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Lithium Alkylamide-Catalyzed Addition Reaction of Alkylamines to Vinyl Monomers. III. Addition Reaction of *p*-Substituted Benzylamines to Styrene and Divinylbenzenes

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The lithium alkylamide-catalyzed addition reaction of *p*-substituted benzylamines with *m*- and *p*-divinylbenzene was examined in order to synthesize new styrene derivatives. Though divinylbenzene possesses two vinyl groups, 1 : 1 adducts, the *N*-(*p*-substituted benzyl)vinylphenethylamines (**6**, **8**) were found to be prepared selectively. The reaction with styrene was also examined as a model reaction. From kinetic studies, the Hammett ρ values for the addition reaction of *p*-substituted benzylamines to the styrene, *m*-divinylbenzene and *p*-divinylbenzene, were −0.72, −0.67, and −1.1, respectively, at 50 °C.

Since the addition reaction of alkylamines to divinylbenzenes has opened a new route for synthesizing styrene derivatives possessing alkylamino groups, the reactions of several primary and secondary amines to vinyl-substituted aromatics have been investigated.[1-8] In previous papers[9,10] the addition reactions of optically active α-methylbenzylamine onto *m*- and *p*-divinylbenzene (DVB) catalyzed by lithium α-methylbenzylamide were reported to produce styrene derivatives possessing an optically active moiety. This may be the first example of a new synthetic route to styrene derivatives having optically active groups.

Investigations concerning the reaction of substituted benzylamines with vinyl-substituted aromatics should be of importance for obtaining information about the mechanism of the addition reaction of benzylamine derivatives toward vinyl-substituted aromatics, since several substituents could be introduced to the aromatic rings of benzylamines. Prior to our investigation on the selective synthesis of styrene derivatives from DVB, the addition reaction of *p*-substituted benzylamines to styrene catalyzed by the corresponding lithium alkylamides was examined as a model. On the basis of the results of the model reaction, new styrene derivatives were synthesized by the addition of several benzylamines to *m*- and *p*-DVB. The pseudo-first-order rate constants of both reactions were analyzed in terms of the Hammett equation. The styrene derivatives possessing benzylamino groups obtained here are expected to serve as the starting materials of reactive polymers.

Experimental

Most of our experiments, such as distillation and anionic addition reactions, were carried out under a purified nitrogen atmosphere so as to preclude both oxygen and moisture. Nitrogen gas was purified by passing it through an activated-copper reducing column and a phosphorus pentoxide column.

Reagents: Styrene, *p*-substituted benzylamines, *m*- and *p*-divinylbenzene (DVB) (Asahi Chemical Industry Co.) were purified by refluxing over calcium hydride and then distilling under reduced pressure. Commercial butyllithium (hexane solution) was used after a determination of the concentration by the double-titration method,[11] other reagents and solvents were purified by usual methods.

Synthesis of *N*-(*p*-Substituted Benzyl)phenethylamine (3): To a toluene (60 ml) solution of *p*-substituted benzylamine (100 mmol), butyllithium (2 mmol) was added in order to synthesize a catalytic amount of the corresponding lithium amide. Styrene (100 mmol) was then introduced and the mixture was kept at 40 °C for 12 h. The product was isolated by fractional distillation.

***N*-Benzylphenethylamne (3a):** Yield, 18%; bp 124 °C (67 Pa); ^{1}H NMR ($CDCl_3$, 60 MHz) δ=1.31 (1H, s, NH), 2.82 (4H, s, CH_2CH_2), 3.73 (2H, s, $NC\underline{H}_2C_6H_5$), 7.00—7.50 (10H, C_6H_5); MS (70 eV) *m*/*z* (rel intensity) 211 (M^+; 0.5), 120 (76), 105 (3), 91 (100), 77 (3), and 65 (7).

***N*-(*p*-Methylbenzyl)phenethylamine (3b):** Yield, 28%; bp 133—134 °C (67 Pa); ^{1}H NMR ($CDCl_3$, 60 MHz) δ=1.33 (1H, s, NH), 2.32 (3H, s, $C\underline{H}_3C_6H_4$), 2.85 (4H, s, CH_2CH_2), 3.76 (2H, s, $NC\underline{H}_2C_6H_4$), 7.00—7.40 (9H, C_6H_4 and C_6H_5); MS (70 eV) *m*/*z* (rel intensity) 225 (M^+; 0.4), 134 (49), 105 (100), 91 (5), 77 (6), and 65 (2).

***N*-(*p*-Methoxybenzyl)phenethylamine (3c):** Yield, 11%; bp 152—153 °C (67 Pa); ^{1}H NMR ($CDCl_3$, 60 MHz) δ=1.32 (1H, s, NH), 2.85 (4H, s, CH_2CH_2), 3.74 (2H, s, $NC\underline{H}_2C_6H_4$), 3.78 (3H, s, CH_3O), 6.70—7.50 (9H, C_6H_4 and C_6H_5); MS (70 eV) *m*/*z* (rel intensity) 241 (M^+; 3), 150 (22), 121 (100), 105 (3), 91 (11), and 77 (9).

Synthesis of *N*-(*p*-Substituted Benzyl)-*N*-phenethylphenethylamine (4): To a toluene (15 ml) solution of *N*-(*p*-substituted benzyl)phenethylamine (25 mmol), 0.5 mmol of butyllithium was added in order to synthesize the corresponding lithium alkylamide. Then, 25 mmol of styrene was introduced into the solution. After the reaction mixture had been kept at 40 °C for 3 d, a small amount of methanol was added to cease the reaction. The product was isolated by fractional distillation.

***N*-Benzyl-*N*-phenethylphenethylamine (4a):** Yield 7%; bp 167 °C (0.7 Pa); ^{1}H NMR ($CDCl_3$, 60 MHz) δ=2.77 (8H, s, CH_2CH_2), 3.72 (2H, s, $NC\underline{H}_2C_6H_4$), 7.05—7.40 (15H, C_6H_5);

MS (CI, 200 eV) m/z (rel intensity) 316 ($M+1^+$; 4), 315 (M^+; 1), 314 ($M-1^+$; 3), (EI, 70 eV) 224 (100), 105 (9), 91 (75), 77 (3), and 65 (5).

***N*-(*p*-Methylbenzyl)-*N*-phenethylphenethylamine (4b):** Yield, 9%; bp 188—189 °C (0.7 Pa); ^{1}H NMR ($CDCl_3$, 60 MHz) δ=2.33 (3H, s, CH_3), 2.77 (8H, s, CH_2CH_2), 3.69 (2H, s, $NC\underline{H}_2C_6H_4$), 6.95—7.42 (14H, C_6H_4 and C_6H_5); MS (CI, 200 eV) m/z (rel intensity) 330 ($M+1^+$; 1), 329 (M^+; 0.7), 328 ($M-1^+$; 3) (EI, 70 eV) 238 (94), 105 (100), 91 (8), 77 (9), and 65 (3).

***N*-(*p*-Methoxybenzyl)-*N*-phenethylphenethylamine (4c):** Yield, 6%; bp 211—212 °C (0.7 Pa); ^{1}H NMR ($CDCl_3$, 60 MHz) δ=2.77 (8H, s, CH_2CH_2), 3.66 (2H, s, $NC\underline{H}_2C_6H_4$), 3.79 (3H, s, CH_3O), 6.65—7.42 (14H, C_6H_4 and C_6H_5). Found: C, 83.19; H, 8.64; N, 3.99%. Calcd for $C_{24}H_{27}NO$: C, 83.43; H, 7.88; N, 4.05%.

Synthesis of *N*-(*p*-Substituted Benzyl)vinylphenethylamine (6, 8): To a toluene (20 ml) solution of lithium (*p*-substituted benzyl) amide and (*p*-substituted benzyl)amine mixture prepared from 100 mmol of *p*-substituted benzylamine and 2 mmol of butyllithium, 100 mmol of *m*- or *p*-DVB was added. After the reaction mixture had been kept at 40 °C for 8 h, a small amount of methanol was added to cease the reaction. The product was isolated by fractional distillation.

***N*-Benzyl-*p*-vinylphenethylamine (6a):** Yield, 26%; bp 139 °C (8 Pa); ^{1}H NMR ($CDCl_3$, 60 MHz) δ=1.14 (1H s, NH), 2.73 (4H, s, CH_2CH_2), 3.67 (2H, s, $C\underline{H}_2C_6H_5$), 5.05—5.70 (2H, dd, J=11 and 18 Hz, C=CH_2), 6.52—6.70 (1H, dd, J=11 and 18 Hz, CH=C), 6.95—7.35 (9H, C_6H_4 and C_6H_5). Found: m/z 237.1497. Calcd for $C_{17}H_{19}N$: M, 237.1517.

***N*-(*p*-Methylbenzyl)-*p*-vinylphenethylamine (6b):** Yield, 20%; bp 151 °C (8 Pa); ^{1}H NMR ($CDCl_3$, 60 MHz) δ=1.35 (1H, s, NH), 2.31 (3H, s, CH_3), 2.82 (4H, s, CH_2CH_2), 3.75 (2H, s, $NC\underline{H}_2C_6H_4$), 5.01—5.85 (2H, dd, J=10 and 17 Hz, C=CH_2), 6.40—6.97 (1H, dd, J=11 and 17 Hz, CH=C), 7.00—7.60 (8H, C_6H_4). Found: m/z 251.1701. Calcd for $C_{18}H_{21}N$: M, 251.1674.

***N*-(*p*-Methoxybenzyl)-*p*-vinylphenethylamine (6c):** Yield, 0.4%; bp 159 °C (8 Pa); ^{1}H NMR ($CDCl_3$, 60 MHz) δ=1.38 (1H, s, NH), 2.82 (4H, s, CH_2CH_2), 3.72 (2H, s, $NC\underline{H}_2C_6H_4$), 3.78 (3H, s, CH_3O), 5.03—5.90 (2H, dd, J=10 and 17 Hz, C=CH_2), 6.43—7.47 (9H, CH=C and C_6H_4). Found: m/z 267.1581. Calcd for $C_{18}H_{21}NO$: M, 267.1623.

***N*-Benzyl-*m*-vinylphenethylamine (8a):** Yield, 15%; bp 130 °C (9 Pa); ^{1}H NMR ($CDCl_3$, 60 MHz) δ=1.45 (1H, s, NH), 2.85 (4H, s, CH_2CH_2), 3.81 (2H, s, $NC\underline{H}_2C_6H_4$), 5.05—5.94 (2H, dd, J=10 and 18 Hz, C=CH_2), 6.93—7.00 (1H, dd, J=11 and 18 Hz, CH=C), 7.00—7.50 (9H, and C_6H_4 and C_6H_5). Found: m/z 237.1490. Calcd for $C_{17}H_{19}N$: M, 237.1517.

***N*-(*p*-Methylbenzyl)-*m*-vinylphenethylamine (8b):** Yield, 14%; bp 156 °C (8 Pa); ^{1}H NMR ($CDCl_3$, 60 MHz) δ=1.53 (1H, s, NH), 2.33 (4H, s, CH_2CH_2), 2.85 (2H, s, $NC\underline{H}_2C_6H_4$), 3.76 (3H, s, CH_3), 5.08—5.94 (2H, dd, J=10 and 16 Hz, C=CH_2), 6.44—7.00 (1H, dd, J=11 and 18 Hz, CH=C), 7.05—7.45 (8H, C_6H_4). Found: m/z 251.1704. Calcd for $C_{18}H_{21}N$: M, 251.1674.

***N*-(*p*-Methoxybenzyl)-*m*-vinylphenethylamine (8c):** Yield, 17%; bp 159 °C (6 Pa); ^{1}H NMR ($CDCl_3$, 60 MHz) δ=1.37 (1H, s, NH), 2.73 (4H, s, CH_2CH_2), 3.78 (5H, CH_3O and $NC\underline{H}_2C_6H_4$), 5.00—5.80 (2H, dd, J=13 and 17 Hz, C=CH_2), 6.40—7.48 (9H, CH=C and C_6H_4). Found: m/z 267.1641. Calcd for $C_{18}H_{21}NO$: M, 267.1624.

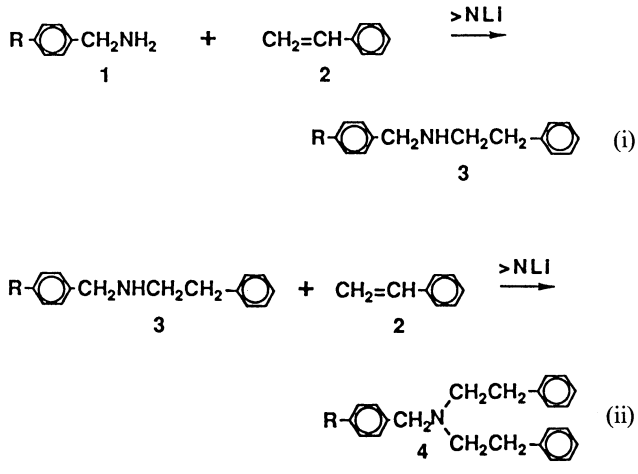
Dependence of the Product Yield on the Reaction Time: An equimolar reaction of benzylamine (50 mmol) with styrene (50 mmol) was carried out in toluene catalyzed by lithium benzylamide. The reaction temperature was kept at 40±0.1 °C. The reaction was quenched after appropriate time intervals by sampling portions of the mixture and adding them to methanol. The concentration of the starting materials and products were determined by vapor-phase chromatography using pentadecane as an internal standard.

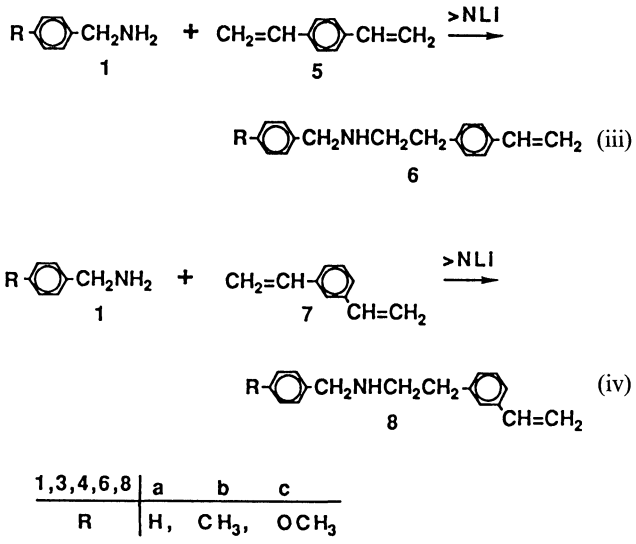
Procedure of Rate Study: The reaction was carried out as follows: toluene, *p*-substituted benzylamine (137.5 mmol), butyllithium (12.5 mmol), tetradecane (internal standard for vapor-phase chromatography) were mixed and stirred. Vinyl-substituted aromatics (12.5 mmol) were added and the total volume of reaction mixture was adjusted to 50 ml. The mixture was kept at 50±0.1 °C and quenched after appropriate time intervals by sampling portions of the solution and adding them to methanol. The concentrations of vinyl-substituted aromatics were determined by vapor-phase chromatography. The rate constants were reproducible to about ±5% on repeated runs.

Measurements: Vapor-phase chromatography was carried out with a HEWLETT PACKARD 5890A equipped with FID by using a DB-1, wide bore fused silica capillary column (15 m×0.53 mm, J&W). The column temperature was programmed from 100 to 300 °C at 20 °C min^{-1}. ^{1}H NMR spectra were recorded at 60 MHz on a Hitachi model R-600 FT-NMR spectrometer. The mass spectra were measured on a JEOL JMS-SX102.

Results and Discussion

Reaction of *p*-Substituted Benzylamine with Styrene. In order to obtain information concerning the appropriate reaction conditions required to synthesize *N*-(*p*-substituted benzyl)-*m*- (or *p*-)vinylphenethylamine from *p*-substituted benzylamines, such as benzylamine, *p*-methylbenzylamine and *p*-methoxybenzylamine with *m*- or *p*-divinylbenzene (DVB), the reaction of styrene with substituted benzylamine was investigated as a model reaction. A second-step addition reaction might take place, to produce the 1 : 2 adduct, as shown in Eq. (ii), since the first-step addition product of *p*-substituted benzylamine with styrene is the secondary amine shown in Eq. (i). Figure 1 shows the time dependence of the





concentrations of the starting materials and the products measured by vapor-phase chromatography. As summarized in Fig. 1 and in the Experimental part, 1 : 1 and 1 : 2 adducts (benzylamine : styrene) were detected and isolated by fractional distillations under reduced pressure. The 1 : 2 adduct was obtained, even in the early stage of the reaction, thus showing a clear contrast to the reaction of α-methylbenzylamine with styrene, which produces only a 1 : 1 addition compound.[9] Twenty percent of benzylamine reacts with styrene within 6 h in the first-step addition reaction, while only 12% of α-methylbenzylamine reacts under the same reaction conditions. These differences in the reactivity between benzylamine and α-methylbenzylamine might be attributed to a steric hindrance by the α-methyl group. The results are consistent with those obtained in a reaction of styrene with propylamine and *s*-butylamine; in this case the reaction rate constant for *s*-butylamine with styrene is less than one forth that for propylamine with styrene.[5]

Kinetic Studies of *p*-Substituted Benzylamines with Styrene. A pseudo-first-order rate analysis of the reaction between benzylamine and styrene might be possible in an early stage of the reaction in the presence of a large excess of benzylamine derivatives in the reaction mixture, since the amount of the 1 : 2 adduct is negligibly small within 6 h, as is shown in Fig. 1. Pseudo-first-order rate plots for the reactions of benzylamine, *p*-methylbenzylamine and *p*-methoxybenzylamine to styrene are shown in Fig. 2. Satisfactory rate analyses are presented, since straight lines were obtained. The pseudo-first-order rate constants measured in toluene are summarized in Table 1. The rate constants for benzylamine derivatives are of the same order of magnitude (10^{-4} s^{-1}) as that of hexylamine with styrene in cyclohexane at 50 °C.[6]

The second-step addition reaction rate for the *N*-benzylphenethylamine (**3a**) with styrene is about one fifth that of the first-step addition reaction, as shown in Table 1. It is thus confirmed that 1 : 1 adducts, *N*-(*p*-substituted benzyl)phenethylamines, can be preferentially prepared by adjusting the reaction conditions.

Preparation of *N*-(*p*-Substituted Benzyl)vinylphenethylamines. On the basis of the results obtained in

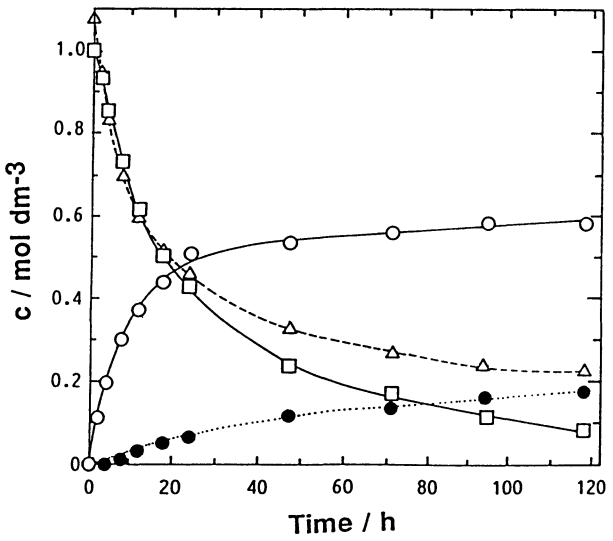


Fig. 1. Time dependence of the reaction of benzylamine with styrene. Reaction conditions: $[St]_0$=$[benzylamine]_0$=1.0 mol dm^{-3}, $[C_6H_5CH_2NHLi]$=0.02 mol dm^{-3} in toluene at 40 °C. Concentrations of styrene (□); benzylamine (△); $C_6H_5CH_2NHCH_2CH_2C_6H_5$ (○); $C_6H_5CH_2N(CH_2CH_2C_6H_5)_2$ (●);

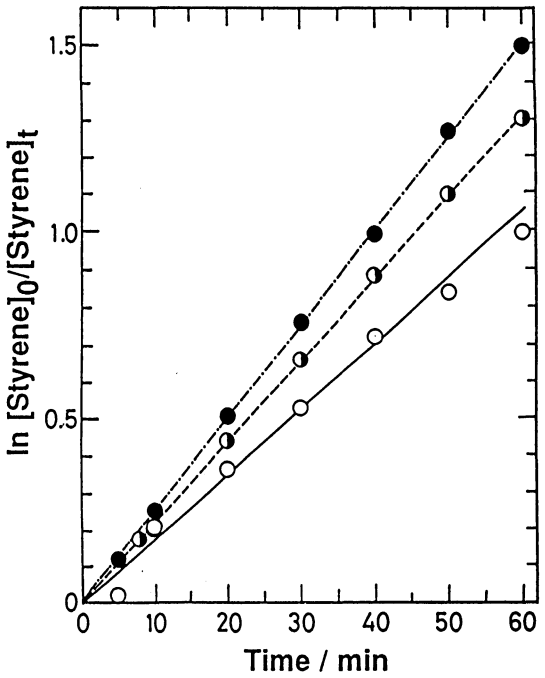


Fig. 2. Pseudo-first-order analysis of the reaction of *p*-substituted benzylamine with styrene in toluene at 50 °C. Reaction conditions: $[St]_0$=$[>NLi]_0$=0.25 mol dm^{-3}, [*p*-substituted benzylamine]$_0$=2.5 mol dm^{-3}; benzylamine (○); *p*-methylbenzylamine (◑), *p*-methoxybenzylamine (●).

Table 1. Pseudo-First-Order Rate Constants, k', of the Addition Reaction of *p*-Substituted Benzylamine with Vinyl-Substituted Aromatics in Toluene at 50 °C[a)]

p-**R**-C_6H_4-CH_2NH_2 **R**	σ[b)]	$10^4\ k'/s^{-1}$		
		St	*m*-DVB	*p*-DVB
H	0	2.7	11	23
CH_3	−0.17	3.7	16	32
CH_3O	−0.27	4.2	17	47
3a	—	0.59	—	—
Hexylamine[c)]	—	5.5	—	—
ρ		−0.72	−0.67	−1.1

a) [vinyl-substituted aromatics]$_0$=[*p*-**R**-$C_6H_4CH_2NHLi$]$_0$ =0.25 mol dm^{-3}, [*p*-**R**-$C_6H_4CH_2NH_2$]$_0$=2.5 mol dm^{-3}. b) Hammett's substituent constant. c) Ref. 6, [St]$_0$= [$C_6H_{13}NHLi$]$_0$=0.25 mol dm^{-3}, [$C_6H_{13}NH_2$]$_0$=2.5 mol dm^{-3} in cyclohexane at 50 °C.

the reaction systems of *p*-substituted benzylamines with styrene, the addition reactions of DVB with *p*-substituted benzylamines were examined. *N*-(*p*-Substituted benzyl)-*p*- (or *m*-) vinylphenethylamines (**6**, **8**), which are the products of the first addition step, could be preferentially prepared, as mentioned in the Experimental part. A small amount of the second-step addition-reaction products was detected from GC-MS analyses of the reaction mixture. In the case of *m*-DVB and *p*-substituted benzylamines, a small amount of the adducts (amine : DVB=2 : 1) were also detected.

Kinetic Studies of the Addition Reactions of *p*-Substituted Benzylamine with DVB. In order to obtain quantitative information concerning the addition reaction with DVB, kinetic studies were carried out. A satisfactory first-order behavior was also observed for the *p*-substituted benzylamine derivatives with *m*- and *p*-DVB during the early stage of the reaction in the presence of a large excess of *p*-substituted benzylamine. The pseudo-first-order rate constants are summarized in Table 1. The reaction rate constants increase with an increase in the electron-donating character of the *p*-substituted groups of benzylamines. The rate constants were found to be according to the order *p*-DVB > *m*-DVB > styrene. Similar results were reported in the reaction systems of lithium α-methylbenzylamide[10)] and lithium diethylamide[8)] with DVB.

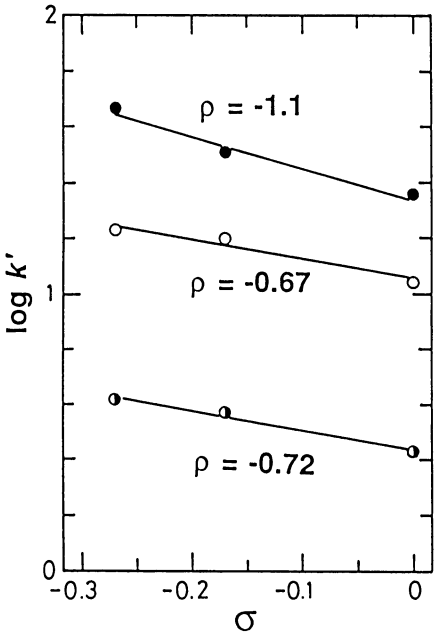
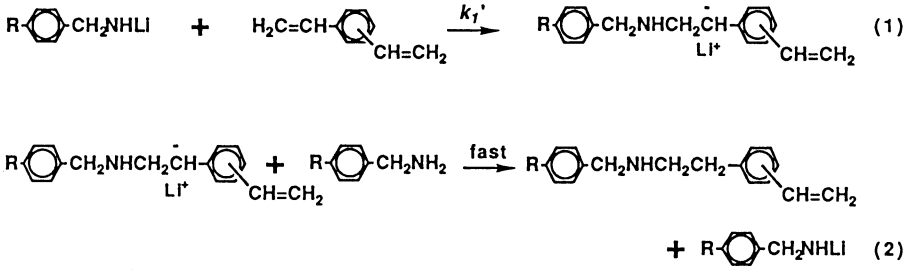


Fig. 3. Hammett σ–ρ plot of lithium *p*-substituted benzylamide with styrene (◑), *m*-DVB (○), and *p*-DVB (●).

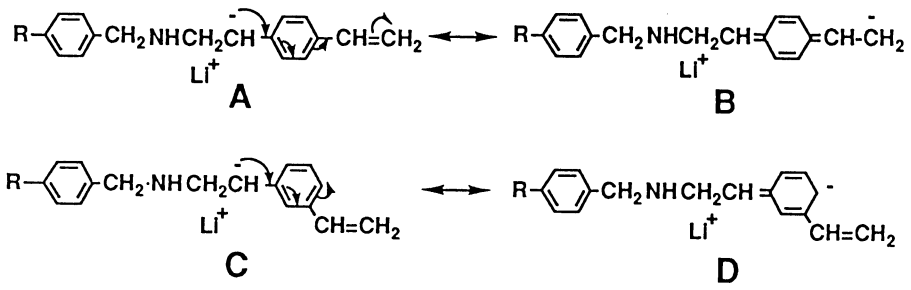
As shown in Fig. 3, the ρ-values are −0.72 for styrene, −0.67 for *m*-DVB, and −1.1 for *p*-DVB, respectively. The negative values of ρ suggest that the lithium *p*-substituted benzylamide is a nucleophile and that vinyl-substituted aromatic is an electorophile. These results support the postulated reaction mechanism shown in Scheme 1. The formation of the adduct of lithium *p*-substituted benzylamide with the vinyl-substituted aromatic is rate-determining.

The larger rate constants of *m*- and *p*-DVB than that of styrene are attributable to two reasons. One is the electron-withdrawing effect of one vinyl group (σ_m=+0.02) on the other vinyl group. The other reason is that DVB possesses two vinyl groups in one molecule and should therefore be statistically twice as reactive.

On the other hand, the higher reactivity of *p*-DVB compared to that of *m*-DVB might be attributed to through-resonance interactions.[12)] The resonance structure of the intermediate formed in the addition reaction shown in Scheme 2 may be probable. Struc-



Scheme 1.



Scheme 2.

ture **B** shown in Scheme 2 makes a considerable contribution to the stabilization of the carbanionic intermediate. The *m*-vinyl group of the intermediate derived from *m*-DVB, on the other hand, has no participation in the resonance structure (**D** in Scheme 2). The vinyl group at the *para* position causes an enhanced reactivity through a conjugative effect.

Interestingly, the *p*-DVB not only shows a higher reactivity, but also a larger absolute ρ value ($\rho=-1.1$). On the other hand, *m*-DVB and styrene show similar ρ values, -0.67 for *m*-DVB and -0.72 for styrene.

Further detailed kinetic studies on a lithium alkylamide-catalyzed addition reaction of benzylamines with vinyl-substituted aromatics are now under way in our laboratory.

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