Chemical Modification of Polymers. VI. Displacement of Reactive Halogens by Isoquinoline Reissert Compound Anions

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ABSTRACT: The anion of 2-benzoyl-1,2-dihydroisoquinaldonitrile reacts with poly(vinylbenzyl chloride) in quantitative yield and conversion with no degradation or cross-linking side reactions. The resultant poly[1-(vinylbenzyl)-2-benzoyl-1,2-dihydroisoquinaldonitrile] undergoes 100% hydrolysis to the fully aromatized poly[1-(vinylbenzyl)-isoquinoline]. These polymers were also prepared from the corresponding monomer, 1-(4′-vinylbenzyl)-2-benzoyl-1,2-dihydroisoquinaldonitrile.

Stability to thermal and oxidative degradation has been a long-standing feature of the study of macromolecules. Nonetheless, in recent years the purposeful modification of polymers by other chemical reactions has received increasing attention.[1-4] A large proportion of the research activity is concerned with the preparation and utility of functionalized polymers as synthetic reagents. This field springs from the original contribution of Merrifield, who first utilized such insoluble polymers for anchoring sequentially synthesized polypeptides.[5] Much of the work still centers on the preparation of such insoluble reagents, the advantages of the process deriving from the insoluble nature of the polymers.

In contrast our work has been concerned with soluble polymers and reactions in solution.[6-10] The primary reason for this is that for most of our potential applications solubility is desirable. Another reason is that the use of soluble polymers allows one to study the reaction processes more easily and in more depth than is possible with insoluble polymers. Using soluble polymers spectroscopic (ir, NMR, uv) studies are more facile and allow a degree of quantitation difficult to achieve otherwise. The solution properties (viscosity, molecular weight data) are observable and are useful in detecting degradative or cross-linking processes which may occur as side reactions. The utility of these techniques for unraveling reaction processes was demonstrated recently in a study of the dimethyl sulfoxide (DMSO) oxidation of poly(vinylbenzyl chloride) (1).[10] A knowledge of molecular weight changes allowed optimization of the process; this could not have been done as readily on the insoluble analogue in the absence of such data. We therefore recommend the study of reactions on soluble polymers even when their ultimate use is to be as insoluble resins.

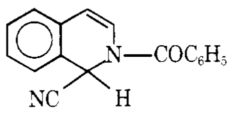
Our interest in this area stems from the possibility of continuous and controlled variation of physicochemical properties of macromolecular systems. The aims of our program of study are to provide new and useful polymers for specific applications as well as series of polymers for studying the mechanistic aspects of physicochemical phenomena of interest.[11]

We perceive the following advantages arising from the chemical modification of polymers. (1) It is possible to synthesize polymers that cannot be prepared by direct polymerization techniques[10] or only with difficulty. (2) A series of structurally related polymers of constant degree of polymerization, namely that of the starting polymer, can be prepared. Such a series is often useful in studying physicochemical phenomena. (3) A series of structurally related polymers of constant tacticity, replicating that of the parent polymer, can be produced. Again such polymers are useful for relating molecular structure to activity in cases when tacticity, i.e., order, plays a role. (4) Copolymers of desired composition can be prepared by stoichiometric control of sequential reactions.

The present paper is a detailed account of the reactions of anions of isoquinoline Reissert compounds with polymers bearing displaceable halogens and supplements our preliminary communication.[8]

Discussion

Reissert compounds are of proven value synthetically.[12-14] They are readily prepared from quinolines or isoquinolines by treatment with an acid chloride in the presence of potassium cyanide.[15] 2-Benzoyl-1,2-dihydroisoquinaldonitrile (1) is a typical Reissert compound. Its anion 2 is formed by reaction with strong base, the most convenient system being sodium hydride in dimethylformamide (DMF).[16] This serves also as a convenient medium for carrying out alkylation reactions with alkyl halides, leading to 1-alkyl-2-benzoyl-1,2-dihydroisoquinaldonitriles (3).[16-19] Hydrolysis of 3 with base leads to 1-alkylisoquinolines (4).[18,20] Thus, this series of reactions results in conversion of isoquinoline to 1-alkylisoquinolines via the Reissert compound 1. This paper describes the application of this synthetic sequence to polymeric alkyl halides.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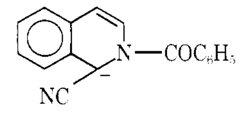
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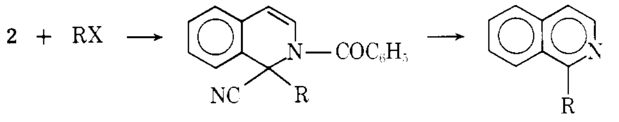
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A. Reaction of 1 and Poly(vinylbenzyl chloride). Our initial work in this area utilized poly(vinylbenzyl chloride) (5), which was prepared by free radical polymerization of a 60:40 mixture of *m*-/*p*-vinylbenzyl chloride (Dow Chemical Co.). Gel permeation chromatographic (GPC) analysis gave $\bar{M}_n = 2.08 \times 10^4$, $\bar{M}_w = 4.39 \times 10^4$ (in terms of polystyrene equivalents), MWD = 2.11.

An unusual aspect of polymer 5 was discovered when it was precipitated from tetrahydrofuran (THF) solution by addition to *n*-hexane; one molecule of *n*-hexane per three monomer units was incorporated into the polymer. It was not removed by drying in vacuo at room temperature. Drying at 78° in vacuo or reprecipitation from THF into methanol did remove the hexane. It is tempting to ascribe this occlusion to a twining of the hexane about the polymer backbone. The phenomenon does, however, seem to be specific to *n*-hexane; *n*-pentane, *n*-heptane, *n*-octane, 2-methylpentane, and 3-methylpentane are not occluded.

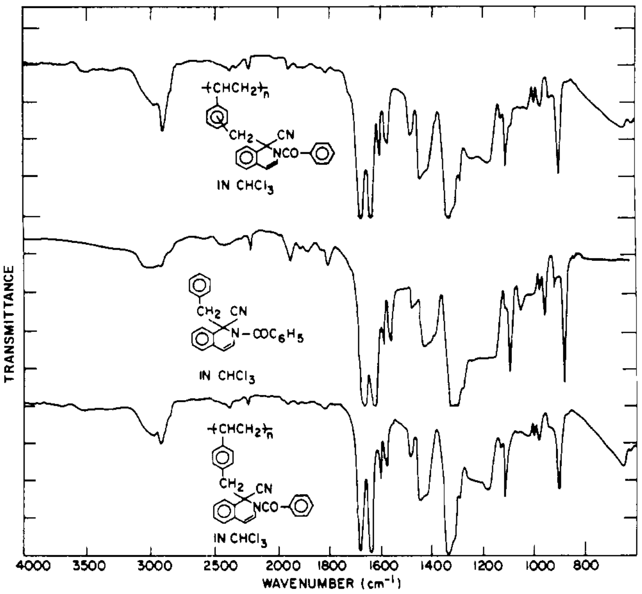


Figure 1. Infrared spectra of $CHCl_3$ solutions of (a) poly[1-(vinylbenzyl)-2-benzoyl-1,2-dihydroisoquinaldonitrile] (**6**) prepared from **1** and **5** (top); (b) 1-benzyl-2-benzoyl-1,2-dihydroisoquinaldonitrile (**3**, R = $CH_2C_6H_5$) (middle); (c) poly[1-(4′-vinylbenzyl)-2-benzoyl-1,2-dihydroisoquinaldontrile] (**17**) prepared by polymerization of **14** (bottom).

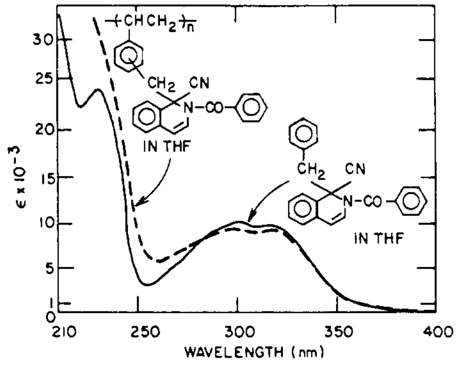


Figure 2. Ultraviolet spectra of THF solutions of (a) poly[1-(vinylbenzyl)-2-benzoyl-1,2-dihydroisoquinaldonitrile] (**6**) (dashed line); (b) 1-benzyl-2-benzoyl-1,2-dihydroisoquinaldonitrile (**3**, R = $CH_2C_6H_5$) (solid line).

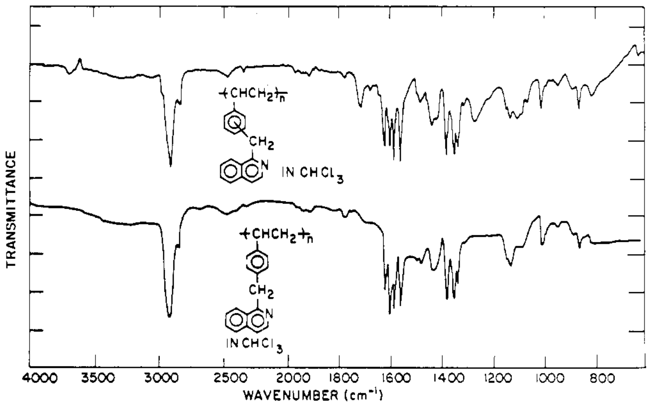


Figure 3. Infrared spectra of $CHCl_3$ solutions of (a) poly[1-(vinylbenzyl)isoquinoline] (**7**) prepared from **6** (top); (b) poly[1-(4′-vinylbenzyl)isoquinoline] (**18**) prepared from **17** (bottom).

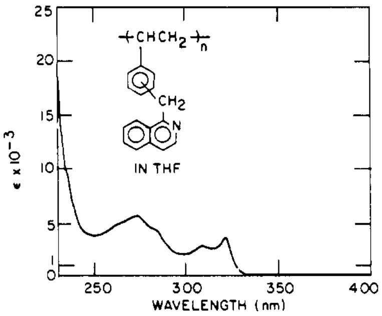
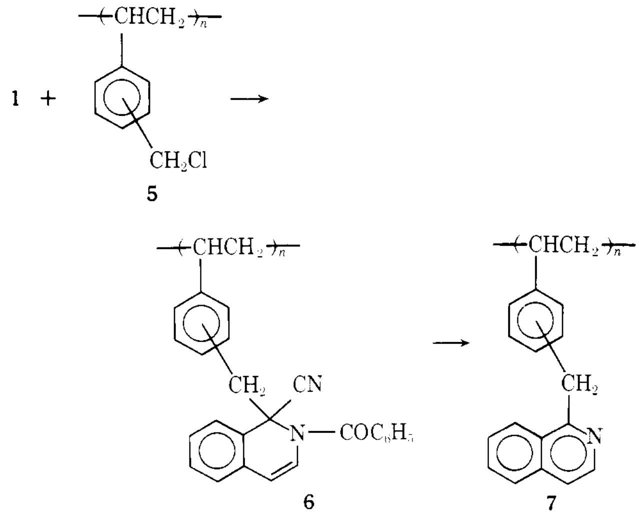


Figure 4. Ultraviolet spectrum of poly[1-(vinylbenzyl)isoquinoline] (**7**) prepared from **6** (in THF).

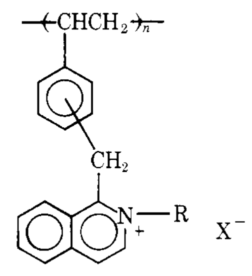


The reaction of **1** and **5** gave poly[1-(vinylbenzyl)-2-benzoyl-1,2-dihydroisoquinaldonitrile] (**6**) in quantitative yield. Its infrared (ir) (Figure 1a) (carbonyl peak at 1695 cm^{-1}, slightly higher than the usual range for monomeric analogues **3**[21]) and ultraviolet (uv) spectra (Figure 2a) are very similar to those of 1-benzyl-2-benzoyl-1,2-dihydroisoquinaldonitrile (**3**, R = $CH_2C_6H_5$)[19] (Figures 1b and 2b). As anticipated both M_n and M_w increase, but MWD is relatively unchanged, indicating that there was no degradation or cross-linking.

Basic hydrolysis of **6** led to poly[1-(vinylbenzyl)isoquinoline] (**7**) in quantitative conversion as indicated by the ir (Figure 3a) (no carbonyl band) and uv spectra (Figure 4) (shift of λ_{max} to longer wavelength[22]). Again MWD is unchanged, indicating no side reactions leading to degradation or cross-linking.

A number of derivatives of **7** were also prepared. Reaction of **7** and methyl iodide in benzene gave poly[1-(vinylbenzyl)isoquinolinium methiodide] (**8**) in nearly quantitative conversion. In DMSO **8** has λ_{max} 348 nm due to the charge transfer ($I^- \rightarrow N^+$) band. Use of gaseous methyl bromide led to the methobromide (**9**) in 63% conversion. It has λ_{max} 350 nm (DMSO). Reaction of **7** and picric acid led to the picrate **10** in a 95% conversion; **10** has λ_{max} 380 nm (DMSO).

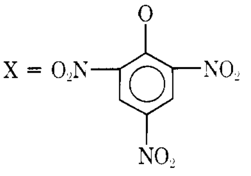
The conversion of poly(vinylbenzyl chloride) to **6** and **7** is surprisingly good on two counts. (1) First, the formation of **6** is cleaner and more efficient than usual monomer reactions involving benzyl halides. The Reissert compound **1** has been reacted with a number of substituted benzyl halides under these same reaction conditions and the yields of **3**, R = p-$CH_2C_6H_4$-X, vary from 65 to 84%,[18,19,22] including X = CH_3 (78%).[18] (2) Second, chemical reactions of pen-



8, R = CH_3; X = I

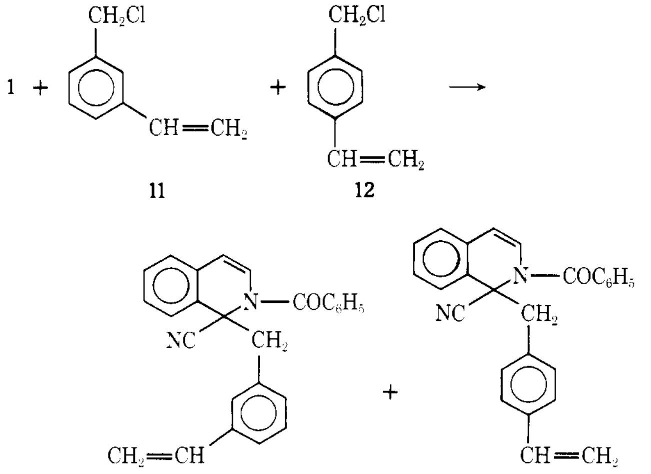
9, R = CH_3; X = Br

10, R = H; X =



dant groups on polymers tend in general to be sluggish[6] and complete conversion is difficult to achieve,[1] though in some cases satisfactory conversions are attainable.[2-4,7,10]

B. Synthesis of 6 by Direct Polymerization. Comparison of the polymer prepared by chemical modification and one of identical structure by direct polymerization was of interest as a structure proof. In order to provide an alternative synthetic route to the individual isomers of polymer 6, the reaction of the Reissert compound 1 with vinylbenzyl chloride was studied. Treatment of a DMF solution of 1 and a 60–40 mixture (Dow Chemical Co.) of 11 and 12, the meta and para isomers, at room temperature with sodium hydride leads to a mixture of the desired 13 and 14 in 78% yield. Compounds 13 and 14 undergo polymerization when heated and purification must be done carefully to minimize polymer formation. By fractional recrystallization of the mixture from ethanol the para isomer 14 was isolated in a pure state in 11% yield as opposed to 40% expected on the basis of the proportion of 12 in the starting material. The more soluble, lower melting isomer 13 was not isolated in pure form.



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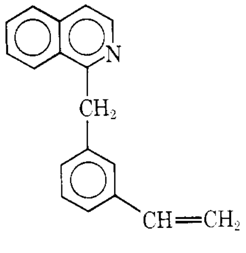
14

The NMR spectrum of 14 contains an AB quartet at δ 3.7 due to the benzylic methylene protons. Analysis of the pattern shows that $\Delta\nu$ (the chemical shift difference) of the diastereotopic benzylic protons is 15 Hz or 0.24 ppm. In the related compound 3, R = $CH_2C_6H_5$, $\Delta\nu$ is 0.22 ppm.[21] The infrared spectrum of 14 contains a carbonyl peak at 1675 cm^{-1}. This is in good agreement with the 1672–1694-cm^{-1} range found for a series of 1-alkyl-2-acyl-1,2-dihydroisoquinoldonitriles.[21] The spectrum also contains bands characteristic of the terminal vinyl group. The ultraviolet spectrum of 14 contains intense ($\epsilon \sim 10^4$) bands at 315, 297, and 287 nm in 95% ethanol.

Hydrolysis of a mixture of 13 and 14 to the fully aromatic 1-(3′-vinylbenzyl)isoquinoline (15) and 1-(4′-vinylbenzyl)isoquinoline (16) with benzyl trimethylammonium hydroxide (Triton B) in methanol proceeded in high yield. The vinyl monomers 15 and 16 are low-melting solids or oils that are difficult to crystallize and were analyzed as the picrates. The monomers polymerize when heated in the absence of solvent. The infrared spectrum of a mixture of 15 and 16 lacks the 1675-cm^{-1} carbonyl peak present in 13 and 14 but retains the terminal vinyl bands.



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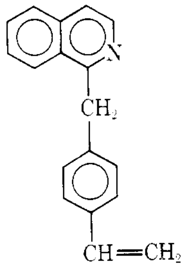

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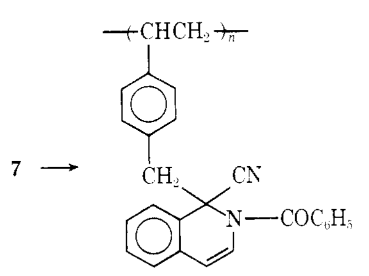
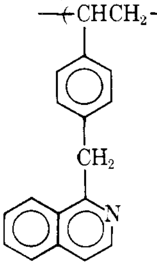


17

Polymerization of 14 at 80°C for about 17 hr in benzene solution using azobis(isobutyronitrile) (AIBN) led to an 81% yield of the colorless polymer 17. GPC analysis yielded $\bar{M}_n = 2.90 \times 10^4$, $\bar{M}_w = 6.87 \times 10^4$ (in polystyrene equivalents), and MWD = 2.4. A second polymerization run was carried out using the same concentrations but at 61° for 64 hr; the polymer, isolated in 91% yield, had $\bar{M}_n = 2.24 \times 10^4$, $\bar{M}_w = 6.76 \times 10^4$ (in polystyrene equivalents), and MWD = 3.16.

The infrared spectrum (Figure 1c) of poly[1-(4′-vinylbenzyl)-2-benzoyl-1,2-dihydroisoquinaldonitrile] (17) prepared from the monomer 14 is virtually identical with the spectrum of the polymer 6 made from reaction of 1 and 5 (Figure 1a). The uv spectra of the polymer 17 prepared from the monomer 14 and 6 prepared by chemical modification of poly(vinylbenzyl chloride) are identical in λ_{max}. Extinction coefficients for the two long-wavelength bands are very similar. However, there does appear to be a difference in the extinction coefficients of the shoulders at 287 and 276 for 6 and 17, those for 6 being up to 13% greater. These minor differences may be due to the presence of ~60% of the meta isomer in 6 or tacticity differences in the two polymers.[23]

The polymers 7 and 18 from hydrolysis of 6 and 17, respectively, were also compared. The infrared spectrum of 7 (Figure 3a) and that of 18 (Figure 3b) are very similar. The ultraviolet spectra of 7 and 18 in THF show good correspondence between λ_{max} values with the exception of the absence of a 267 peak in 7. The extinction coefficients for 322, 316, 308, and 280 nm are 11 to 16% higher for 7 than for 18, while for the 272-nm absorption ϵ of 18 is 15% higher than that of 7. The 272-nm band is most likely the ${}^1L_b$ transition of the benzyl moiety; the higher extinction coefficient in 18, the para isomer, relative to 7, the 60–40 meta-para mixture, is consistent with results for *p*- and *m*-xylenes.[24] The longer wavelength bands are associated with $\pi \rightarrow \pi^*$ transitions of the isoquinoline chromophore. These could be sensitive to the substitution pattern of the benzyl group. Again, tacticity differences[23] could contribute as well.



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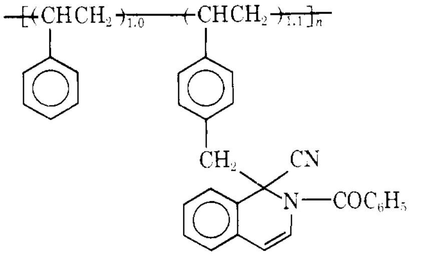
Monomer **14** was also copolymerized with styrene in a 1:1 feed ratio using AIBN in benzene solution at 61° for 97 hr (63% conversion). The copolymer (**19**) had a mole ratio of the isoquinoline monomer to styrene of 1.1 to 1.0 according to elemental analysis. Thus the monomer **14** appears to be of the same order of reactivity as styrene in free radical polymerization. The polymer had $\bar{M}_n = 2.35 \times 10^4$, $\bar{M}_w = 9.40 \times 10^4$ (in polystyrene equivalents), and MWD = 3.99.



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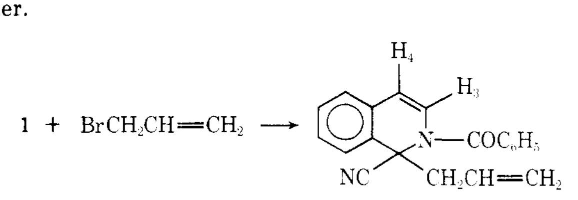
In another reaction similar to that for synthesis of **13** and **14**, **1** was reacted with allyl bromide. 1-Allyl-2-benzoyl-1,2-dihydroisoquinoldonitrile (**20**) was isolated in 100% yield. The NMR spectrum shows the methylene protons of the allyl group as an upfield multiplet (AB part of an ABX pattern) at ca. δ 2.98. First-order analysis of the AB pattern gives $\Delta\nu$ (the chemical shift difference) of the diastereotopic methylene protons equal to 17 Hz or 0.28 ppm. This is very close to the value of 0.27 for the corresponding 1-isobutyl analogue.[21] In another attempt to prepare a polymerizable monomer, **1** failed to react with 2-chloroethyl vinyl ether.



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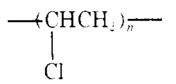
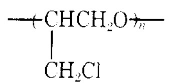
C. Reaction of 1 with Other Polymers Bearing Halogens. In an attempt to extend this reaction **1** was converted to its anion **2** by use of phenyllithium in THF and this was exposed to 0.67 equiv of poly(vinyl chloride) (**21**) at −45 to −50° and the temperature was raised in 15° increments every hour. Of the **21**, 84% was recovered unreacted (ir); none of the expected product was found.



$-\!\!(\underset{\mathrm{Cl}}{\mathrm{CH}}\mathrm{CH_2})_n\!\!-$

21



$-\!\!(\underset{\mathrm{CH_2Cl}}{\mathrm{CH}}\mathrm{CH_2O})_n\!\!-$

22

Similarly the anion **2** prepared by treatment of **1** with sodium hydride in DMF was exposed to 0.80 equiv of poly(epichlorohydrin) (**22**) at room temperature; 76% of the **22** was recovered. None of the expected product was found. **2** does not react with monomeric epichlorohydrin either apparently.[17]

D. Rationalization of Reactivity Patterns. The facile reaction of **1** and **5** is noteworthy. The lack of reactivity of **21** was not unexpected; however, the lack of significant dehydrochlorination also seems significant. It is useful to put these results in perspective by comparison to other reported work in which potassium *O-tert*-butylthiocarbonate (**23**) was the nucleophile; a side reaction leading to cross-linking products notwithstanding, the extents of reaction by nucleophilic displacement of Cl^- from **5**, **21**, and **22** were 92, 55, and 95% in DMF.[25] With the exception of **5** the present results are in contrast.

$K^+ \quad {}^-SCOOBu\text{-}t$

23

While a number of factors influencing polymer reactivity have been considered,[26] the principle of hard and soft acids and bases[27] does not seem to have been discussed in this regard. The rationalization of the above results exemplifies the use of these principles. Anion **23** is a very soft anion and thus the greater its reactivity with a given substrate the softer the substrate. On this basis the softness of the polymers is **22** > **5**. (**21** is left out of this scheme since in reaction with **23** steric inaccessibility very likely contributes to the low reactivity; on the basis of softness **21** would be softer than **5** and probably softer than **22**. We believe the lack of reaction of **2** with **21** is primarily a consequence of steric hindrance to approach to the nucleophilic site, which is part of the backbone.) The lack of reactivity of **2** with **21** and **22** then suggests that anion **2** is significantly harder than **23**. However, it is not hard enough to abstract a proton and bring about dehydrochlorination of **21**, though the soft solvent DMF also tends to minimize this. This hardness of **2** suggests that it would also be reactive toward aldehydes, while **23** would not be. Of course anion **2** does react with aldehydes,[12,13] while **23** would most likely react via its harder oxygen anion. A later paper will describe such reactions of **2** with polymeric aldehydes.[9]

The increased yield of the reaction of the Reissert anion with poly(vinylbenzyl chloride) relative to that with benzyl chloride may in part be due to the greater ease of isolation of the polymer. However, the reaction is not as messy in the polymer case and this suggests greater specificity. This could arise from the soft environment provided by the hydrocarbon backbone of the polymer, which would disfavor side reactions of the harder type, such as proton abstraction leading to carbene.

On this basis the sluggishness of aminolysis of *n*-butyl methacrylate polymers with aliphatic amines and the lack of solvent dependence[6] may be attributed to the hardness of the ester carbonyl and the amine nucleophile in contrast to the soft shielding effect of the polymer backbone. It thus appears that consideration of the hard and soft acid and base principles may be of particular advantage in understanding and controlling reactions of polymers due to the local environment of the reactive site provided by the rest of the polymer.

Conclusions

The reaction of the anion of 2-benzoyl-1,2-dihydroisoquinaldonitrile (**1**) and poly(vinylbenzyl chloride) (**5**) is essentially quantitative. This is noteworthy from the point of view of polymer reactivity and also for such a reaction of **1** with benzyl halides. Moreover, the hydrolysis of the resultant poly[1-(vinylbenzyl)-2-benzoyl-1,2-dihydroisoquinaldonitrile] (**6**) to the fully aromatic isoquinoline polymer, poly[1-(vinylbenzyl)isoquinoline] (**7**), is also quantitative. These structures have been confirmed by synthesis from the corresponding vinyl monomer. In contrast poly(vinyl chloride) and poly(epichlorohydrin) are not reactive toward the Reissert anion. The former case seems to be a steric problem, while the latter may be rationalized by hard and soft acid–base principles.

Experimental Section

General. Ir spectra were determined on a Perkin-Elmer Model 267, NMR spectra on a JOELCO C-60H and uv spectra (λ in nm) on a Cary Model 15. Polymer extinction coefficients are reported on a monomer unit basis. Melting points were determined in capillaries on a Thomas-Hoover apparatus and are corrected. Thermal properties of the polymers were determined on a Perkin-Elmer Model 1B differential scanning calorimeter. Elemental analyses were performed by Spang Microanalytical Laboratories, Ann Arbor, Mich. GPC was performed on 0.25% THF solutions using a Waters instrument; all molecular weights are in terms of polystyrene equivalents.

2-Benzoyl-1,2-dihydroisoquinaldonitrile (1). This compound was prepared in 85% yield by the literature procedure.[15] Mp 125–126°, reported mp 124–126°.[15]

Vinylbenzyl Chloride(chloromethylstyrene). This compound was obtained from Dow Chemical Co. as experimental monomer NC-19156, Lot. No. TI-4-10-25-71-14. It was used as received.

Poly(vinylbenzyl chloride) (5). This was synthesized from vinylbenzyl chloride using dibenzoyl peroxide as initiator. It was purified by precipitation from THF solution (~0.3 g/ml) with *n*-hexane three times and dried in vacuo. T_g = 78°, endotherm at 175°. Anal. Calcd for C_9H_9Cl: C, 70.82; H, 5.94; Cl, 23.23. Found: C, 73.17; H, 7.39; Cl, 19.55. Calcd for $C_9H_9Cl\cdot\frac{1}{3}C_6H_{14}$: C, 72.85; H, 7.60; Cl, 19.55. This sample was then dried in vacuo at 78° for 20 hr. Anal. Found: C, 71.15; H, 5.94; Cl, 23.23. A separate sample of the crude polymer was precipitated from THF using methanol, T_g = 91°. Anal. Found: C, 70.89; H, 5.80; Cl, 23.12. Gel permeation chromatography (THF) gave $\bar{M}_n = 2.08 \times 10^4$, $\bar{M}_w = 4.39 \times 10^4$, MWD = 2.11. Intrinsic viscosity (THF): 2.35 cl/g.

Poly[1-(vinylbenzyl)-2-benzoyl-1,2-dihydroisoquinaldonitrile] (6). To a stirred solution of 1.90 g (7.31 mmol) of **1** and 0.76 g (5.06 meq) of **5** in 30 ml of dry DMF was added 0.34 g (8.0 mmol) of 57% NaH. The mixture turned dark brown then red-orange and straw-colored. After 1 hr it was poured into 200 ml of water. The solid was filtered, washed with water, and dried to yield 1.88 g (100%). After three precipitations from THF with hexane a cream colored solid resulted, T_g = 154°. Anal. Calcd for $C_{26}H_{20}N_2O$: C, 82.95; H, 5.36; N, 7.44. Found: C, 82.81; H, 5.36; N, 7.35. Ir($CHCl_3$): C=O, 1695 cm^{-1} (see Figure 1a). NMR ($CDCl_3$): δ 0.9–2.0 (m, 3 H, backbone CH,CH_2), 3.7 (s, 2 H, benzylic CH_2), 5.0–8.2 (m, 13 H, aromatic and vinyl). The uv spectrum is shown in Figure 2a. Gel permeation chromatography gave $\bar{M}_n = 3.26 \times 10^4$, $\bar{M}_w = 6.45 \times 10^4$, MWD = 1.98.

Poly[1-(vinylbenzyl)isoquinoline] (7). To a refluxing solution of 10.0 g (26.6 mequiv) of polymer **6**, 6.0 g of water, 20 g of ethoxyethanol, and 46.0 g of THF was added a few pellets at a time 3.15 g (49 mmol) of potassium hydroxide. During the addition water soluble platelets (sodium benzoate presumably) precipitated. The mixture was refluxed 2 hr and poured into 400 g of ice/400 g of water, filtered, and washed with water. After two precipitations from THF solution using water, 6.80 g (100%) of cream colored solid, T_g = 64°, was obtained. Anal. Calcd for $C_{18}H_{15}N$: C, 88.13; H, 6.16; N, 5.71. Found: C, 88.61; H, 6.22; N, 5.68. Ir($CHCl_3$): no C=O (Figure 3a). The uv spectrum is shown in Figure 4. Gel permeation chromatography gave $\bar{M}_n = 2.05 \times 10^4$, $\bar{M}_w = 4.20 \times 10^4$, MWD = 2.05.

Poly[1-(vinylbenzyl)isoquinolinium methiodide] (8). A solution of 1.00 g (4.08 mequiv) of **7**, 5 ml of methyl iodide, and 7.5 ml of dry benzene was refluxed 2 hr and cooled and the resultant solid was filtered and washed with benzene to afford 1.58 g (100%) of an orange solid. After precipitation from DMF with methanol: T_g = 84°, T_m = 112°. Anal. Calcd for $C_{19}H_{18}NI$: C, 58.89; H, 4.68; I, 32.75. Found: C, 57.63; H, 4.51; I, 32.13. Uv (DMSO): $\lambda_{max}(\epsilon \times 10^3)$ 292 (12.0), 348 (6.32).

Poly[1-(vinylbenzyl)isoquinolinium methobromide] (9). Through a solution of 1.00 g (4.08 mequiv) of **7** in 7.5 ml of dry benzene in a flask equipped with a dry ice condenser was bubbled about 2 l. of gaseous methyl bromide over a period of several hours. The mixture was then refluxed using a water cooled condenser for 0.5 hr, cooled, filtered, and washed with benzene and dried to yield 1.4 g (100%) of a resinous solid. It was precipitated from DMF solution once with THF and again with ethyl acetate to yield a cream colored solid, T_g = 97°, T_m = 127°. Anal. Calcd for $C_{18}H_{15}N\cdot CH_3Br$: C, 67.06; H, 5.33; N, 4.12; Br, 23.49. Found: C, 73.25; H, 5.04; N, 4.80; Br, 16.14. Calcd for $C_{18}H_{15}N\cdot 0.63CH_3Br$: C, 73.35; H, 5.58; N,4.59; Br, 16.8. Uv (DMSO): $\lambda_{max}(\epsilon \times 10^3)$ 287 sh (8.82), 309 (5.50), 322 (5.67), 350 sh (1.86).

Poly[1-(vinylbenzyl)isoquinoline picrate] (10). A solution of 4.59 g (20.0 mmol) of picric acid in 10 ml of dry THF was added with stirring to a solution of 1.00 g (4.08 mequiv) of polymer **7** in 10 ml of dry THF. A yellow precipitate formed immediately. After 1 hr refluxing with stirring, it was filtered, washed with THF and ether, and dried to give 1.93 g (100%) of powdery yellow solid. After precipitation twice from DMF solution with benzene, T_g = 125°. Anal. Calcd for $C_{18}H_{15}N\cdot C_6H_3N_3O_7$: C, 60.75; H, 3.82; N, 11.81. Found: C, 61.45; H, 4.30; N, 11.39. Calcd for $C_{18}H_{15}N\cdot 0.95C_6H_3N_3O_7$: C, 61.48; H, 3.89; N, 11.65. Uv (DMSO): $\lambda_{max}(\epsilon \times 10^3)$ 283 sh (9.92), 287 sh (7.33), 310 sh (6.38), 332 (8.28), 380 (16.7).

1-(3′- and 4′-Vinylbenzyl)-2-benzoyl-1,2-dihydroisoquinaldonitriles (13 and 14). To a solution of 26.0 g (100 mmol) of 2-benzoyl-1,2-dihydroisoquinaldonitrile (**1**) and 15.3 g (100 mequiv) of a 60–40 mixture of **11** and **12** (Dow Chemical Co.) in 150 ml of dry DMF under nitrogen at room temperature was added 4.0 g (100 mmol) of 57% sodium hydride. The mixture was stirred 2 hr, poured into ice–water, and filtered. The resultant gum was recrystallized from ethanol to give 29.4 g (78%) of crystals of **13** and **14**, mp 120–150°. One recrystallization gave crystals, mp 140–145°. A recrystallization from ethanol gave colorless crystals, mp 146–150°. Three more recrystallizations gave an analytical sample of pure **14** (4.1 g, 11%), mp 150.5–152.5°. Anal. Calcd for $C_{26}H_{20}N_2O$: C, 82.95; H, 5.36; N, 7.44. Found: C, 82.89; H, 5.43; N, 7.44. NMR ($CDCl_3$): δ 3.37 (q, J_{AB} = 12 Hz, 2 H(CH_2)), 4.6–5.3 (m, 3 H (=CH_2,H_4)), 5.9–7.2 (m, 15 H (arom + -CH=)). Ir ($CHCl_3$): 1675 (s) (C=O), 1820 (w), 1640 (s), 1420–1450 (m), 1335 (s), 990 (m), 910 cm^{-1} (m) (terminal vinyl). The uv spectrum in 95% ethanol had λ_{max} 315, 297, 287 nm (ϵ's all ~10^4).

1-(3′- and 4′-Vinylbenzyl)isoquinolines (15 and 16). A solution of 1.50 g (5.0 mmol) of a mixture of **13** and **14** (mp 146–150°, see above) and 3.0 ml of 40% methanolic benzyltrimethylammonium hydroxide (Triton B) in 37 ml of dry DMF was stirred under nitrogen at room temperature for 45 min and poured into 400 g of ice water. The ether extract was washed with 10% HCl then water and dried. Concentration of the ether gave 0.84 g of yellow oil. The infrared spectrum contained a carbonyl peak at 1720 cm^{-1} due apparently to DMF impurity but different from that of **13**. It showed a positive $KMnO_4$ test for unsaturation. The oil yielded a picrate, mp 159.0–159.5° (ethanol). Anal. Calcd for $C_{24}H_{18}N_4O_7$: C, 60.76; H, 3.82; N, 11.81. Found: C, 59.3 H, 3.45; N, 11.3. The HCl extract was made basic and extracted with ether. The ether extract was washed with water, dried, and concentrated to afford 0.50 g of a yellow oil. The infrared spectrum contains a weak peak at 1720 cm^{-1} due presumably to a small amount of DMF and is similar to but distinct from that of the oil described above. The picrate after two recrystalizations from ethanol had mp 154.0–155.5°, mixed with the above picrate mp 134–152°. Anal. Calcd for $C_{24}N_{18}N_4O_7$: C, 60.75; H, 3.82; N, 11.81. Found: C, 60.61; H, 3.94; N, 11.66.

Poly[1-(4′-vinylbenzyl)-2-benzoyl-1,2-dihydroisoquinaldonitrile] (17). 1. A solution of 1.85 g (49.2 mmol) of **14** in 20 g of dry benzene was flushed with dry nitrogen for 20 min. Then 9.3 mg (0.057 mmol) of azobisisobutyronitrile (AIBN) was added and the solution temperature was set at 58°. The temperature rose during a 17.5-hr period to reflux. After this the solution was cooled and kept at 27° for an additional 48 hr. All these operations were under a nitrogen blanket. The polymer (1.5 g, 81% conversion) was collected by precipitation with hexane. After three precipitations from THF into methanol, there remained 0.51 g of a white powder. Anal. Calcd for $C_{26}H_{20}N_2O$: C, 82.95; H, 5.36; N, 7.44. Found: C, 83.32; H, 5.57; N, 7.18. The infrared spectrum (shown in Figure 1c) is nearly identical with that of **6** prepared by chemical modification of **5** (Figure 1a). Uv (THF): λ_{max} ($\epsilon \times 10^3$) 317 (9.15), 300 (9.30), 287 sh (8.27), 276 sh (6.66). GPC analysis gives $\bar{M}_n = 2.9 \times 10^4$, $\bar{M}_w = 6.87 \times 10^4$, MWD = 2.4. 2. A similar polymerization was run on a twofold scale at 61° in a sealed ampoule for 64 hr. The initial product (3.35 g, 91%) was precipitated twice more from THF with methanol (2.98 g). Anal. Calcd for $C_{26}H_{20}N_2O$: C, 82.95; H, 5.36; N, 7.44. Found: C, 81.59; H, 5.25; N, 7.51. The infrared spectrum was identical with that of the above polymer. Uv (THF): λ_{max} ($\epsilon \times 10^3$) 317 (9.01), 300 (9.08), 287 sh (8.50), 267 sh (6.7). GPC analysis gave $\bar{M}_n = 2.24 \times 10^4$, $\bar{M}_w = 6.7 \times 10^4$, MWD = 3.16.

Poly[1-(4′-vinylbenzyl)isoquinoline] (18). To a refluxing solution of 1.00 g (2.66 mequiv) of **17** (from run 2 above), 0.60 g of water, 3.5 g of ethoxyethanol, and 21.5 g of THF was added slowly 0.32 g (4.9 mmol) of 87% KOH. After 3.2 hr of refluxing the mixture was poured into water and filtered. The crude solid was precipitated from THF into water, washed with methanol, and dried to a weight of 0.56 g (86%). Two more precipitations left 0.33 g. Anal. Calcd for $C_{18}H_{15}N$: C, 88.13; H, 6.16; N, 5.17. Found: C, 88.6; H, 5.94; N, 5.63. The infrared spectrum (Figure 3b) is virtually identical with that of **7**(Figure 3a) prepared by hydrolysis of **6**. Uv (THF): λ_{max} ($\epsilon \times 10^3$) 321 (3.25), sh 316 (2.24), 308 (2.50), sh 280 (4.09), 272 (5.07), 267 (4.67). GPC analysis yields $\bar{M}_n = 1.20 \times 10^4$, $\bar{M}_w = 5.60 \times 10^4$, MWD = 4.66.

Poly{styrene-*co*-[1-(4′-vinylbenzyl)-2-benzoyl-1,2-dihydroisoquinaldonitrile]} (19). A solution of 3.76 g (10.0 mmol) of **14** (2.66 g of solid, mp 146–150°; 1.10 g of solid, mp 140–145°), 1.04 g (10.0 mmole) of deinhibited styrene, 22.4 mg of AIBN, and 45 ml of dry benzene was maintained at 61° in a sealed ampule for 97 hr. The solid initially obtained by precipitation into methanol was precipitated from THF into methanol twice and dried to a weight of 2.97 g (63%). Anal. Calcd for $C_8H_8 \cdot 1.1C_{26}H_{20}N_2O$: C, 84.82; H, 5.84, N, 5.95. Found: C, 84.72; H, 6.03; N, 6.02. The infrared spectrum is very similar to that of **17**. The ultraviolet spectrum has the following: λ_{max} ($\epsilon \times 10^{-3}$ calculated on isoquinoline equivalent basis) 317 (7.94) and 300 (8.23). GPC gave $\bar{M}_n = 2.35 \times 10^4$, $\bar{M}_w = 9.40 \times 10^4$, MWD = 3.99.

1-Allyl-2-benzoyl-1,2-dihydroisoquinaldonitrile (20). To a solution of 2.60 g (10.0 mmol) of **1**, 4.80 g (40.0 mmol) of allyl bromide, and 25 ml of dry DMF at 0° was added 0.40 g (10.0 mmol) of 57% sodium hydride. The solution was stirred for 0.5 hr and poured into 400 g of ice–water. A stream of air was used to evaporate the excess allyl bromide and then the solution was filtered, yielding 3.00 g (100%) of tan solid. Recrystallization from hexane-ethyl acetate gave large colorless crystals, mp 101.0–103.5°. Anal. Calcd for $C_{20}H_{16}N_2O$: C, 79.98; H, 5.37; N, 9.33. Found: C, 80.06; H, 5.40; N, 9.43. The ultraviolet spectrum (ethanol) has the following: λ_{max} (ϵ) 321 sh (1×10^4), 297 (1×10^4), 287 sh (1×10^4), 228 nm (3×10^4). NMR ($CDCl_3$): δ 2.98 (septet, AB part of ABX system, $J_{AB} = 13$ Hz, $J_{AX} = 4.2$ Hz, $J_{BX} = -4.2$ Hz), 2 H ($-CH_2-$)), 4.5–5.7 (m, 3 H ($-CHCH_2-$)), 5.35 (d, $J = 8$ Hz, 1 H (H_4)), 6.06 (d, $J = 8$ Hz, 1 H (H_3)), 6.5–7.4 (m, 9 H (arom)).

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References and Notes

(1) E. M. Fettes, Ed., "High Polymers", Vol. XIX, Interscience, New York, N.Y., 1964.

(2) M. Okawara, T. Endo, and Y. Kurusu, *Prog. Polym. Sci., Jpn.*, **4**, 105 (1970).

(3) J. A. Moore, Ed., "Reactions on Polymers", D. Reidel Publishing Co., Boston, Mass., 1973.

(4) C. C. Leznoff, *Chem. Soc. Rev.*, **3**, 65 (1974).

(5) R. B. Merrifield, *Science*, **150**, 178 (1965).

(6) Part I: H. W. Gibson and F. C. Bailey, *J. Polym. Sci., Polym. Chem. Ed.*, **10**, 3017 (1972).

(7) Part II: H. W. Gibson and F. C. Bailey, *J. Polym. Sci., Polym. Chem. Ed.*, **12**, 2141 (1974).

(8) Part III: H. W. Gibson, *Macromolecules*, **7**, 711 (1974).

(9) Part IV: H. W. Gibson, *Macromolecules*, **8**, 89 (1975).

(10) Part V: H. W. Gibson and F. C. Bailey, *J. Polym. Sci., Polym. Chem. Ed.*, **13**, 1951 (1975).

(11) For example, H. W. Gibson, *J. Am. Chem. Soc.*, **97**, 3832 (1975).

(12) W. E. McEwen and R. L. Cobb, *Chem. Rev.*, **55**, 511 (1955).

(13) F. D. Popp, *Adv. Heterocycl. Chem.*, **9**, 1 (1968).

(14) F. D. Popp, *Heterocycles*, **1**, 165 (1973).

(15) F. D. Popp and A. Soto, *J. Chem. Soc.*, 1760 (1963), and earlier references cited therein.

(16) F. D. Popp and J. M. Wefer, *J. Chem. Soc., Chem. Commun.*, 207 (1966).

(17) F. D. Popp and J. M. Wefer, *J. Heterocycl. Chem.*, **4**, 183 (1967).

(18) B. C. Uff and J. R. Kershaw, *J. Chem. Soc. C*, 666 (1969).

(19) H. W. Gibson, *J. Heterocycl. Chem.*, **7**, 1169 (1970).

(20) V. Boekelheide and J. Weinstock, *J. Am. Chem. Soc.*, **74**, 660 (1952).

(21) H. W. Gibson, *J. Org. Chem.*, **38**, 2851 (1973).

(22) J. L. Neumeyer, K. H. Oh, K. K. Weinhardt, and B. R. Neustadt, *J. Org. Chem.*, **34**, 3786 (1969).

(23) W. G. Lloyd and T. E. Durocher, *J. Appl. Polym. Sci.*, **8**, 953 (1964).

(24) P. E. Stevenson, *J. Chem. Educ.*, **41**, 234 (1964).

(25) W. H. Daly and C.-D. S. Lee, ref 3, p 351.

(26) For example, H. J. Harwood, ref 3, p 188.

(27) R. G. Pearson, *Surv. Prog. Chem.*, **5**, 1 (1969).

Multifunctional Hydrolytic Catalyses. IV. The Catalytic Hydrolysis of *p*-Nitrophenyl Acetate by Copolymers Containing Complementary Functional Groups (Hydroxamate and Imidazole)

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ABSTRACT: Water-soluble bifunctional polymers which contained *N*-phenylacrylohydroxamate unit and 4(5)-vinylimidazole unit were prepared, and the catalytic hydrolysis of *p*-nitrophenyl acetate was studied at 30°C in 28.9% $EtOH-H_2O$. Under ordinary substrate concentrations (10^{-4}–10^{-5} *M*), the reaction followed the simple first-order kinetics, indicating the complete turnover of the catalytic group. At higher substrate concentrations, the time course of the reaction was biphasic and the hydrolysis was shown to proceed mainly via the formation and the subsequent decomposition of the acetyl hydroxamate intermediate. The acylation rate at the hydroxamate anion unit was affected only insignificantly by the presence of the imidazole unit, and was much more efficient than those at the imidazole site. In contrast, the decomposition of the acetyl intermediate was remarkably accelerated (up to 10^3-fold) by the introduction of the imidazole unit. Thus, the appropriate combination of the nucleophilic functions of complementary nature led to much enhanced turnover rates of the catalytic site.

It is generally believed that the cooperative action of several functional groups at the active site is crucial for the remarkable efficiency of enzyme catalyses, and, in fact, it has been shown that a combination of functional groups named the charge relay system catalyzes hydrolyses of esters and amides very efficiently in some serine proteases.[2a]

In much simpler systems, attempted observation of the multifunctional catalysis (polymeric[2b–4] and nonpolymeric