NOTES

Oligomerization of Protoanemonin with *n*-Butyllithium

Tadamichi HIRABAYASHI and Kenji YOKOTA

*Department of Materials Science and Engineering, Faculty of Engineering,
Nagoya Institute of Technology, Gokiso-cho, Showa-ku, Nagoya 466, Japan*

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While synthesizing¹ polymers which possess the lactone structure in their backbone chains, protoanemonin (ProtoAn), [5-oxo-2-methylene-2,5-dihydrofuran] formulated as **1** in eq 1, was considered useful for the purpose. ProtoAn and its dimer[=anemonin] **2**, are antibiotics present in some kinds of plants² and several investigations on their action against bacteria have been reported.^{3–5} Although ProtoAn has an interesting structure, the so-called “exo-ene conjugated diene system,” no study from the standpoint of the monomer in polymer syntheses has been made as yet. If this monomer should be (co)polymerized successfully under conventional conditions, lactone unit could be readily realized in the backbone chain of the resulting (co)poly-

mer(s).

In this note, we report that ProtoAn can give rise to 1,4-addition along the conjugated system in the presence of a catalytic amount of *n*-butyllithium (*n*-BuLi) and produce linear oligomers but no polymer.

EXPERIMENTAL

Protoanemonin (ProtoAn)

ProtoAn was synthesized from levulinic acid according to eq 1.^{6,7} For its preparation in high (45—53%) yield *without dimer*, it was required to shut out light in the dehydrobromination step and add benzoquinone as an inhibitor.

The IR spectrum [in CHCl₃, 1780, 1770, 1755, 1650, and 890 cm⁻¹] and UV spectrum [λ_{max} (Ethanol)=259 nm, $\epsilon=1.26 \times 10^4$] of **1**, and its

bp (47—48°C/2.5 mmHg) agreed with those described in the literature.^{7,8} The ¹H NMR (60 MHz) data measured in C₆D₅CD₃ at 0°C

are given below:

$\delta = 5.25$ (d-d, $|J| = 3.6, 1.7$; $\text{H} \setminus \text{C} = \text{C} \setminus \text{O}$), 5.55 (d-d-d, $|J| = 3.6, 3.3, 0.9$; $\text{H} / \text{C} = \text{C} \setminus \text{O}$), 6.56 (d-d-d, $|J| = 11.0, 0.3, 1.7$, $\text{C} = \text{C} \setminus \text{H} / \text{C} = \text{O}$), and 7.77 ppm (d-d, $|J| = 11.0, 0.9$ Hz, $\text{C} = \text{H} / \text{C} = \text{C}$).

Polymerization

All polymerizations were run carefully in the dark, otherwise regioselective photodimerization would occur, resulting in anemonin (mp 154°C). A typical procedure is as follows. *n*-BuLi in tetrahydrofuran (THF) was added into ProtoAn solution in THF at -78°C , adjusting $[\text{ProtoAn}]/[n\text{-BuLi}]$ to 40. The mixture was kept at 0°C for 29 h, and then poured into large amounts of cold ether-methanol (95:5 in vol%). A yellowish solid was collected in 35 wt% yield. So as to remove the small amount of dimer, the crude product was washed with warm ethanol and subjected to hydrolysis in acidic aqueous methanol at 40°C for 2 h. The remaining solid oligomers were collected by filtration under a nitrogen atmosphere and dried *in vacuo*. The filtrate was allowed to evaporate, extracted again with ether, and dried.

Analyses of Products

^1H NMR (60 MHz) and IR spectra were recorded in Hitachi R-24A and JASCO IR-E

spectrometers, respectively. Gel permeation chromatography (GPC) was determined on a Toso HLC-803 model with the TSK G4000-, G2000-, and G1000-HXL column system at 35°C , monitored by differential refractometric detectors. The molecular weight was calibrated by standard polystyrene samples. THF-DMSO (9:1, v/v) mixture was used as eluent to make the solubility of the oligomers better. For analysis of the products from an equimolar reaction of ProtoAn and *n*-BuLi, gas chromatography (GC) was performed on a Shimadzu GC-4C with column packed Triton-X305, increasing the temperature from 120 to 180°C . GC-Mass spectrum (GC-MS) was measured on a Hitachi M-52 connected to the above column.

RESULTS AND DISCUSSION

Structure of Oligomers

Results of the oligomerization of ProtoAn with *n*-BuLi are summarized in Table I. Figures 1(A) and (B) show GPC charts of the solid products and anemonin, respectively. These suggest that the products consist not only of the dimer **2** but also oligomers whose molecular weights were distributed in the range of 2600 to 300, ($\bar{M}_n = 730$). The GPC eluent was divided into several fractions and then each was allowed to evaporate under reduced pressure, leaving yellow solids behind. A fraction of 36–37 ml on an elution volume must contain products with molecular weights of 580–

Table I. Oligomerization of protoanemonin (protoAn) with *n*-butyllithium (*n*-BuLi)^a

Run No.	ProtoAn	<i>n</i> -BuLi	Solvent	Time	Yield of products/g	
	mmol	mmol			Solid oligomers	Others ^b
1	23.6	0.59	THF, 10	19	0.56 (24%) ^c	0.62
2	23.6	0.59	THF, 10	29	0.72 (32%)	0.67
3	23.6	0.59	THF, 16	40	0.60 (27%)	0.72
4	23.6	0.59	Toluene, 10	48	0.55 (24%)	0.58

^a In the dark at 0°C .

^b Obtained from filtrates. Details are given in the text.

^c Weight % on the basis of feed ProtoAn is shown in ().

680 (*i.e.*, mainly consisted of hexamers); its IR spectrum is given in Figure 2. The IR spectra of other fractions were essentially the same except for different strengths of absorption due to the *n*-butyl group. Therefore, these oligomers must be composed of the same repeating structure. In Figure 2, absorptions at 1800, 1675, and 835 cm^{-1} appear strongly, while the bending vibrations of C-H assigned to both $\text{CH}_2=$ and $-\text{CH}=\text{CH}-$ (*cis*) moieties have disappeared entirely. In the ^1H NMR spectra, three broad (multiplet) resonances were centered at 2.20, 3.65, and 5.25 ppm, roughly 2:1:1 in an intensity ratio, being in accord with the NMR data⁹ of β,γ -unsaturated γ -lactones. Thus the structure of the present oligomers may be pictured as 3 in eq 2.

Figure 1. Gel permeation chromatographs for (A) solid products from oligomerization of protoanemonin and (B) anemonin (=one of dimers). See the text for GPC conditions.

Figure 2. IR spectrum of solid oligomer(s) contained in the fraction of the elution volume of 36 to 37 ml on GPC.

Oligomers **3** must be formed *via* 1,4-addition of *n*-BuLi to the conjugated system. However, the 1,3-prototropic rearrangement might take place at least partly because a very small shoulder at 1750 (and 1775) cm^{-1} due to α,β -unsaturated γ -lactone was observed in the IR spectra.

Products other than the solid oligomers were detected in filtrates after removing the solid oligomers. On the GC charts of the ether-extracts about fifteen components were found. The major one (13% of the extracts) was the 1:1 adduct, **4**, described in Scheme 1 and its identification was made by GC-MS. The MS data for **4** [m/z = 154 (M^+ , 25), 153 (9.3), 152 (6.2), 100 (10), 99 (100), 85 (4.7), 72 (32), 71 (24), 57 (12), and 55 (17% relative intensity based on the 100%-peak)] agreed with those of

the literature.¹⁰ The others remain obscure because of their paucity and insufficient peak-separation. Some peaks will be described in the next section, relating them with products from an equimolar reaction.

In general, such behaviour as 1,3-diene of exo-ene conjugated heterocycles has been reported rarely. Merely, 2-dichloromethylene pseudooxazolone¹¹ and dichloroprotoanemonin¹² reacted in a similar manner in the radical copolymerization with styrene.

Equimolar Reaction of ProtoAn and *n*-BuLi

It is unlikely that no carbonyl addition (1,2-addition) which competes with the 1,4-addition to the conjugated diene system take place with a strong nucleophilic reagent like *n*-BuLi during the oligomerization. To make products

Scheme 1. The reaction of ProtoAn with *n*-BuLi.

Figure 3. Gas chromatograph of liquid products obtained from an equimolar reaction of protoanemonin (ProtoAn) with *n*-butyllithium (*n*-BuLi). Numbers with peaks correspond to the compound numbers illustrated in the scheme 1. GC conditions: carrier, Hydrogen 43 ml min⁻¹; column, 3 m × ϕ 3 mm stainless steel, packed Triton X-305/Uniport-B; temperature, inj., 200, det., 220, and col., 120–180°C increasing by 5°C min⁻¹.

other than the solid oligomers and compound **4** clearer, the equimolar reaction of ProtoAn and *n*-BuLi was examined at 0°C for 5 h. After filtering the solid oligomers of only ~5 wt% yields, the filtrate was subjected to evaporation under reduced pressure, dissolved again in ether, and washed with dilute hydrochloric acid to remove inorganic compounds. Liquid products were finally obtained in a 51 wt% yield and their GC are shown in Figure 3. The main products **4**, **5**, and **6** have already appeared in the GC charts of the liquid products of oligomerization where, however, both peaks **4** and **5** were not so large (6% or so). GC-MS analysis became possible by the improved peak-separation. Based on the mass fragmentation and IR analyses, it was revealed that the compounds C₁₁H₁₈O₂, **6** (55% of liquid products), [MS: m/z = 182 (P⁺, 2%), 143 (100%); IR: 1600, 1455, 1375, 1135, 990, and 900 cm⁻¹], C₉H₁₈O, **7** (18%), [MS: m/z = 142 (P⁺, 5%), 57 (100%); IR: 1250 and 840 cm⁻¹], C₁₁H₂₀O₃, **5** (9%), [MS: m/z = 200 (P⁺, very

small), 97 (100%); IR: 1705, 1600, 1450, 1380, 1225 and 1045 cm⁻¹], and the 1,4-adduct **4** (8%) were contained in the products. The minor peaks have not been thoroughly elucidated yet.

Main reaction paths of ProtoAn with *n*-BuLi can be recognized in Scheme 1. Compounds **6** (and **7**) must be derived from the intermediate (**B**) via carbonyl addition. But **4** and **5** should be derived from the 1,4-addition intermediate (**A**), as in the case oligomers. The methoxy fragment may be secondarily introduced by methanolysis of the primary products (lactones).

It seems reasonable to assume that a carbanion of the A-type intermediate is apt to convert a less reactive oxanion (A*-type) or ambident anion (**C**), and this would be the reason why no polymer can be obtained against expectation where we supposed ProtoAn most useful for the purpose.

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