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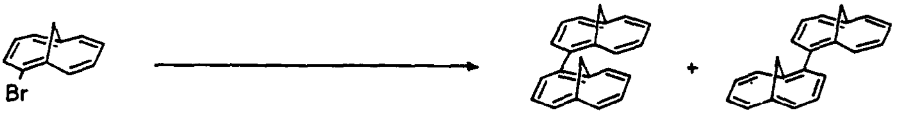
NICKEL-CATALYZED COUPLING OF BROMIDES OF 1,6-METHANO[10]ANNULENE AND AZULENE. A FACILE SYNTHESIS OF BIANNULENE AND BI-, TER-, QUATER-, AND POLYAZULENES

Masahiko Iyoda*, Koichi Sato, and Masaji Oda
Department of Chemistry, Faculty of Science, Osaka University,
Toyonaka, Osaka 560, Japan

Summary: The active nickel complex generated *in situ* by reduction of $NiBr_2(PPh_3)_2$ with zinc in the presence of Et_4NI is a useful reagent for the dehalogenative coupling of 2-bromo-1,6-methano[10]annulene and 1-bromo- and 1,3-dibromoazulenes.

The reductive coupling of aryl or alkenyl halides in the presence of zerovalent nickel complexes has been widely investigated.[1] Although the nickel-catalyzed Ullmann-type coupling has been proved to be a useful reaction because of the mild conditions and high yields, the reaction has not been widely extended so far in organic synthesis. Recently, we have reported the reductive coupling of alkenyl and benzyl halides using the active nickel complex generated *in situ* by reduction of $NiX_2(PPh_3)_2$ with zinc in the presence of Et_4NI.[2] We report here the use of the active nickel catalyst to synthesize bi-1,6-methano[10]annulenes (2 and 3) and bi-, ter-, quater- and polyazulenes (6, 7, 8 and 9).



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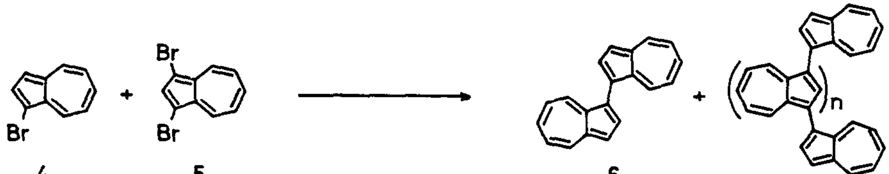


4 5 6 7:n=1, 8:n=2, 9:polymer

We initially examined the reductive coupling of bromobenzene with $NiX_2(PPh_3)_2$-Zn in the presence of Et_4NI (Table 1). The nickel-catalyzed coupling of bromobenzene in various solvents (50 °C, 2 h) proceeded smoothly in the presence of 1 equiv. of Et_4NI to give biphenyl in good yields. The nickel-catalyzed coupling of aryl halides have been reported to proceed effectively only in DMF or HMPA as solvents.$^{3)}$ However, our results demonstrate the coupling reaction to take place cleanly in THF, acetonitrile and acetone, when the reaction is carried out in the presence of Et_4NI.

Table 1. Coupling of bromobenzene with $NiX_2(PPh_3)_2$-Zn-Et_4NI.$^{a)}$

Catalyst	Solvent	Yield (%)
$NiCl_2(PPh_3)_2$	THF	92
$NiBr_2(PPh_3)_2$	THF	94
$NiI_2(PPh_3)_2$	THF	94
$NiBr_2(PPh_3)_2$	DMF	84
$NiBr_2(PPh_3)_2$	Acetonitrile	88
$NiBr_2(PPh_3)_2$	Acetone	80

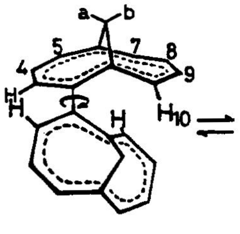
a) Bromobenzene (10 mmol), $NiX_2(PPh_3)_2$ (1 mmol), Zn (15 mmol), Et_4NI (10 mmol), solvent (15 ml), 50 °C, 2 h.

On the basis of the results mentioned above, we applied the coupling reaction to synthesize 2,2'-bi-1,6-methano[10]annulenes (**2** and **3**). Treatment of 2-bromo-1,6-methano-[10]annulene (**1**)$^{4)}$ with $NiBr_2(PPh_3)_2$ (0.1 equiv.) and zinc (2 molar equiv.) in the presence of Et_4NI (1 equiv.) at 50 °C for 2 h afforded a mixture of *meso*- and *racemic*-biannulenes (**2** and **3**), which could be easily separated by column chromatography on silica gel (**2**,$^{5)}$ pale yellow oil, 44.5%; **3**,$^{5)}$ yellow oil, 42.5%). Although stereochemical assignments of the two biannulenes (**2** and **3**) were difficult to make from spectroscopic analysis, the configurations were assigned on the basis of their chiral properties. Optical resolution of the *racemic*-biannulene (**3**) by HPLC [column: "CHIRALPAK OP(+)" or "CHIRALCEL OK"$^{6)}$] revealed two peaks corresponding to the (+)- and (-)-isomers, whereas HPLC of the *meso*-biannulene (**2**) with the same columns showed only one peak.

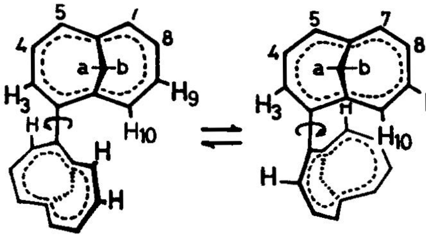
In the aromatic system containing two aromatic rings joined by a single bond (*e.g.*, biphenyls, binaphthyls, etc.), the barrier to rotation is often large enough to prevent the easy interconversion of the conformations and sometimes permit the isolation of conformers. Therefore, we examined the rotational barrier of the annulene rings about the 2,2'-carbon-carbon bond in the biannulenes (**2** and **3**).

The ^1H-NMR spectrum of the *racemic*-biannulene (**3**) is temperature dependent and shows very broad signals at room temperature. Since the spectra at higher temperatures (>80 °C) reveal the sharp signals corresponding to the biannulene (**3**), the broadening of the spectrum at room temperature is attributable to the hindered rotation about 2,2'-single bond (*i.e.*, **3a** $\rightleftarrows$ **3b**). Actually, the spectra at lower temperatures (<-10 °C) show the sharp and complex signals corresponding to the two conformers (**3a** and **3b**). The 360MHz ^1H-NMR data of **3a** and **3b** at -20 °C are summarized in Table 2. The protons (H_3 in **3a**, and H_9 and H_{10} in **3b**) reveal an upfield shift, due to the shielding effect of the other annulene-ring. The bridge protons of **3** reveal that the compound exists at -20 °C as a 2:1 mixture of **3a** and **3b**. Therefore, **3a** is *ca* 0.3 kcal/mol more stable than **3b**. The activation energy was estimated to be $\Delta G^{\ddagger} = 15$ kcal/mol (-25 °C), which is appreciably smaller than that for 1,1'-binaphthyl.$^{7)}$

In contrast to the results for the *racemic*-biannulene (3), the *meso*-biannulene (2) exhibits averaged ^{1}H-NMR spectra at room temperature and the signals begin to broaden at -80 °C. Therefore, the rotational barrier about the 2,2'-bond is apparently small in this case. As shown in Table 2, the annulene protons of 2 except for H_5 and H_7 show an upfield shift to some extent as compared with those of 3. The upfield shift of H_9 and H_{10} depends on the ring current effect of the other ring.



2a 2b



3a 3b

The nickel-catalyzed coupling of aryl halides can be also applied to the synthesis of bi-, ter-, quater- and polyazulenes (6, 7, 8 and 9). Bromination of azulene with NBS (1 equiv.) is known to afford a mixture of 1-bromo- and 1,3-dibromoazulenes (4 and 5).[8] Since 1-bromoazulene (4) decomposed slowly during column chromatography, we examined the nickel-catalyzed coupling of the mixture of 4 and 5 without separation. Treatment of 4 and 5 (*ca* 4:1), which were prepared by bromination of azulene with 1 equiv. of NBS in benzene, was carried out in a similar manner as above [0.1 equiv. of $NiBr_2(PPh_3)_2$, 2 molar equiv. of Zn, 1 equiv. of Et_4NI, THF, 50 °C, 2 h]. The reaction mixture was chromatographed on silica gel to give 1,1'-biazulene (6,[9] 55%), 1,1':3',1''-terazulene (7,[10] 13%), and 1,1':3',1'':3'',1'''-quaterazulene (8,[11] 7.5%). Although the synthesis of biazulenes has been reported recently using the Ullmann reaction of iodoazulenes and their derivatives,[9] the nickel-catalyzed coupling described in this paper provides a simple and versatile method for the synthesis of biazulenes. Furthermore, the reductive coupling of 1,3-dibromoazulene (5)[8] prepared from azulene with 2 equiv. of NBS afforded polyazulene (9, deep green powder, 39%). Recently, Bargon *et al.* reported the synthesis of polyazulene containing perchlorate or tetrafluoroborate ion by electrochemical oxidation of azulene.[12] However, our method provides a way for the synthesis of anion-free polyazulene (9).

Table 2. ^{1}H-NMR parameters of 2 and 3 (360MHz, CD_2Cl_2, δ ppm, $CDHCl_2$$^{i)}$ as internal standard).

	H_3	H_4	H_5	H_7	H_8	H_9	H_{10}	H_a	H_b
2$^{ii)}$	7.06-7.10 m		7.45 d	7.50 d	7.12 t	6.96 t	6.89 d	-0.21 d	-0.43 d
		($J_{7,8}$ = $J_{8,9}$ = $J_{9,10}$ = $J_{a,b}$ = 9.0 Hz)							
3a$^{iii)}$	6.89 d	7.08 t	7.53 d	7.53 d	7.18-7.27 m		8.15 d	-0.11 d	-0.27 d
		($J_{3,4}$ = $J_{4,5}$ = $J_{7,8}$ = $J_{9,10}$ = $J_{a,b}$ = 9.0 Hz)							
3b$^{iii)}$	8.05 d	7.29 t	7.51 d	7.44 d	7.06 t	6.83 t	6.77 d	-0.16 d	-0.44 d
		($J_{3,4}$ = $J_{4,5}$ = $J_{7,8}$ = $J_{8,9}$ = $J_{9,10}$ = $J_{a,b}$ = 9.0 Hz)							

i) $CDHCl_2/CD_2Cl_2$ = δ 5.30. ii) At room temperature. ii) At -20 °C.

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5) The *meso*- and *racemic*-biannulenes (**2** and **3**) were also synthesized by Prof. Vogel's group using the coupling of the organocopper derivative of 1,6-methano[10]annulene (E. Vogel, private communications). **2**: Mass(m/z) 282 (M+); IR (CCl_4) 3035, 2944, 1450, 1255 cm^{-1}; UV $\lambda_{max}^{cyclohexane}$ (ε) 259 (66,300), 320 (11,600) nm; ^{13}C-NMR ($CDCl_3$) δ 141.6, 129.6, 129.4, 128.6, 128.1, 126.5, 125.5, 117.0, 114.7, 35.4; **3**: Mass(m/z) 282 (M$^+$); IR (CCl_4) 3035, 2944, 1450, 1255 cm^{-1}; UV $\lambda_{max}^{cyclohexane}$ (ε) 248 (47,700), 275 (35,300), 361 (11,800) nm; ^{13}C-NMR ($CDCl_3$) δ 140.7, 130.4, 129.7, 129.6, 128.3, 127.5, 127.3, 126.3, 117.1, 116.3, 35.5.

6) "CHIRALPAK OP(+)" and "CHIRALCEL OK" are commercially available from Japan Spectroscopic Co., Ltd.

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10) **7**: deep green cryst., mp 97-98 °C; Mass(m/z) 380 (M+); UV $\lambda_{max}^{cyclohexane}$ (ε) 240sh (35,200), 262.5 (49,200), 276sh (43,600), 312 (39,400), 399 (20,800), 635 (671) nm; ^{1}H-NMR ($CDCl_3$) δ 8.47 (d, J=9.5 Hz, 2H, $H_{4'}$), 8.37 (d, J=9.5, 4H, H_4, H_8), 8.32 (s, 1H, $H_{2'}$), 8.19 (d, J=4.0, 2H, H_2), 7.4-7.7 (m, 5H, H_3, H_6, $H_{6'}$), 6.9-7.2 (m, 6H, H_5, $H_{5'}$, H_7).

11) **8**: dark green cryst., mp 140-142 °C; Mass(m/z) 506 (M$^+$); UV $\lambda_{max}^{cyclohexane}$ (ε) 250sh (61,900), 263 (63,900), 298.5 (54,300), 314sh (50,300), 401 (24,300), 640 (992) nm; ^{1}H-NMR ($CDCl_3$) δ 8.2-8.6 (m, 12H, H_2, $H_{2'}$, H_4, $H_{4'}$, H_8, $H_{8'}$), 7.45-7.7 (m, 6H, H_3, H_6, $H_{6'}$), 6.9-7.2 (m, 8H, H_5, $H_{5'}$, H_7, $H_{7'}$).

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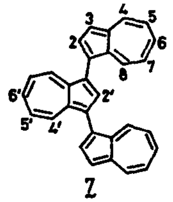

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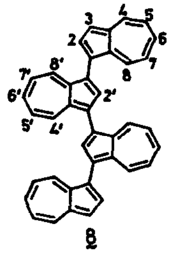

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