled to GC. [e] Isolated as deprotected product.

(different from iodides) into much more reactive aryl iodides.[20]

In Table II we have reported the results of a study performed on bromo- and chlorobenzenes with NiCRA-bpy in THF.

It appears that addition of alkali iodides improves the procedure by increasing the yields or the reaction rate or both. As expected phenyl chloride is more sensitive to the salt effect. A number of unreported experiments showed that the same salt effect took place in benzene added with a small amount of THF.

It was thus concluded that *if the results of a given coupling performed with NiCRA-bpy alone were judged as not acceptable, it would be possible to improve the condensation by the simple addition of alkali iodides.*

In the experiment described below we used KI when necessary. Note that NaI had an equivalent action.

Homo-Coupling of Aryl Halides. From the above observations we devised three possible procedures: NiCRA-bpy in THF (method A) and NiCRA-bpy–KI in THF (method B) or in C_6H_6–small amount of THF (method C) (it was found that addition of KI was always preferable for couplings performed in benzene).

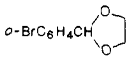
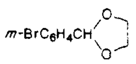
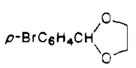
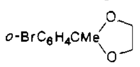
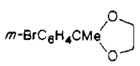
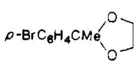
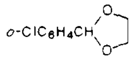
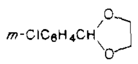
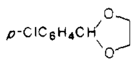
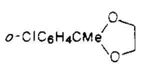
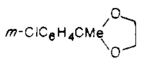
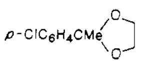
The best results obtained in THF and benzene are reported in Tables III and IV, respectively.

It is noteworthy that whatever the method was, yields of coupling varied from good to excellent. The main by-product came from reduction.

It appeared that NiCRA-bpy's solved a number of the problems mentioned above. Thus they work in convenient solvents such as THF or benzene, easily removed from the condensation products. Ortho-substituted aryl halides coupled very easily and phenol derivatives led also to good results.

Moreover, the procedure tolerated amines, acetals, ketals, nitriles, and ethers as well as the trifluoromethyl group. Unfortunately halobenzoic acids were found to be unreactive and nitroaryl halides led to untractable mixtures due to reduction of the nitro group.[21]

Table IV. Coupling of Aryl Halides by NiCRA-bpy-KI [4/2/1/2/1][a] in Benzene at 63 °C (Method C)[b]

entry	compound	time, h	yield, %[c]	lit. ref
1	*o*-BrC_6H_4Me	0.75	80	25a
2	*m*-BrC_6H_4Me	0.75	83	25c
3	*p*-BrC_6H_4Me	0.5	82	25b, 26
4	*o*-BrC_6H_4OMe	1.5	68	25a
5	*m*-BrC_6H_4OMe	0.15	82	25e
6	*p*-BrC_6H_4OMe	1.5	84	25d, 26
7	*o*-BrC_6H_4OH	0.5	63	25a
8	*p*-BrC_6H_4OH	1.75	76	25a
9	*p*-$BrC_6H_4NMe_2$	2.5	81	25a, 33
10	*o*-BrC_6H_4F	3	57	25a
11	*m*-BrC_6H_4F	0.5	74	
12	*p*-BrC_6H_4F	2.25	64	25a, 34
13		2	57[d]	29
14		0.5	71[d]	
15		1	63[d]	28
16		2.5	62[d]	32
17		1.75	68[d]	
18		2.5	64[d]	30
19	*p*-BrC_6H_4CN	1	72	30
20	*o*-$BrC_6H_4CF_3$	1.25	62	31
21	*m*-$BrC_6H_4CF_3$	2	80	
22	*p*-$BrC_6H_4CF_3$	0.25	87	
23	*o*-ClC_6H_4Me	5	80	25a
24	*m*-ClC_6H_4Me	8	77	25c
25	*p*-ClC_6H_4Me	5	74	25b, 26
26	*o*-ClC_6H_4OMe	2	74	25a
27	*m*-ClC_6H_4OMe	1.75	73	25e
28	*p*-ClC_6H_4OMe	2	71	25d, 26
29	*m*-ClC_6H_4OH	27	70	25a
30	*o*-ClC_6H_4F	3.75	60	25a
31	*m*-ClC_6H_4F	0.75	84	
32	*p*-ClC_6H_4F	2.5	75	25a, 34
33		3.5	64[d]	29
34		2	75[d]	
35		3	76[d]	28
36		4	65[d]	32
37		3.5	73[d]	
38		8	72[d]	30
39	*p*-ClC_6H_4CN	2	80	30
40	*o*-$ClC_6H_4CF_3$	3.25	70	31
41	*m*-$ClC_6H_4CF_3$	4	77	
42	*p*-$ClC_6H_4CF_3$	1	77	

[a] Reaction performed on a 10-mmol scale with a molar ratio Ni/ArX = 1 in the presence of 10 mmol of KI. [b] See Experimental Section. [c] Isolated yields. [d] Isolated as deprotected product.

The results gathered in Tables III and IV also pointed out that, just like the copper-promoted Ullmann reaction,[1]

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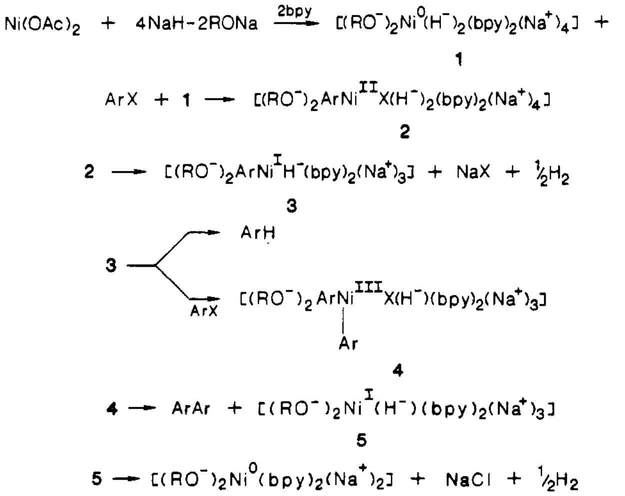
Scheme I



electron-donating as well as electon-withdrawing substituents favored the reaction. However, broadly speaking electon-withdrawing groups were a little bit more efficient. This result agrees with the fact that NiCRAL's (constituted by Ni(0) centers surrounded by alkoxide and hydride anions)[18] are very electon-rich nucleophiles and would more easily condense with electron-poor aryl halides.

Finally, procedures using Zn necessitate an excess of the reducing agent.[5] So, we wondered if an excess of NaH would not improve our procedure. A number of unreported experiments performed with NiCRA-bpy [5.5/2/1/2] showed that the results varied with the substrate. Generally speaking, an increase in NaH increases the rate of conversion. However, yields might be higher or lower, depending on the nature of the ring substituents.

Concerning the mechanism, it must not be basically different from the ones given in the literature.[2,6,8,12,22-24]

Thus it may be guessed that the first step must be an oxidative addition of aryl halides with Ni(0) species in NiCRA.[18] Then successive steps analogous to those invoked by Colon and Kelsey[8] could intervene as symbolized (since the actual structures of CRA's are not completely elucidated) in Scheme I, where the polymeric aspects of CRA's[14] have been omitted for sake of simplicity.

The part played by the alkoxide would be the stabilization of the complexes as already proposed to explain the properties of CRA's.[14]

Formation of the reduced product has just been symbolized.

Examination of this mechanism leads to the following observations: (i) One nickel atom couples two molecules of aryl halides. So under the conditions used during the present work it ought to be possible to couple two times the amount of aryl halides. This was completely verified. For example, 10 mmol of phenyl bromide was coupled with 10 mmol of nickel species in 1 h in 84% yield. Under the same conditions, 20 mmol of phenyl bromide led to 82% coupling after 2.5 h. In fact we chose to work under the given conditions in order to have the shortest reaction times. (ii) On the other hand Ni(0) species by themselves are able to couple aryl halides.[2] So if our mechanistic hypothesis was right the Ni(0) species **5** should be able to couple some more aryl halides althought more slowly and less efficiently than **1**. Indeed, under the above conditions (10 mmol of Ni species) 30 mmol of PhBr was coupled after 9 h in 73% yield and 40 mmol led to 71% yield after 21 h. Note, that means more than 140% yield relative to Ni. (iii) Finally, it should be expected that in the presence of NaH in excess, **5** could be transformed into **1**, allowing a catalytic procedure provided that the reaction between **5** and NaH was fast enough.

This hypothesis was completely verified. Thus 100 mmol of C_6H_5Cl was reacted with a NiCRA-bpy containing 100 mmol of NaH, 10 mmol of *t*-AmONa, 5 mmol of Ni(0), and 10 mmol of bpy in the presence of 5 mmol of KI. After 24 h, 90% of conversion of the chloride was observed. The yield of coupling relative to Ni was 350% and 39% relative to chlorobenzene. In other words the reactions are catalytic in nickel but, for the present time, the part taken by the reduction is too important for this to be used for synthetic purposes. Current works performed in our laboratory aim at suppressing or at least diminishing this side reaction.

Conclusion

This study displays that NiCRA-bpy are very efficient in a nickel-promoted Ullmann-type reaction and may be situated among the best reagents known till now. They are devoid of a number of the disadvantages encountered with the reagents described in the literature. The main drawback is the side reduction during catalytic couplings. However, it must be emphasized that in the present procedure and relative to Ni more than 140% yields of coupling may be obtained. Moreover, we shall see in the following paper that NiCRA-bpy are the first nickel-containing reagents able to efficiently perform cross-couplings.

Experimental Section

Instrumentation. GC analyses were performed on a Girdel 330 apparatus (flame-ionization detector) equipped with 10-ft long SE 30 columns. IR spectra were recorded on 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.

Solvents. THF was distilled from a benzophenone–sodium adduct and stored over sodium wires. DME (Fluka) was distilled from sodium. Hexane was distilled from $KMnO_4$. Anesthetic ether was distilled from P_2O_5. Anisole, benzene, and cyclohexane were distilled from sodium; xylene isomer mixture was distilled from sodium. DMF was distilled from CaH_2. NMP was distilled in vacuo. *tert*-Amyl alcohol was distilled from sodium. For Et_2O, THF, and DME, the absence of peroxide was checked before each

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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.

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

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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-

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