Polymer Journal, Vol. 29, No. 5, pp 467—470 (1997)

NOTES

Synthesis of Polyisoxazolines *via* 1,3-Dipolar Cycloaddition Using *O,O'*-Bis(tributylstannyl)ether of Isophthalaldoxime

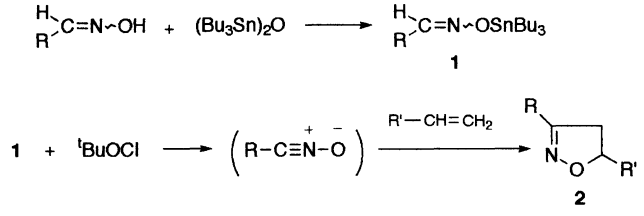
Osamu MORIYA† and Takeshi ENDO*

Department of Chemistry, The National Defense Academy, Hashirimizu, Yokosuka 239, Japan
** Research Laboratory of Resources Utilization, Tokyo Institute of Technology, Nagatsuta, Midori-ku, Yokohama 227, Japan*

(Received June 26, 1996)

KEY WORDS *O*-Tributylstannylated Aldoxime / 1,3-Dipolar Cycloaddition / Nitrile Oxide / Polyisoxazoline / Diallyl Dipolarophile / Isophthalaldoxime /

The synthetic and mechanistic aspects of 1,3-dipolar cycloadditions using nitrile oxides to give a variety of heterocyclic compounds have been investigated.[1,2] The synthesis of isoxazole derivatives *via* the cycloaddition of nitrile oxide to unsaturated dipolarophiles is one successful example.[3] In these reported reactions, aldoximes have been used as starting materials. The widely used procedure to generate the dipolar from aldoximes is halogenation by an active halogen compound and successive dehydrohalogenation by a basic reagent, *i.e.*, the reactions are usually conducted under basic conditions. We proposed a new method to generate nitrile oxides by the use of *O*-tributylstannylated aldoximes **1**, readily obtained from aldoximes and bis(tributyltin) oxide [$(Bu_3Sn)_2O$], under mild and neutral conditions.[4] The method, in which the reaction of **1** and *tert*-butylhypochlorite (^{t}BuOCl) proceeds efficiently to give nitrile oxide intermediates *in-situ*, is applicable to the synthesis of various isoxazole derivatives **2** (Scheme 1). The reaction of terephthalaldoxime with dipolarophiles was effective to prepare the corresponding bis-isoxazolines.[5]



Scheme 1.

The 1,3-dipolar cycloaddition has been utilized in the field of polymer synthesis and several groups have reported the preparations of polyisoxazoles employing intermediary nitrile oxides as a representative procedure of polycycloaddition reaction.[6-8] These works have been primarily devoted to obtain aromatic polyisoxazoles, which are insoluble in common organic solvents, by employing the reactions of nitrile oxides obtained from phthalaldoximes with vinylic or nitrile dipolarophiles.

The above prompted us to examine the adaptability of our procedure to the polycycloaddition directed toward a convenient synthetic route to polymers having the isoxazoline ring in the main chain. The report describes the polymerizations using *O,O'*-bistributylstannylated isophthalaldoxime **3** as the precursor of nitrile oxide with allylic and vinylic ester dipolarophiles **4**. The use of such dipolarophiles may be expected to improve the solubility of polyisoxazolines in common organic solvents by the introduction of methylene and functional units such as ester and ether.

EXPERIMENTAL

IR spectra were recorded on a JASCO A-3 spectrometer. ^{1}H NMR and ^{13}C NMR spectra were measured on a JEOL FX 90 Q and on a JEOL FX 270 using tetramethylsilane as an internal standard, respectively. Molecular weights of polymers and distribution were determined by GPC using a Shimadzu LC-6A system equipped with Shim-pack GPC-802 and GPC-804, in which tetrahydrofuran (THF) was used as an eluent at 50°C. The GPC chromatogram was calibrated against a standard polystyrene sample.

Isophthalaldoxime was prepared from isophthalaldehyde according to the reported procedure.[9] All solvents used for the polymerizations were dried and distilled in the usual manner. Other reagents including $(Bu_3Sn)_2O$ were used as received.

Monomer Synthesis

Isophthaldialdoxime *O,O'*-bis(tributylstannyl) ether (**3**) was prepared according to the procedure reported previously.[5] A mixture of isophthalaldoxime (0.30 g, 1.83 mmol) and $(Bu_3Sn)_2O$ (1.10 g, 1.85 mmol) in benzene (2 ml) was heated for 1 h in an oil bath maintained at 110°C under atmospheric pressure to distill out the volatile fraction. The remaining mixture was placed at a pressure of 1 mmHg in a bath of the same temperature for 3 h to leave **3** as a colorless oil (1.38 g). Product **3** was found to contain a trace of unreacted $(Bu_3Sn)_2O$, but it was used for the polymerizations without further purification: IR (neat) 2970, 2925, 950, 695 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.15 (s, 2H), 7.30—7.70 (m, 4H), 1.00—1.80 (m, 36H), 0.90 (t, J = 7.0 Hz, 18H).

Polymer Synthesis

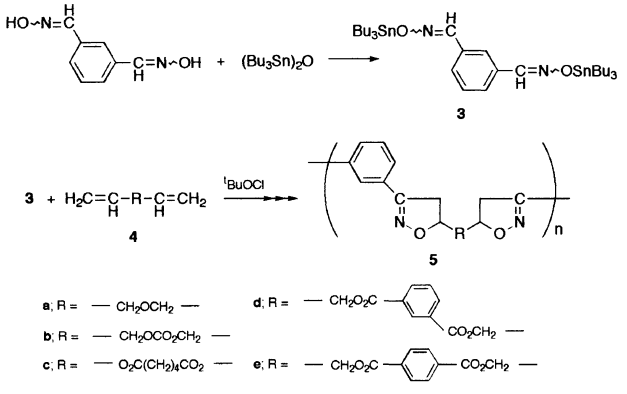
Polyisoxazolines were prepared from reactions of stan-

† To whom all correspondence should be addressed.

nylated aldoxime **3** with the dipolarophile **4** in the presence of ^{t}BuOCl. The influence of the solvents and concentration of the monomers on the polycycloaddition was examined to obtain some information about the nature of polymerizations. A typical procedure for polycycloaddition to give the polyisoxazoline **5** was as follows: To a solution of **3** (1.00 g, 1.35 mmol) and diallyl ether **4a** (0.13 g, 1.32 mmol) in 1,2-dichloroethane (DCE) (2 ml), ^{t}BuOCl (0.30 g, 2.76 mmol) was added dropwise at a temperature below -10°C under argon. After stirring for 30 minutes, the mixture was allowed to warm to room temperature and kept for 7 h. The resulting solution was poured into *n*-hexane to give slight yellowish precipitates. The precipitates were collected and dissolved in dimethylformamide (DMF) and reprecipitated with ethanol. After drying *in vacuo* at room temperature, 0.32 g of the desired polymer **5a** was obtained (Table I, Run 2): IR (KBr) 2900, 2850, 1330, 1120, 900 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.10 (br, 4H, Aromatic proton), 4.86 (br, 2H, CH at 5-position of isoxazoline ring), 3.00—3.90 (br, m, 8H, CH_2 at 4-position of isoxazoline ring and CH_2-O); ^{13}C NMR ($CDCl_3$) δ 157.0, 129.2, 128.6, 127.2, 116.0, 79.4, 71.4, 35.6. *Anal.* Calcd for $(C_{14}H_{14}N_2O_3)_n$: C, 65.11%; H, 5.46%; N, 10.84%. Found: C, 64.29%; 5.11%; N, 11.23%.

Reactions of **3** and diallyl ether **4a** with ^{t}BuOCl under various conditions afforded the polyisoxazoline **5** (Run 3—8).

Other polyisoxazolines **5** were also obtained from the corresponding dipolarophiles such as diallylcarbonate **4b**, divinyl adipate **4c**, diallyl isophthalate **4d**, and diallyl terephthalate **4e** (Table I, Scheme 2).



Scheme 2.

Polycycloaddition from **3** and diallylcarbonate **4b** afforded polyisoxazolines **5b** having carbonate groups (Run 9—11): IR (KBr) 1750, 1260, 910 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 7.87—8.00 (br m, 4H, Aromatic proton), 5.00 (br, 2H, CH at 5-position of isoxazoline ring), 4.30 (br m, 4H, CH_2–OCO–), 3.35—3.50 (br, 4H, CH_2 at 4-position of isoxazoline ring); ^{13}C NMR ($CDCl_3$) δ 156.2, 154.2, 129.6, 129.0, 128.1, 124.5, 118.4, 78.1, 68.3, 36.2. *Anal.* Calcd for $(C_{15}H_{14}N_2O_5)_n$: C, 59.60%; H, 4.67%; N, 9.26%. Found: C, 57.59%; H, 4.58%; N, 9.28% (Run 9).

Polycycloaddition from **3** in the presence of divinyl adipate **4c** gave polyisoxazolines **5c** having ester groups (Run 12): IR (KBr) 1740, 1130, 950, 870 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.20—8.00 (br m, 4H, Aromatic proton), 6.80 (br, 2H, CH at 5-position of isoxazoline ring), 3.20—3.80 (br m, 4H, CH_2 at 4-position of isoxazoline ring), 2.30 (br, 4H, CH_2–CO_2), 1.20—1.80 (br, 4H, CH_2). *Anal.* Calcd for $(C_{18}H_{18}N_2O_6)_n$; C, 60.33%; H, 5.06%; N, 7.81%. Found; C, 59.56%; H, 4.96%; N, 7.61%.

Polycycloaddition from **3** and diallyl isophthalate **4d** afforded polyisoxazolines **5d** having ester groups (Run 13): IR (KBr) 1715, 1300, 1230, 900, 720 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 7.20—8.10 (br, 8H, Aromatic proton), 5.06 (br, 2H, CH at 5-position of isoxazoline ring), 4.50 (br, 4H, CH_2–OCO), 3.00—3.80 (br, 4H, CH_2 at 4-position of isoxazoline ring). *Anal.* Calcd for $(C_{22}H_{18}N_2O_6)_n$; C, 65.02%; H, 4.46%; N, 6.89%. Found; C, 64.38%; H, 4.32%; N, 7.03%.

Polycycloaddition from **3** and diallyl terephthalate **4e** afforded polyisoxazolines **5e** having ester groups (Run 14): IR (KBr) 1710, 1260, 1110, 900, 720 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 7.40—8.00 (br, 8H, Aromatic proton), 5.10 (br, 2H, CH at 5-position of isoxazoline ring), 4.20 (br, 4H, CH_2–OCO), 3.30—3.80 (br, 4H, CH_2 at 4-position of isoxazoline ring). *Anal.* Calcd for $(C_{22}H_{18}N_2O_6)_n$; C, 64.92%; H, 4.41%; N, 6.78%. Found; C, 64.45%; H, 4.37%; N, 6.93%.

Polycycloaddition from **3** without a dipolarophile afforded polymeric furoxan **5** (Run 1): IR (KBr) 1590, 1580, 685 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.55—7.79 (br, Aromatic proton).

Table I. Preparation of polyisoxazolines **5** from *O,O'*-tributylstannylated isophthalaldoxime **3**

Run	Dipolarophile	Solvent[a]	Initial concentration of **3**, [M]	Polymer **5** Yield[b] %	M_n[c]	M_w/M_n[c]
1	None	DCE	0.67	27	9200	1.23
2	**4a**	DCE	0.67	91	9900	1.07
3	**4a**	DCE	0.67	43[d]	9930	1.06
4	**4a**	DCE	0.34	32	9200	1.01
5	**4a**	DCE	0.23	17	9800	1.06
6	**4a**	DCM	0.67	54	7040	1.09
7	**4a**	Benzene	0.67	40	9450	1.08
8	**4a**	DMF	0.67	40	9670	1.05
9	**4b**	DCE	1.35	100[e]	10870	1.06
10	**4b**	DCE	0.67	98[e]	10530	1.09
11	**4b**	DCE	0.34	78	10580	1.06
12	**4c**	DCE	0.67	46	11960	1.10
13	**4d**	DCE	0.67	97	9730	1.11
14	**4e**	DCE	0.67	96	11120	1.13

[a] DCE = 1,2-Dichloroethane; DCM = Dichloromethane. [b] Reprecipitated with *n*-hexane/chloroform. [c] Determined by GPC (polystyrene standard). [d] The polymerization was carried out without the distillation to remove water in the step of *O,O'*-tributylstannylation of the aldoxime. [e] Small amount of precipitates insoluble in the solvent was obtained.

RESULTS AND DISCUSSION

As reported previously, the *O,O'*-distannylation of isophthalaldoxime was easily conducted by mixing isophthalaldoxime and $(Bu_3Sn)_2O$ at room temperature in benzene within 20 minutes. The resulting solution was dried under reduced pressure to leave an oil, regarded as stannylated dialdoxime **3**, which was soluble in common organic solvents such as methanol, diethyl ether,

dichloromethane, benzene, and hexane. Trials to isolate **3** by a column chromatography on silica gel or neutralized alumina and distillation under reduced pressure were unsuccessful. **3** was hydrolyzed to the starting aldoxime. The thermal decomposition of **3** into a nitrile derivative took place due to its high boiling point. Therefore, after drying *in vacuo*, the formation of **3** was confirmed by the spectral data of IR and ^{1}H NMR, which exhibited good agreement to those of the related compound such as *O*-stannylated benzaldoxime.[5] The purity of the oily product **3** was speculated to be over 95% by its ^{1}H NMR spectrum, in which no detectable signal due to hydroxyl group of the aldoxime was observed and the ratio of the protons due to aromatic ring and to those due to butyl groups attached to tin was reasonable. For the polycycloaddition, **3** was used after treatment as mentioned above. Using diallyl ether **4a** as a dipolarophile (Run 3), polymerization was carried out without distillation to remove H_2O, *i.e.*, all the reactions for the polymerization were conducted in the presence of H_2O as the side product at stannylation. This was conducted to examine the effects of H_2O, which was not observed apparently in the reactions using a low molecular weight materials,[5] on the polymerizations.

The *O*-stannylated aldoxime was thought to react with ^{t}BuOCl to generate the intermediary nitrile oxide for 1,3-dipolar cycloaddition with dipolarophile **4**. This procedure using *O*-stannylated aldoxime is more practical and convenient than that using nitrile oxide,[6-8] because, nitrile oxides without a bulky substituent are not enough stable to be isolable, *i.e.*, a limited sort of nitrile oxides are available for the polymerization.[9] The yields of **5** varied from 17% to 100% according to polymerization conditions (Table I). Higher yields were obtained in the case of high concentration of **3** over 0.67 M. In polymerizations with lower concentration of **3** below 0.67 M, the yields of **5** decreased significantly (Run 4 and 5). Decrease in yield was also observed when the polymerization was conducted without removal of water in *O*-stannylation of the dialdoxime (Run 3). The yields varied from 40% to 90% depending on a type of solvents (Run 2, 6, 7, and 8). Almost quantitative yields of **5** were observed in polymerization in dichloroethane (DCE) as a solvent. The polycycloadditions of **3** with diallyl ether **4a** in dichloromethane (DCM), benzene, and dimethylformamide (DMF) resulted in the formation of the polymers **5** in lower yields.

Most of polymers **5** obtained here were soluble in common organic solvents. However, using diallylcarbonate **4b** as a dipolarophile, the corresponding polyisoxazolines **5b** contained small amounts of product insoluble in organic solvents such as DMSO, DMF, THF, DCE, and DCM (Run 9 and 10).

The molecular weights (M_n) of polymers **5**, soluble in THF, were estimated to be in the range of 9000 to 11000 by GPC based on the polystyrene standard. These values appeared to be independent of polymer yield as shown in Table I. As a typical example, the relationship between the time of polymerization *vs.* M_n curve in the polymerization using diallyl ether **4a** as the dipolarophile, is shown in Figure 1, indicating that M_n increased with reaction time and reached to 8000 at 2 h, but further increase of M_n was hardly observable after 5 h.

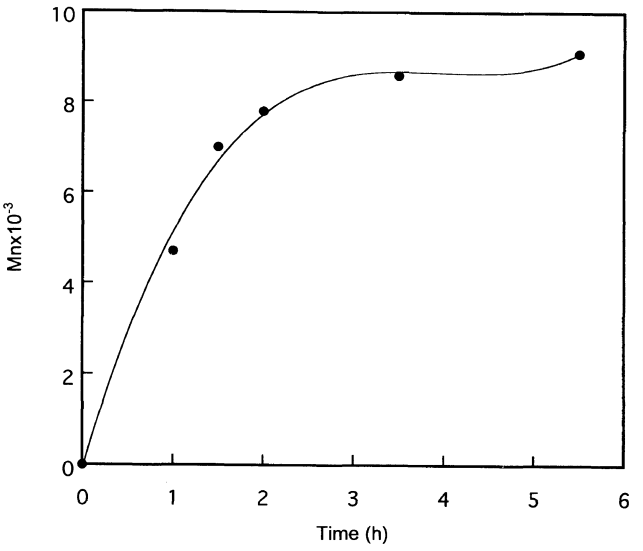


Figure 1. Plots of molecular weight (M_n) *vs.* reaction time on the polymerization of **3** with diallyl ether **4a** in 1,2-dichloroethane; initial monomer concentration [**3**] = 0.35 M.

The structures of the polymers **5** were confirmed by spectral data and elemental analyses. In the IR spectra of **5a**, absorptions at 2900 cm^{-1} and 2850 cm^{-1} were assigned to $\nu(CH_2)$ attached to C-5 position of isoxazoline ring. Several absorptions in the region from 900 cm^{-1} to 1300 cm^{-1} were attributed to N–O and C–O bonds of the isoxazoline ring and substituent of the ring. For **5b**, **5c**, **5d**, and **5e**, absorption due to $\nu(C=O)$ was observed at 1750, 1740, 1715, and 1710 cm^{-1}, respectively. The signal due to the proton at C-5 position of isoxazoline ring was observed from 4.80 ppm to 5.20 ppm in the ^{1}H NMR spectra of **5a**, **5b**, **5d**, and **5e**, and at 6.80 ppm in that of **5c**. The signals in the region from 3.00 ppm to 4.50 ppm were assigned to the protons at C-4 position of isoxazoline ring of the polymers **5**. Such spectral data were almost identical with those of 3-phenylisoxazoline derivatives having respective substituents.[5,10] The spectral data of ^{13}C NMR analysis also supported the structures of polymers **5a** and **5b**, in which signals appearing around 157 ppm and 36 ppm were thought assignable to the carbons at C-3 (C=N) and C-4 position of the isoxazoline rings, respectively. The polymerization of **3** without a dipolarophile was carried out to obtain the polymer having a furoxan unit in the main chain (Run 1). Yield of polymer such as 27% was considerably lower than those of the polyisoxazolines obtained in the presence of a dipolarophile under analogous reaction conditions. The IR spectrum of the polymer showed strong absorption at 1590 cm^{-1}.[11] In the ^{1}H NMR spectrum, only aromatic protons were observed in region from 7.55 ppm to 7.79 ppm. A comparison of the IR spectrum of polyfuroxan with those of **5a—e** seemed to indicate the polymers obtained from the reactions in the presence of a dipolarophile mainly consist of isoxazoline units. The strong absorption of furoxan unit at 1590 cm^{-1} was not found in the IR spectra of **5a—e**. The IR spectra of the polymer **5b** and polyfuroxan was shown in Figure 2. The ^{13}C NMR data of **5a** and **5b**, in which only one distinguishable signal assigned to C-3 (C=N) was observed at 157 and 154 ppm respectively, support the speculated structure. The results

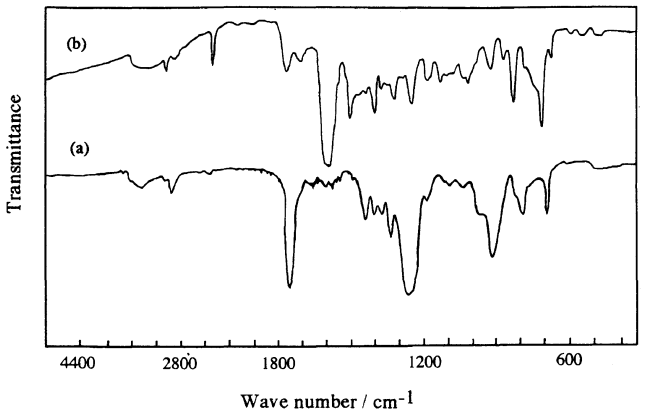


Figure 2. IR spectra of (a) polyisoxazoline **5b** and (b) polyfuroxan.

of elemental analysis of all polymers **5** were in good agreement with the calculated values of carbon, nitrogen, and hydrogen. Although more detailed analytical data were required to confirm the exact structures of the polymer **5**, it might be said at the moment that the poly-1,3-dipolar cycloaddition essentially proceeded to give isoxazoline rings.

Thus, the use of the *O*-stannylated aldoxime **3** as a precursor of nitrile oxide is effective for polycycloaddition with the allylic dipolarophiles **4a**—**e**, possibly due to the analogous effects of tributyltin chloride, the side product in the step of the generation of nitrile oxide, to those of a weak Lewis acid, which are reported to accelerate the regioselective dipolar cycloaddition of nitrile oxide to allylic dipolarophiles.[12,13] The use of isophthalaldoxime and allylic dipolarophiles appeared to prompt to synthesis of polyisoxazolines **5** owing to high solubility in common organic solvents compared to poly-isoxazolines and -isoxazoles obtained from the cycloadditions of terephthalnitrile oxide to allene, diethynylbenzene, and terephthalnitrile.[7]

REFERENCES

1. R. Huisgen, *Angew. Chem.*, **75**, 604 (1963).
2. P. Caramella and P. Grunanger, "1,3-Dipolar Cycloaddition Chemistry," A. Padwa, Ed., Wiley, Chichester, 1984, p 291.
3. C. Grundmann, *Synthesis*, 344 (1970).
4. O. Moriya, Y. Urata, and T. Endo, *J. Chem. Soc., Chem. Commun.*, 17 (1991).
5. O. Moriya, H. Takenaka, M. Iyoda, Y. Urata, and T. Endo, *J. Chem. Soc., Perkin Trans. 1*, 413 (1994).
6. Y. Iwakura, M. Akiyama, and S. Shiraishi, *Bull. Chem. Soc. Jpn.*, **38**, 335 (1965).
7. C. G. Overberger and S. Fujimoto, *J. Polym. Sci., B*, **3**, 735 (1965).
8. K. Itoya, M. Kakimoto, Y. Imai, and O. Fukunaga, *Polym. J.*, **24**, 979 (1992)
9. E. H. Ungnade and A. D. McLaren, *J. Org. Chem.*, **10**, 29 (1945).
10. D. P. Curran and S. T. Gothe, *Tetrahedron*, **44**, 3945 (1988).
11. C. Grundmann and S. K. Datta, *J. Org. Chem.*, **34**, 2016 (1969).
12. J. H. Boyer, U. Toggweiler, and G. A. Stoner, *J. Am. Chem. Soc.*, **79**, 1748 (1957).
13. S. Kanemasa, S. Kobayashi, M. Nishiuchi, H. Yamamoto, and E. Wada, *Tetrahedron Lett.*, **32**, 6367 (1991).