Stereochemical Evidence for Participation of a Donor–Acceptor Complex in Alternating Copolymerization. 1. Model Compound Synthesis

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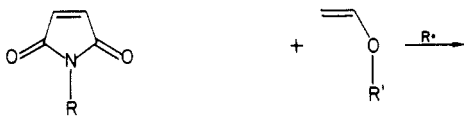
ABSTRACT: The stereospecific synthesis of a series of model compounds for N-substituted maleimide/vinyl ether alternating copolymers is described. The stereochemistry of the compounds prepared could be unambiguously deduced via utilization of ^{1}H NMR coupling constants. Comparison of the ^{13}C NMR chemical shifts of the model compounds with those of the copolymers suggests that the predominant stereochemistry at the succinimide units in the copolymers is erythro. A detailed comparison of the several properties of the copolymers with those of the model compounds is reported in an accompanying paper.

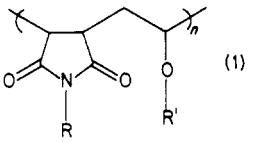
Introduction

During the course of our investigations into the effect of varying reaction conditions on the stereochemistry of alternating copolymers of N-substituted maleimides and vinyl ethers,[1] it became necessary to determine what effect differing stereochemistry at the succinimide units of the copolymers had on their ^{13}C NMR chemical shifts. We report here the synthesis, stereochemical assignment, and ^{13}C NMR chemical shifts of a series of model compounds for these alternating copolymers.

It has been shown that copolymers of N-substituted maleimides and vinyl ethers produced via free radical initiation possess predominantly alternating sequence distributions (eq 1).[1] It was found that the appearance of



R = C_6H_5, C_6H_{11}, *p*-$CF_3C_6H_4$, *p*-CNC_6H_4, *p*-FC_6H_4, *p*-ClC_6H_4, *p*-BrC_6H_4, *p*-$OAcC_6H_4$, *p*-$CH_3C_6H_4$, *p*-$CO_2EtC_6H_4$, *p*-$OCH_3C_6H_4$, OAc



(1)

R' = 2-chloroethyl, ethyl, *n*-butyl, methyl

the ^{13}C NMR spectra of these copolymers (especially the carbonyl region) was markedly dependent on such reaction conditions as temperature, solvent, total monomer concentration, the initial ratio of comonomers, and the relative donor and acceptor strengths of the comonomers. Although the sequence distribution is also changed slightly with reaction conditions, the sequence distribution changes did not adequately explain the observed differences in the ^{13}C NMR spectra, leading to the hypothesis that the observed changes were due to stereochemical differences in the copolymers. The present study was undertaken to determine how much of an effect varying stereochemistry has on the ^{13}C NMR chemical shifts of model compounds for these copolymers and to determine if any inferences could be made about the predominant stereochemistry of the copolymers.

In addition to ^{13}C NMR spectral data, both 100-MHz and 300-MHz ^{1}H NMR spectral data were heavily relied upon to establish the structure and stereochemistry for the model compounds. Also, IR spectral data, and in some instances, low- and high-resolution mass spectral data, were relied upon. However, since ^{13}C NMR data were the major spectral data employed for establishing copolymer structure and stereochemistry, in order to conserve space, the other spectral data are deleted from this paper; they are made available as supplementary material.

Experimental Section

General. All temperatures are uncorrected and reported in degrees centrigrade. Melting points were determined in open capillary tubes using a Thomas-Hoover melting point apparatus. Infrared spectra were obtained by using a Perkin-Elmer Model 281 infrared spectrometer. Vibrational transition frequencies are expressed in wavenumbers (cm^{-1}), with bands being assigned as weak (w), medium (m), strong (s), very strong (vs), and broad (b). Proton nuclear magnetic resonance spectra (60 MHz) were obtained on either a Varian A-60A or a Jeol JNM-PMX-60 spectrometer. Carbon-13 (25 MHz) and 100-MHz proton NMR spectra were recorded on a Jeol JNM-FX-100 instrument. Chemical shifts are expressed in parts per million (ppm) downfield from tetramethylsilane unless stated otherwise. Multiplicities of proton-decoupled and off-resonance-decoupled ^{13}C resonances are designated as singlet (s), doublet (d), triplet (t), quartet (q), or multiplet (m). Coupling constants (J) are expressed in hertz (Hz). A 300-MHz ^{1}H NMR spectrum was obtained on a Nicolet NTC-300 instrument. Mass spectra [low resolution (LRMS) and high resolution (HRMS)] were recorded on an Associated Eletronics Industries Model MS-30 spectrometer. Catalytic hydrogenations were carried out in a low-pressure shaker type Parr Series 3910 catalytic hydrogenation apparatus. Chemical analyses were performed by Atlantic Microlab, Inc., Atlanta, GA. Compound headings appear with the common name listed first, followed by the systematic name in parentheses.

Reagents and Solvents. Unless otherwise noted, reagents were obtained from Aldrich Chemical Co. Deuterated solvents [chloroform-*d* ($CDCl_3$), acetone-d_6, dimethyl-d_6 sulfoxide (Me_2SO-d_6), and tetrachloroethane-d_2 (TCE-d_2)] were obtained from Merck and Co., Inc., Stohler Isotope Chemical, or Aldrich Chemical Co. and were used without further purification. *N*-Phenylmaleimide was obtained from Aldrich Chemical Co. and was recrystallized from cyclohexane before use.

Model Compound Synthesis. *N*-Phenylsuccinimide (1-Phenyl-2,5-pyrrolidinedione) (1). Method A. By the procedure of Umrigar,[2] this compound was synthesized in 51.4% yield from succinic anhydride and aniline, mp 154–155 °C (lit.[3] mp 156 °C). ^{13}C NMR ($CDCl_3$) δ 28.39 (t), 126.32 (d), 128.42 (d), 128.42 (d), 131.83 (s), 176.03 (s).

The ^{1}H NMR, IR, LRMS, and HRMS data are omitted from the paper; however, they are available as supplementary material. Because of the importance of the ^{13}C NMR data in correlation of polymer structure with model compound structure, these data are included in the paper.

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Method B. *N*-Phenylsuccinimide (1) was also obtained by reduction of *N*-phenylmaleimide (NPM) in 39% yield by the procedure of Medvedeva and Belotsvetov.[4] The spectral properties (IR, NMR) and melting point were identical with those of 1 synthesized via method A.

3,4-Dimethyl-*N*-phenylmaleimide (3,4-Dimethyl-1-phenyl-1*H*-pyrrole-2,5-dione) (2). Dimethylmaleic anhydride (Aldrich) (5.0 g, 39.6 mmol) was dissolved in 75 mL of $CHCl_3$. This solution was stirred magnetically while 5.0 g (53.7 mmol) of freshly distilled aniline was added dropwise, after which it was stirred on a hot plate at 40–45 °C for 91 h. No precipitation of the expected maleic acid was noted. The $CHCl_3$ was removed on a rotary evaporator to leave an orange crystalline mass. This residue was dissolved in a small amount of acetone and precipitated dropwise into rapidly stirred acidic water (100 mL + 5 drops of 18 M H_2SO_4). The precipitate was suction filtered, washed with water, and dried overnight in a vacuum oven (50 °C). After drying, the residue was recrystallized from cyclohexane to yield 4.6 g (57.6%) of pale-green needles, mp 90–91 °C.

^{13}C NMR ($CDCl_3$) δ 8.82, 125.69, 127.33, 128.94, 132.03, 137.39, 170.85.

***cis*-3,4-Dimethyl-*N*-phenylsuccinimide (3,4-Dimethyl-1-phenyl-2,5-pyrrolidinedione) (3).** To a 250-mL-capacity hydrogenation bottle were added 1.0 g (5.0 mmol) of 3,4-dimethyl-*N*-phenylmaleimide, approximately 150 mL of 95% ethanol, and 0.01 g of PtO_2 (Engelhard Industries). The bottle was placed on the Parr shaker, and the system was pressurized to 55 psi with hydrogen gas. The solution was shaken for about 5 min, and the apparatus was then evacuated (aspirator). The system was pressurized with H_2 and evacuated twice more and then pressurized to 55 psi. The solution was shaken for 18.5 h at room temperature. The catalyst was removed by filtration, and the solvent was removed via rotary evaporation. The residue was recrystallized from CCl_4 to yield 0.97 g (95%) of very fine, colorless needless, mp 128–129 °C (lit.[11] mp 127 °C.). The cis:trans isomer ratio (calculated from ^{13}C NMR peak intensities) was ≥14, or expressed as a percentage, the product was ≥94% cis.

^{13}C NMR ($CDCl_3$) δ 11.55, 38.40, 126.38, 128.28, 128.57, 128.96, 132.08, 179.35.

***trans*-3,4-Dimethyl-*N*-phenylsuccinimide (*trans*-3,4-Dimethyl-1-phenyl-2,5-pyrrolidinedione) (4).** The trans isomer of 3,4-dimethyl-*N*-phenylsuccinimide could be conveniently prepared by epimerization of the cis compound (3). Thus, approximately 0.2 g of 3 was dissolved in 0.4 mL of Me_2SO-d_6, and the resulting solution was filtered into a clean NMR tube. A ^{13}C NMR spectrum was run (see below for chemical shifts of cis isomer in Me_2SO-d_6). A drop of 2,2,6,6-tetramethylpiperidine (TMP) (Aldrich) was then added to the tube, and the tube was placed in a 60 °C water bath. After being heated overnight, another ^{13}C NMR spectrum was run. The peaks due to the small amount of the trans isomer originally present (~5–6%) had grown at the expense of the peaks attributed to the cis compound. Indeed, the trans isomer was in excess. Continued epimerization at 60 °C (monitored periodically with ^{13}C NMR) for about 1 week gave a maximum trans:cis ratio of about 6 (86% trans), as judged from ^{13}C NMR peak intensities. That no epimerization took place in the absence of TMP was verified by heating another sample of the cis isomer at 60 °C in Me_2SO-d_6 for several days and observing the ^{13}C NMR spectrum. No change was observed. An analytical sample of 4 was isolated by evaporation of most of the Me_2SO-d_6, followed by extraction of the residue with boiling cyclohexane. The hot cyclohexane was decanted from the residue, and upon cooling, 4 crystallized as colorless needles, mp 145–147 °C (lit.[11] mp 146 °C.).

Compound 3 ^{13}C NMR (Me_2SO-d_6, internal reference Me_2SO-d_6 = 39.5[5]) δ 11.28, 37.99, 127.18, 128.30, 128.88, 132,69, 179.72.

Compound 4 ^{13}C NMR (Me_2SO-d_6, internal reference Me_2SO-d_6 = 39.5[5]) δ 13.94, 42.42, 126.98, 128.06, 128.71, 132.78, 178.45.

***cis*-Hexahydrophthalanilic Acid (*cis*-2-[(Phenylamino)carbonyl]cyclohexanecarboxylic Acid) (5).** *cis*-1,2-Cyclohexanedicarboxylic anhydride (Aldrich) (5.0 g, 32.4 mmol) was dissolved in 20 mL of $CHCl_3$ in a 500-mL Erlenmeyer flask. Freshly distilled aniline (3.0 g, 32.2 mmol) was slowly added (dropwise over 10 min) while rapidly stirring the solution. The solution was stirred for 3 h, during which time a white powdery precipitate formed. The precipitate was suction filtered and dried in a 50 °C vacuum oven to yield 7.0 g of 5 (87.4%), mp 176–177 °C (lit.[12] mp 172–173 °C).

^{13}C NMR (Me_2SO-d_6, internal reference Me_2SO-d_6 = 39.5[5]) δ 22.49, 24.10, 25.32, 27.85, 42.13, 42.67, 119.19, 122.74, 128.54, 139.66, 172.70, 175.18.

***cis*-Hexahydro-*N*-phenylphthalimide (*cis*-Hexahydro-2-phenyl-1*H*-isoindole-1,3(2*H*)-dione) (6).** Compound 5 (6.7 g, 27.1 mmol) was dissolved in 30 mL of acetic anhydride and stirred magnetically at 80 °C for 24 h. The solution was cooled and slowly added to vigorously stirred water (dropwise over 1.5 h). The cream colored precipitate that formed was suction filtered and dried overnight in a 50 °C vacuum oven. The precipitate was mixed with 100 mL of $CHCl_3$, filtered, and washed several times with $CHCl_3$. The chloroform-insoluble part proved to be unreacted starting material (2.6 g). The chloroform was removed from the filtrate on a rotary evaporator, leaving 3.8 g of residue. This residue was recrystallized from CCl_4 to give 3.2 g of fine, white needles (84.2% based on recovered starting material), mp 130–133 °C (lit.[12] mp 132–133 °C).

^{13}C NMR ($CDCl_3$) δ 21.81, 23.93, 40.06, 126.25, 128.28, 129.03, 132.15, 178.55.

***trans*-Hexahydrophthalanilic Acid (*trans*-2-[(Phenylamino)carbonyl]cyclohexanecarboxylic Acid) (7).** To a 125-mL Erlenmeyer flask were added 2.0 g (13.0 mmol) of *trans*-cyclohexanedicarboxylic anhydride (Aldrich) and 75 mL of $CHCl_3$. The resulting solution was stirred magnetically while 1.3 g (14.0 mmol) of distilled aniline was added dropwise. The solution was stirred at 50 °C for 1 h, during which time a white, powdery precipitate formed. The precipitate was suction filtered and dried in a vacuum oven to yield 2.9 g of product (90.2%), mp 206–212 °C (lit.[12] mp 224–225 °C).

^{13}C NMR (Me_2SO-d_6, internal reference Me_2SO-d_6 = 39.5[5]) δ 24.93, 25.12, 28.58, 28.88, 29.53, 44.35, 44.47, 46.54, 119.12, 122.79, 128.47, 139.53, 173.48, 175.94, 176.04.

***trans*-Hexahydro-*N*-phenylphthalimide (*trans*-Hexahydro-2-phenyl-1*H*-isoindole-1,3(2*H*)-dione) (8).** To a 125-mL Erlenmeyer flask were added 2 g of 8 and 100 mL of acetic anhydride. The resulting solution was stirred at 80 °C for 22 h and then allowed to cool to room temperature. The solution was added dropwise to a vigorously stirred aqueous NaCl solution (500 mL), and some white precipitate formed. The mixture was cooled in an ice bath for several hours, and the white crystalline solid that formed was suction filtered, washed with water, and dried overnight in a 50 °C vacuum oven. Recrystallization from CCl_4 yielded 1.2 g of colorless, very-fine crystals, mp 194–196 °C (lit.[12] mp 195–196 °C).

^{13}C NMR ($CDCl_3$) δ 25.15, 25.54, 47.52, 126.25, 128.03, 138.98, 132.15, 175.77.

1-Methoxy-3-(trimethylsiloxy)butadiene (9). This compound was made according to the procedure of Danishefsky and Kitahara[13] from 4-methoxy-3-buten-2-one (Aldrich) and chlorotrimethylsilane (Pierce) in 56.5% yield, bp 48–50 °C (4.5 mmHg) (lit.[13] bp 54–55 °C, 5 mmHg).

^{13}C NMR ($CDCl_3$, internal reference $CDCl_3$ = 77.0[5]) δ −0.34 (q), 55.87 (q), 90.62 (t), 102.85 (d), 150.06 (d), 153.71 (s).

***cis*-3-Methoxy-*N*-phenyl-2a,3,6,6a-tetrahydro-4-(trimethylsiloxy)phthalimide (*cis*-4-Methoxy-2-phenyl-3a,4,7,7a-tetrahydro-6-(trimethylsiloxy)-1*H*-isoindole-1,3(2*H*)-dione) (10).** This compound was synthesized by the Diels–Alder addition of compound 9 to NPM in 89.4% yield, mp 114–116 °C.

^{13}C NMR ($CDCl_3$) δ 0.121 (q), 27.07 (t), 37.43 (d), 45.69 (d), 55.54 (q), 73.06 (d), 100.94 (d), 126.64 (d), 128.35 (d), 128.98 (d), 132.35 (s), 156.20 (s), 176.06 (s), 178.77 (s).

Anal. Calcd for $C_{18}H_{23}NO_4Si$: C, 62.58; H, 6.71; N, 4.05. Found: C, 63.63; H, 6.54; N, 3.90.

***cis*-Hexahydro-3-methoxy-5-oxo-*N*-phenylphthalimide (*cis*-Hexahydro-4-methoxy-6-oxo-2-phenyl-1*H*-isoindole-1,3(2*H*)-dione) (11).** Silyl enol ether 10 was hydrolyzed to ketone 11 via two different methods. The first utilized the procedure of Danishefsky et al.[6] in which silyl enol ether 10 was treated with a solution comprised of 0.1 N HCl and THF (1:4 by volume) to form 11 in 90.9% yield, mp 107–108 °C.

The second method, that of Semmelhack et al.[17] was preferrable for the desilylation, yielding 10 in 95% yield, mp 107–108 °C.

^{13}C NMR ($CDCl_3$) δ 36.10 (d), 36.83 (t), 40.46 (t), 44.38 (d), 57.25 (q), 75.21 (d), 126.54 (d), 128.65 (d), 129.09 (d), 132.02 (s), 175.31 (s), 177.56 (s), 205.91 (s).

Anal. Calcd for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.12. Found: C, 65.98; H, 5.54; N, 5.09.

***cis*-Hexahydro-5-hydroxy-3-methoxy-*N*-phenylphthalimide (*cis*-Hexahydro-6-hydroxy-4-methoxy-2-phenyl-1*H*-isoindole-1,3(2*H*)-dione) (12).** Ketone **11** was reduced to alcohol **12** by catalytic hydrogenation. Thus, 2.5 g (9.15 mmol) of ketone **11** was dissolved in 200 mL of 95% ethanol in a 500-mL-capacity hydrogenation bottle. A catalytic amount (~0.01 g) of PtO_2 (Engelhard Industries) was added to the solution, and the bottle was placed in the Parr shaker. The hydrogenation apparatus was flushed with hydrogen several times and finally pressurized to 46 psi with hydrogen. The shaker was started, and the solution was shaken at room temperature for 4 h. At the end of this time, the apparatus was depressurized, and the catalyst was removed by filtration. The solvent was removed by rotary evaporation to yield a pale-green oil that crystallized on standing in a desiccator for several days. This procedure yielded 2.5 g (99%) of colorless crystals of alcohol **12**, mp 125–127 °C.

^{13}C NMR ($CDCl_3$) δ 28.80 (t), 32.21 (t), 36.48 (d), 43.86 (d), 57.73 (q), 64.97 (d), 76.18 (d), 126.60 (d), 128.52 (d), 129.11 (d), 132.18 (s), 176.33 (s), 178.16 (s).

Anal. Calcd for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.22; N, 5.09. Found: C, 65.42; H, 6.22; N, 5.09.

***cis*-3,5-Dimethoxyhexahydro-*N*-phenylphthalimide (*cis*-4,6-Dimethoxyhexahydro-2-phenyl-1*H*-isoindole-1,3(2*H*)-dione) (13).** This compound was prepared by methylation of alcohol **12** using trimethoxyoxonium tetrafluoroborate.[7] Alcohol **12** (1.5 g, 5.45 mmol) was dissolved in 250 mL of freshly distilled (from P_2O_5) CH_2Cl_2 in a 500-mL Erlenmeyer flask with a ground glass stopper. Excess (~3 g) trimethyloxonium tetrafluoroborate (Alfa) was added under a blanket of dry nitrogen; i.e., the bottle was opened and the transfer made under an inverted funnel connected to a nitrogen line. The trimethyloxonium tetrafluoroborate was largely insoluble in CH_2Cl_2. The flask was tightly stoppered, and the suspension was stirred magnetically for 60 h at room temperature. At the end of this time, 100 mL of H_2O was added. Solid $NaHCO_3$ was then added to the stirred solution in small increments until further additions no longer resulted in the evolution of CO_2 bubbles. The organic layer was separated, and the aqueous layer was extracted further with $CHCl_3$ (2 × 20 mL). The combined organic layers were dried over anhydrous $MgSO_4$ for several hours. The $MgSO_4$ was separated by filtration, and the solvent was removed by rotary evaporation to yield a yellow-orange oil. This oil was purified by percolation through a short (15 cm) silica gel column using hexane–CH_2Cl_2–MeOH (50:20:1). A pale-yellow oil remained after solvent evaporation. This oil solidified on standing in a desiccator for about 1 week. Recrystallization of this solid residue from absolute ethanol gave 1.4 g (89%) of colorless crystals, mp 120–122 °C.

^{13}C NMR ($CDCl_3$) δ 25.46 (t), 31.19 (t), 37.16 (d), 43.42 (d), 55.95 (q), 56.71 (q), 74.25 (d), 75.59 (d), 126.60 (d), 128.35 (d), 128.69 (d), 132.32 (s), 176.33 (s), 178.33 (s).

Anal. Calcd for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.32; H, 6.64; N, 4.82.

5-Methoxy-8-[(phenylamino)carbonyl]-2-oxabicyclo-[2.2.2]octan-3-one (14). Attempted reduction of ketone **11** to alcohol **12** by using sodium borohydride ($NaBH_4$) as a reducing agent led to bicyclic lactone **14** instead. Thus, 0.2 g (5.3 mmol) of $NaBH_4$ (Eastman) was added to a stirred solution of 1.0 g (3.7 mmol) of ketone **14** in 75 mL of 95% ethanol. The solution was stirred for 0.5 h at room temperature, after which 12 M HCl was slowly added dropwise until the solution was acidic to litmus. Upon rotary evaporation of the bulk of the solvent, a crystalline material formed. This material was broken up and washed several times with water. The residue was treated with chloroform, but was largely insoluble. Recrystallization of the residue from ethanol–water (3:1) yielded colorless crystals that had a sharp melting point (201–202 °C). On the basis of the spectral information given below, the compound was assigned the bicyclic lactone structure **14**.

^{13}C NMR (Me_2SO-d_6) δ 27.78 (t), 33.26 (t), 38.28 (d), 43.23 (d), 55.54 (q), 73.01 (d), 75.91 (d), 119.19 (d), 123.31 (d), 128.59 (d), 138.93 (s), 170.58 (s), 170.65 (s).

Anal. Calcd for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.22; N, 5.09. Found: C, 65.53; H, 6.38; N, 5.05.

1-Methoxy-1,3,3-triethoxybutane (15). To a 125-mL Erlenmeyer flask were added 20 g (200 mmol) of 4-methoxy-3-buten-2-one (Aldrich), 30 g (202 mmol) of triethyl orthoformate (Aldrich), 0.1 g of *p*-toluenesulfonic acid monohydrate (Aldrich), and 50 mL of absolute ethanol. The solution turned deep black soon after the addition of the *p*-toluenesulfonic acid, the reaction being somewhat exothermic. The flask was stoppered and allowed to stand at room temperature for 16 h, after which the mixture was fractionally distilled through a Vigreux column. Distillation at atmospheric pressure yielded a fraction boiling at 52–57 °C (~20 mL) presumed to be ethyl formate (lit.[8] bp 54.5 °C). Excess ethanol was also removed at atmospheric pressure. The distillation flask was allowed to cool, and the pressure was reduced to 10 mmHg. Continued distillation gave 16.6 g (37.7%) of a colorless liquid with a boiling range of 85–95 °C (10 mm). The product proved to be a mixture of isomers (various monomethoxy- and triethoxybutanes).

^{13}C NMR (acetone-d_6) δ 15.64, 15.74, 22.51, 22.56, 23.03, 23.07, 41.18, 41.64, 42.13, 47.86, 47.91, 51.73, 55.75, 60.58. 60.67, 60.94, 61.16, 100.54, 100.59, 101.40.

***cis*-2a,6a,3,4-Tetrahydro-3,5-diethoxy-*N*-phenylphthalimide (4,6-Diethoxy-2-phenyl-3a,7a,4,5-tetrahydro-2*H*-isoindole-1,3(2*H*)-dione) (16).** *N*-Phenylmaleimide (5.0 g, 29.0 mmol) and 1-methoxy-1,3,3-triethoxybutane (6.7 g, 30.4 mmol) were mixed in a 100-mL, one-necked, round-bottomed flask. Hydroquinone (0.3 g) and Na_2HPO_3 (0.3 g) were also added. The flask was evacuated to 25 mmHg with a vacuum pump and immersed in a 70 °C oil bath. The yellow crystalline mass soon dissolved, and the resulting solution was stirred magnetically at 70–80 °C and 25 mmHg, until its weight decreased by about 2.5 g (2 equiv of ethanol). This took about 1 week (6.8 days). The temperature was controlled so that it did not exceed 85 °C at any time. The flask was cooled to room temperature, and the yellow solid mass was triturated with absolute ethanol. The cream-colored precipitate that formed was filtered, and the ethanol was removed from the filtrate via rotary evaporation. The residue was triturated again to yield more cream-colored powder, which was filtered. This process was repeated again, and the combined precipitates were recrystallized from ethanol–water (3:1) to yield 5.2 g (56.9%) of colorless plates, mp 156–157 °C.

^{13}C NMR ($CDCl_3$) δ 14.45 (q), 15.30 (q), 30.85 (t), 39.21 (d), 44.47 (d), 62.53 (t), 65.02 (t), 72.50 (d), 86.68 (d), 126.60 (d), 128.33 (d), 129.01 (d), 132.35 (d), 152.72 (s), 176.16 (s), 176.94 (s).

Anal. Calcd for $C_{18}H_{21}NO_4$: C, 68.55; H, 6.71; N, 4.44. Found: C, 68.54; H, 6.74; N, 4.44.

***cis*-3,5-Diethoxyhexahydro-*N*-phenylphthalimide (4,6-Diethoxyhexahydro-2-phenyl-1*H*-isoindole-1,3(2*H*)-dione) (17).** Compound **16** (1.75 g, 5.5 mmol) was dissolved in 200 mL of 95% ethanol in a 250-mL hydrogenation bottle, and moist, freshly prepared Raney nickel catalyst[9] was added. The solution was heated to ~70 °C with a heating tape wrapped around the bottle, and the bottle was placed in the Parr hydrogenation apparatus. The apparatus was pressurized with hydrogen, evacuated (aspirator) several times, and finally pressurized to 51 psi. The solution was shaken at this hydrogen pressure and 70–80 °C for 1.5 h. At the end of this time, the solution was cooled to room temperature and the pressure released. The solution was filtered into a round-bottomed flask, and the solvent was removed by rotary evaporation to leave 1.6 g of oily residue. NMR analysis showed that the residue was about 25% starting material. The residue was treated with absolute ethanol, and the cream-colored precipitate that formed was isolated by filtration (0.25 g). Rotary evaporation of the filtrate left 1.2 g (91.4% based on recovered starting material) of a pale-green oil. This oil was purified further by percolation through a short (~15 cm) silica gel column using isooctane–CH_2Cl_2–methanol (50:20:1).

^{13}C NMR ($CDCl_3$) δ 15.30 (q), 15.55 (q), 25.98 (t), 32.58 (t), 37.48 (d), 43.72 (d), 63.75 (t), 64.43 (t), 72.89 (d), 74.03 (d), 126.57 (d), 128.40 (d), 129.03 (d), 132.30 (s), 176.67 (s), 178.43 (s).

Anal. Calcd for $C_{18}H_{23}NO_4$: C, 68.12; H, 7.30; N, 4.41. Found: C, 67.98; H 7.32; N, 4.36.

Epimerization of *cis*-4,6-Diethoxyhexahydro-2-phenyl-1*H*-isoindole-1,3(2*H*)-dione (17). Compound **17** (~200 mg) was dissolved in 0.4 mL of Me_2SO-d_6, and the solution was transferred

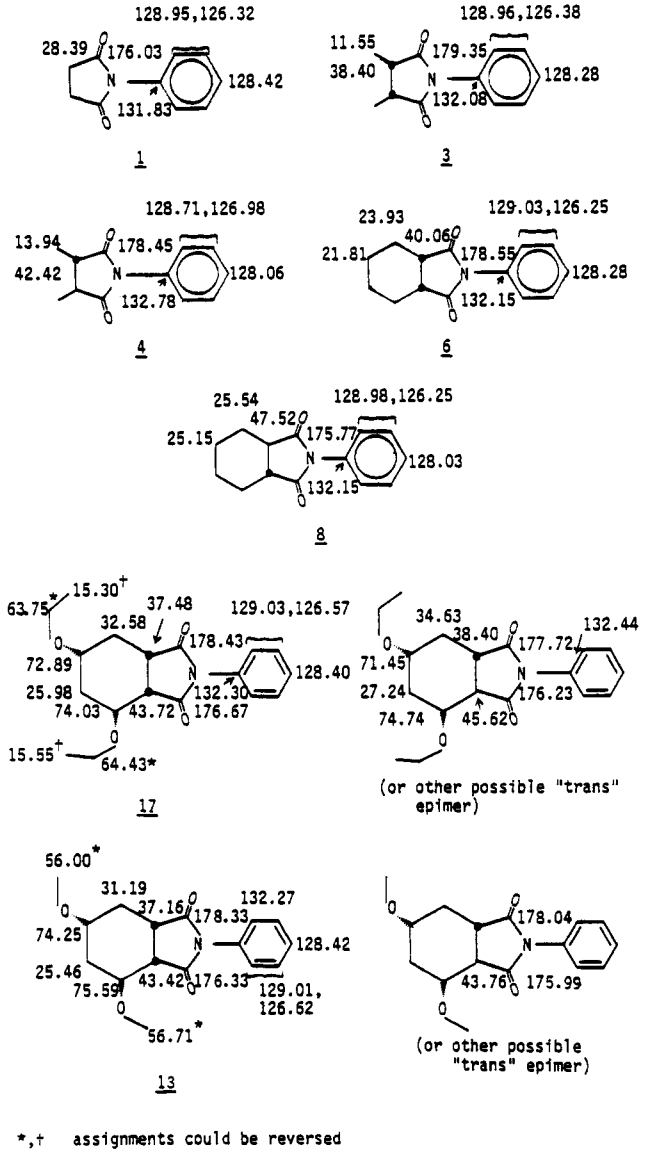


Figure 1. Model compound ^{13}C NMR chemical shifts ($CDCl_3$, ppm from Me_4Si).

to an NMR tube. A ^{13}C NMR spectrum was obtained on this sample. Several drops of 2,2,6,6-tetramethylpiperidine (Aldrich) were then added to the tube, and the tube was placed in a 60 °C water bath. The epimerization was monitored by periodically obtaining ^{13}C spectra over a period of several weeks (54 days). Nine peaks with distinctly different chemical shifts from the original compound were observed to increase in intensity with time. The final cis:trans ratio was about 3 (75% cis).

Results and Discussion

Model Compound Synthesis and Stereochemical Assignments. The model compounds synthesized in this study, their assigned stereochemistry, and their ^{13}C NMR chemical shifts are shown in Figure 1. *N*-Phenylsuccinimide (1) could be synthesized by the reaction of succinic anhydride and aniline, followed by thermal dehydration in dimethylformamide. Alternatively, 1 could be synthesized by reduction of *N*-phenylmaleimide (NPM) with iron and acetic acid.

Reaction of aniline with dimethylmaleic anhydride in chloroform at low temperature (40–45 °C) yielded 3,4-dimethyl-*N*-phenylmaleimide (2). It is interesting that 2 formed under such mild conditions. In general, maleimide synthesis involves the isolation of the chloroform-insoluble intermediate acid–amide, followed by dehydration to the imide using acetic anhydride–sodium acetate, temperature,

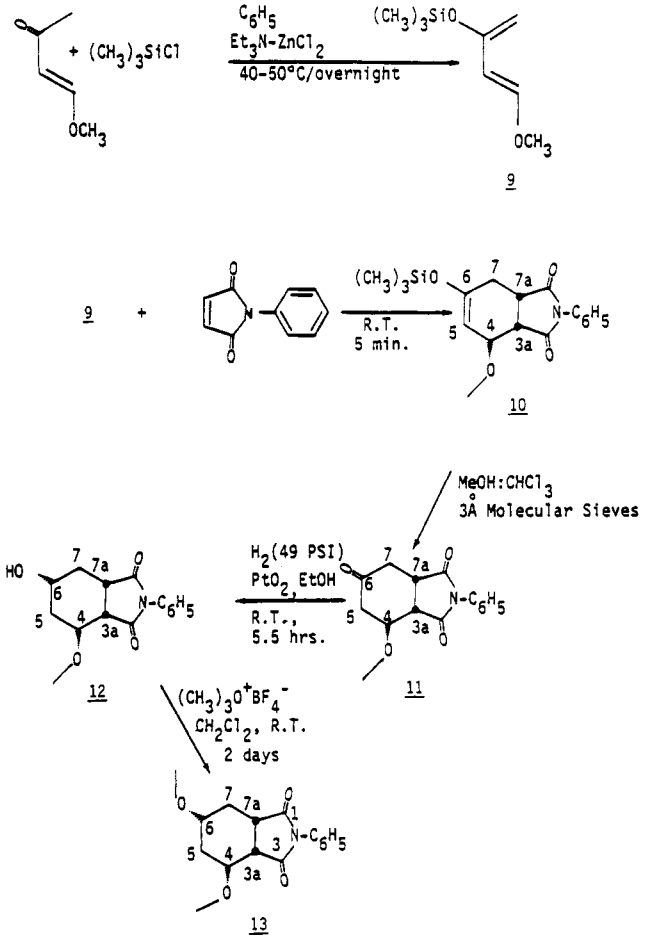


Figure 2. Synthetic scheme for model compound 13.

or both.[1,10] Apparently, steric repulsion of the two methyl groups considerably lowers the activation energy of the dehydration step. The cis compound 3 was prepared by catalytic hydrogenation (H_2, PtO_2) of 2. The product mixture proved to have a cis:trans ratio of ~14:1 (as judged by ^{13}C NMR peak heights). The assignment of cis stereochemistry to the major product was based on comparison of spectral and melting point data with data found in the literature[11] for 3. The trans compound 4 was synthesized by equilibrium epimerization of 3 with 2,2,6,6-tetramethylpiperidine (TMP) in Me_2SO-d_6. Epimerization at 60 °C for 1 week gave a maximum trans:cis ratio of ~6:1. Since the trans compound is expected to be more thermodynamically stable because of the steric repulsion of the methyl groups in the cis compound, the above epimerization results are consistent with the assigned stereochemistry for compounds 3 and 4. The spectral properties of an isolated analytical sample of 4 are in agreement with those reported in the literature.[11]

Reaction of aniline with *cis*-1,2-cyclohexanedicarboxylic anhydride in chloroform yielded *cis*-2-[(phenylamino)-carbonyl]cyclohexanecarboxylic acid (5). Dehydration of 5 with hot (80 °C) acetic anhydride yielded the imide 6. Similar, *trans*-1,2-cyclohexanedicarboxylic anhydride was treated with aniline to yield *trans*-2-[(phenylamino)-carbonyl]cyclohexanecarboxylic acid 7. This compound gave the trans imide 8 on dehydration with hot acetic anhydride. Spectral and melting point data for compounds 5–8 were consistent with those reported in the literature.[4]

The synthesis of 13 is outlined in Figure 2. Compound 9 was made according to the procedure of Danishefsky and Kitahara[13] (see Experimental Section). Simply mixing 9 with NPM at room temperature produced 10 as a white

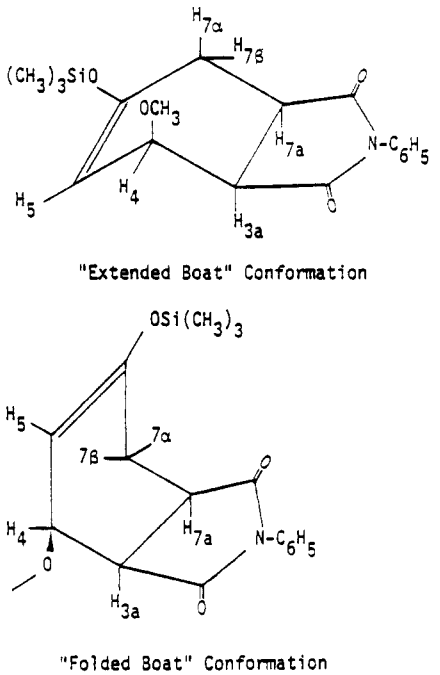


Figure 3. Possible conformations of endo Diels–Alder adduct **10**.

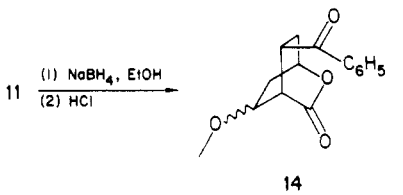
crystalline product. Danishefsky et al.[14] pointed out that compounds such as **10** can exist in either of two stable conformations, which they have termed the "folded boat" and the "extended boat" conformations. These conformations are illustrated in Figure 3. The two possible conformations could be distinguished by examination of the proton–proton coupling constants, which were determined from the ^{1}H NMR spectrum obtained at 100 MHz in $CDCl_3$ (see supplementary material). All of these couplings, taken together, are consistent only with the "extended boat" conformation of the endo adduct depicted in Figure 3. The observed couplings are also nearly identical with those determined by Danishefsky et al.[14] for the corresponding maleic anhydride adduct, with those described by Becker,[15] and with those determined by Overman et al.[16] for similar adducts.

Mildly acidic hydrolysis of trimethylsilyl enol ether **10** with 3-Å molecular sieves[17] gave ketone **11** as colorless crystals. Both 100-MHz and 300-MHz ^{1}H NMR spectral data and coupling constants are consistent with the stereochemistry for **11** shown in Figure 2 if its conformation is the "extended boat" type, similar to that shown for **10** in Figure 3. Thus, it was concluded that no epimerization took place at carbon 4 during the hydrolysis of **10**.

Ketone **11** was catalytically reduced (PtO_2, H_2) to alcohol **12**, which was isolated as colorless crystals. The ^{13}C NMR spectrum of **12** exhibited the theoretical number of peaks, so the reduction was presumed to be stereospecific. (For 100-MHz ^{1}H NMR spectral data, see supplementary material.) These observations, along with the similarities between the couplings discussed and those determined for compound **13** at 300 MHz (all of the ring coupling constants could be determined at this field strength; vide infra), suggest that the stereochemistry of **12** is that shown in Figure 2.

Support for the assigned stereochemistry at carbon 6 was obtained indirectly, by the isolation of bicyclic lactone **14** after attempted reduction of ketone **11** with sodium borohydride in ethanol, as shown in eq 2.

The structure of **14** was deduced based on the appearance of an N–H stretch at 3302 cm^{-1} in its IR spectrum and a resonance at 10.08 in its ^{1}H NMR spectrum. The



(2)

IR spectrum of **14** also exhibits two carbonyl absorptions—one at 1736 cm^{-1} and the other at 1689 cm^{-1}. The absorption at 1689 cm^{-1} is characteristic of six-membered lactones[18] (see supplementary material). Lactonizations of this type, carried out with $NaBH_4$, are not uncommon.[19]

The production of **14** is possible only if the stereochemistry of the presumably intermediate alcohol is that shown for **12** in Figure 2. This evidence by itself cannot be regarded as conclusive, however, because the assumption must be made that the stereochemistry of the reduction of ketone **11** is the same whether $NaBH_4$ or Pt/H_2 is the reducing agent.

Compound **13** was prepared in crystalline form by methylation of alcohol **12** with trimethyloxonium tetrafluoroborate in CH_2Cl_2. The 100-MHz ^{1}H NMR spectrum of **13** exhibited the same extensive overlap of the ring proton resonances as did that of compound **12**. (See supplementary material, Figures 1 and 2, for 300-MHz ^{1}H NMR spectral data.) The coupling constants are consistent with the stereochemistry and conformation for compound **13**.

The ^{13}C NMR assignments for compound **13** (shown in Figure 1) were made by using selective decoupling techniques. Selective irradiation of proton 4 caused more of an increased in the intensity of the carbonyl peak at δ 176.33, relative to the peak at δ 178.33, due to the removal of the three-bond coupling between proton 4 and carbonyl 3. Thus, the peak at δ 178.33 was assigned to carbonyl 1, and the peak at δ 176.33 was assigned to carbonyl 3.

The selective decoupling described caused a collapse of the doublet centered at δ 75.59, in the coupled spectrum of **13**, to a singlet. Therefore, the methine ^{13}C resonance at δ 75.59 was assigned to carbon 4, and the methine at δ 74.25 was assigned to carbon 6.

Selective irradiation of protons 7α and 7β caused a collapse of the triplet centered at δ 31.19 in the coupled spectrum. This observation allowed assignment of the δ 31.19 resonance to carbon 7, and the remaining methylene carbon resonance (δ 25.46) was assigned to carbon 5.

Another experiment was performed by setting the decoupler frequency slightly downfield of the overlapping resonances due to protons 7a and 3a in the ^{1}H NMR spectrum while observing the ^{13}C NMR spectrum. A greater intensity was observed for the ^{13}C NMR methine peak at δ 37.16 than for the methine peak at δ 43.42. Since proton 7a appears at lower field than proton 3a, this experiment allows assignment of the ^{13}C NMR resonance at δ 37.16 to carbon 7a and the peak at δ 43.42 to carbon 3a.

Compound **17** was synthesized as shown in Figure 4. Compound **1k** was obtained as a mixture of isomers by treating 4-methoxy-3-buten-2-one with triethyl orthoformate and an acid catalyst in absolute ethanol.

Pyrolysis[20] of **15** was not successful. However, heating **15** in the presence of NPM, radical (hydroquinone), and acid (Na_2HPO_4) scavengers produced **16** as a colorless crystalline material.

It is interesting that the double bond in **16** is not in the position expected for a typical Diels–Alder product. The position of the double bond in **16** was established by ^{1}H NMR homonuclear decoupling studies (see supplementary

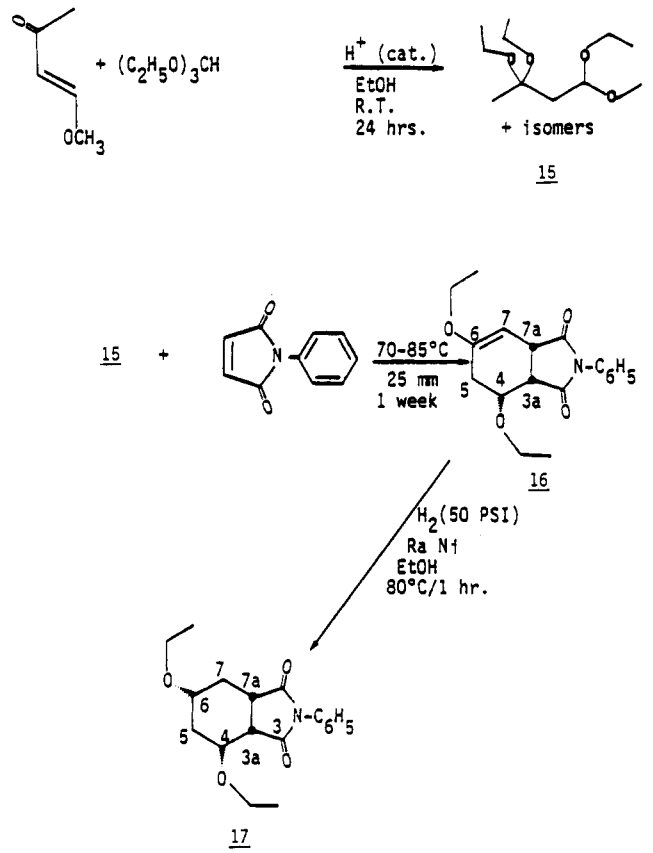
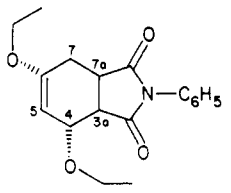


Figure 4. Synthetic scheme for model compound 17.

material). The 100-MHz ^1H NMR spectral data also supported the assigned stereochemistry for **17**. These observations are consistent with the assigned structure **16** shown in Figure 4, but not with structure **18**.



18

The reason for the anomalous position of the double bond in **16** is unknown at present. It is reasonable to assume, however, that the "normal" Diels–Alder adduct **18** is formed first, followed by an allylic hydrogen shift. A similar double bond migration has been observed in the Diels–Alder reaction of 2-ethyl-3-methoxybutadiene with cyclopentenone.[21] Vinyl ethers are known to rearrange so as to form the compound with the double bond in the most energetically favored position.[22] Apparently, the position of the double bond shown in **16** is energetically favored over that shown in **18**. Perhaps this finding indicates that there is less ring strain in the cis-fused compound **16** than in **18**.

Catalytic hydrogenation of **16** in ethanol using Raney nickel catalyst and high temperature (70–80 °C) produced **17** as a pale-green oil. The similarity of the ^{13}C NMR chemical shifts of **17** and **13** (see Figure 1) suggests that the stereochemistry of these two compounds is very similar (see supplementary material).

Equilibrium epimerization of **17** in Me_2SO-d_6 with TMP at 60 °C resulted in the appearance of nine new peaks in its ^{13}C NMR spectrum. These peaks were assumed to be due to one of the two possible trans epimers of **17**. No evidence was found for the formation of the other trans epimer. The final cis:trans ratio of the product mixture was about 3, implying that the cis-fused compound **17** is more thermodynamically stable than its trans-fused stereoisomer. The cis-fused compound **6** has also been found to be more thermodynamically stable than the trans-fused hexahydrophthalimide **8**.[23,24] On epimerization of **13** with TMP in Me_2SO-d_6, the peaks in the ^{13}C NMR spectrum due to the small amount of trans compound originally present (~5–10%) decreased in intensity with time. This interesting result implies that the energy difference between cis- and trans-fused **13** is greater than that between cis- and trans-fused **17**.

Conclusions

The ^{13}C NMR chemical shifts of the compounds synthesized in this work were used to help assign the peaks in ^{13}C NMR spectra of *N*-phenylmaleimide (NPM)–2-chloroethyl vinyl ether (CEVE) copolymers.[1] More significantly, the ability to construct stereospecific model compounds allowed inferences to be made as to the predominant stereochemistry of the copolymers. The relationship between the model compounds and the copolymers studied has been summarized and discussed in an accompanying paper.[1b]

Acknowledgment. We thank Dr. Roy W. King, Dr. Thieo E. Hogen-Esch, and Dr. David P. Vanderbilt for helpful discussions and suggestions. Thanks are also due to Dr. Wallace Brey and Mr. Paul Kanyha, for the 300-MHz NMR spectrum. Financial support for this work by the National Science Foundation (Grant DMR 80-20206), the Center for Macromolecular Science and Engineering, the Department of Chemistry, and the Graduate School of the University of Florida, the Tennessee Eastman Co., and the Gulf Oil Co. is gratefully acknowledged.

Supplementary Material Available: ^1H NMR and IR spectral data on the model compounds reported and low-resolution and/or high-resolution mass spectral data on certain model compounds (these data were relied upon extensively in establishing structures for the compounds), the relationship of these data to the structural assignments made, the 300-MHz ^1H NMR spectrum of model compound **13** (supplemental Figure 1), and an expansion of critical regions of this spectrum (supplemental Figure 2) (19 pages). Ordering information is given on any current masthead page.

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Stereochemical Evidence for Participation of a Donor–Acceptor Complex in Alternating Copolymerization. 2. Copolymer Structure

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ABSTRACT: Various N-substituted maleimides have been shown to alternately copolymerize with several vinyl ethers. The stereochemistry of these copolymers, as deduced from ^{13}C NMR spectroscopy, is markedly dependent on such copolymerization conditions as temperature, solvent, total monomer concentration (M_T), comonomer concentration ratio at fixed total monomer concentration, and the donor–acceptor character of the comonomer pair. Copolymerization conditions favoring the formation of a comonomer donor–acceptor complex (DA) invariably gave higher cis:trans stereochemical ratios at the succinimide units in the resulting copolymers. The results are interpreted as indicating that copolymer succinimide unit stereochemistry is dependent on the fraction of maleimide monomer in complex form and that the DA participates significantly in the propagation steps of the copolymerization.

Introduction

The question of participation of a donor–acceptor complex (DA) in alternating copolymerizations has long been debated. Bartlett and Nozaki[2] first proposed such participation as an explanation for the alternating nature of some copolymers as early as 1946. Walling et al.[3] postulated that the observed alternation resulted from a lowering of the activation energy for cross propagation reactions relative to homopropagations due to polarity differences between the radical chain end and the incoming monomer. Tsuchida and Tomono[4] introduced the concept that both "free" and "complexed" comonomers may participate in alternating copolymerizations. Methods have recently been developed which utilize kinetic[5,6] data in order to quantify the extent of DA participation in copolymerizations. Better fits to copolymer composition[7-9] and triad fraction[10] data have been obtained by invoking kinetic schemes that include participation of DA in copolymerization propagation steps. In spite of the large amount of data (especially composition data) that has been amassed over the years, several authors[11,12] have suggested that there has been no unambiguous experimental proof of any of the above mechanisms. This could be due to errors inherent in the determination of copolymer compositions, triad fractions, and copolymerization rates, or due to the fact that assumptions of relative values of certain rate constants are often made in these kinetic analyses. Thus, in order to clarify the mechanism of alternating copolymerization, a new source of data was deemed necessary.

Mulliken theory[13] predicts that the maximum amount of charge-transfer stabilization is to be expected if a complex adopts a conformation in which there is maximum overlap between the HOMO of the donor and the LUMO of the acceptor. It is therefore conceivable that if a DA adds to the radical chain end in a concerted manner (as opposed to a stepwise addition of the complex components), then a certain amount of stereoregularity may be induced into the copolymer chain. The degree of stereoregularity may be related to the amount of complex participation in the propagation steps.

In this paper, we show that the appearance of the ^{13}C NMR spectra of certain alternating copolymers of N-substituted maleimides and vinyl ethers varies with the copolymerization conditions. The changes in the ^{13}C NMR spectra are shown to be due to stereochemical differences in the copolymers. Copolymerization conditions that favored the formation of a DA invariably resulted in more stereoregular copolymers. Some of these results have been previously reported.[14] We now report the details of this study.

Experimental Section

General. All temperatures are uncorrected and are reported in degrees centigrade. Melting points were determined in open capillary tubes using a Thomas-Hoover melting point apparatus.

Infrared (IR) spectra were obtained by using a Perkin-Elmer Model 281 infrared spectrophotometer. Vibrational transition frequencies are expressed in wavenumbers (cm^{-1}), with bands being assigned the following classifications: weak (w), medium (m), strong (s), very strong (vs), and broad (b). Proton nuclear magnetic resonance (NMR) spectra (60 MHz) were obtained on either a Varian A-60A or a Jeol JNM-PMX-60 spectrometer. Carbon-13 (25.00 MHz) and 100-MHz proton NMR spectra were recorded on a Jeol JNM-FX-100 instrument. Chemical shifts are expressed in parts per million (ppm) downfield from tetramethylsilane unless stated otherwise. Multiplicities of proton-decoupled and off-resonance-decoupled ^{13}C resonances are des-

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