Synthesis and Potential Radical Copolymerization of New Monomers Based on Diallylguanidine

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ABSTRACT: Methods were elaborated for the synthesis of new monomers, derivatives of diallylguanidine. These monomer salts (acetate and trifluoroacetates) have the ability to polymerize in water and organic solvents in the presence of radical initiators. Radical copolymerization of diallylguanidine and diallyldimethylammonium chloride was investigated. High biocide ability of obtained copolymers was demonstrated. © 2003 Wiley Periodicals, Inc. J Appl Polym Sci 91: 439–444, 2004

Key words: monomers; radical polymerization; copolymerization; water-soluble polymers; NMR

INTRODUCTION

Substances with guanidine groups, as is known, exhibit noticeable biocide activity.[1] The introduction of such groups in polymer chains results in reinforcement of these properties. Many medicines also contain guanidine groups. The purpose of this work was to synthesize diallyl monomers with guanidine groups, to investigate their properties, and to ascertain the possibility of obtaining products with biocidal activity based on their polymers.

EXPERIMENTAL

^{1}H-NMR spectra were measured using a Bruker MLS-300 instrument (Bruker Instruments, Billerica, MA) in D_2O, $CDCl_3$ at about 20°C. IR spectra were recorded with a Spekord M82 (Carl Zeiss, Jena, Germany) in KBr tablets.

Viscosities were measured with Ubbelohde-type viscometer (Cannon-Ubbelohde, State College, PA) in 1*N* NaCl aqueous solution at 30°C.

Solvents were dried by conventional methods and distilled before use. Diallylamine (DAA) was distilled before use over NaOH under dry nitrogen (bp 109–110°C). ^{1}H-NMR data are given in Table I.

Cyanamide, acetic acid, and trifluoroacetic acid were commercial products used without further purification.

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Synthesis of diallylguanidine acetate (DAGA, 1)

A typical method was used and details of the syntheses are presented in Table II). Glacial acetic acid (1.00 mol) was added with stirring to cooled DAA (1.05 mol) in a one-neck flask (0.5 L). Then to the resulting mixture of DAA acetate and DAA a solution of cyanamide (1.00 mol) in acetonitrile (~ 60 mL) was added. After this the reaction mixture was stirred for about 10 min without cooling. The prepared mixture was added dropwise to reflux acetonitrile (25–250 mL) in a three-neck flask (1.0 L) with a reflux condenser and dropping funnel over a period of about 1 h 40 min (crystalline product appeared after addition of half of the mixture), then this mixture was refluxed an additional nearly 1 h 40 min. The precipitate was filtered off; washed many times with acetonitrile, *n*-batanol, and acetone; and dried *in vacuo* at about 20°C to give DAGA (**1**; m.p. 212–214°C). ^{1}H-NMR data are given in Table I.

Synthesis of diallylguanidine (DAG, 2)

A solution of sodium ethylate was prepared in ethanol (~ 30 mL of ethanol per 0.1 mol of sodium) and then mixed with ethanol solution of equimolar DAGA (~ 30 mL of dry ethanol per 0.1 mol of DAGA) with stirring. After addition the reaction solution was stirred for 1.5 h, then kept 12 h. After filtering off the precipitate of sodium acetate the filtrate was evaporated on a rotary evaporator, yielding DAG (**2**; m.p. 166–169°C). ^{1}H-NMR data are given in Table I.

TABLE I
^{1}H-NMR Spectral Characteristics of Monomer and Polymer Substances[a,b]

Entry	Substance	CH_3–	–CH_2—N [for polymer: CH_2—N (ring)]	CH_2═ [for polymer: CH_2–(chain)]	–CH═ [for polymers–CH– (chain)]
			Monomer substances[c]		
1	DAGA	1.91	4.04	5.28, 5.34	5.89
2	DAGTFA	—	4.30	5.57, 5.62	6.16
3	DAG	—	3.88	5.15, 5.19	5.79
4	DAA	—	3.21	5.06, 5.13	5.86
5	DADMAC	3.03	3.91	5.41, 5.45	6.07
			Polymer substances[d]		
6	PDAGA	1.94	3.14, 3.27, 3.54, 3.71	1.12, 1.35, 1.52, 1.73	2.06, 2.39
7	PDAGTFA	—	3.53, 3.84, 3.97	1.26, 1.41, 1.78, 1.97	2.33, 2.67
8	PDADMAC	3.45,3.55	3.56, 4.12	1.63, 1.85	2.60, 2.99
9	Copolymer of DAGA:		Signals of DAGA links (lower line)		
	DADMAC = 25:75	2.17	3.81, 3.97	1.47, 1.70, 1.80, 1.90	2.30, 2.58
		3.43,3.55	3.58, 4.10	1.62, 1.84	2.64, 3.00
			Signals of DADMAC links (higher line)		

[a] Spectra were measured in D_2O at about 20°C, except entry 4: in $CDCl_3$; chemical shifts δ in ppm.
[b] The numbers of protons on integral magnitudes correspond to predictable structures.
[c] Allyl parts of monomers spectra are $ABMX_2$-type with different multiplicity of their signals; signals of methyl group are singlets.
[d] All signals are broadened and a number of these signals are partially overlapping with each other.

Synthesis of diallylguanidine trifluoroacetate (DAGTFA, 3)

To obtain this monomer salt a solution of DAG (without base isolation) in ethanol was used. Trifluoroacetic acid (TFAA; 2.8 mL, 0.036 mol) was added dropwise to a solution of DAG (5.0 g, 0.036 mol) in ethanol (20 mL) under ice cooling, then stirred 3 h and kept 12 h. The resulting solution was evaporated on a rotary evaporator, yielding 8.2 g (90%) of DAGTFA (**3**; m.p. 156–157°C). (Precipitation of this salt from ethanol into dry acetone can be used for its isolation and additional clarification.) When threefold excess of TFAA was used monomer salt **3** was obtained in 85% yield (m.p. 156–158°C). ^{1}H-NMR data are given in Table I.

Synthesis of diallyldimethylammonium chloride (DADMAC)

This comonomer was prepared as previously described.[2] ^{1}H-NMR data are given in Table I. In addition, ^{1}H-NMR data of DAGA and DADMAC homopolymers and their copolymers are given in Table I.

RESULTS AND DISCUSSION

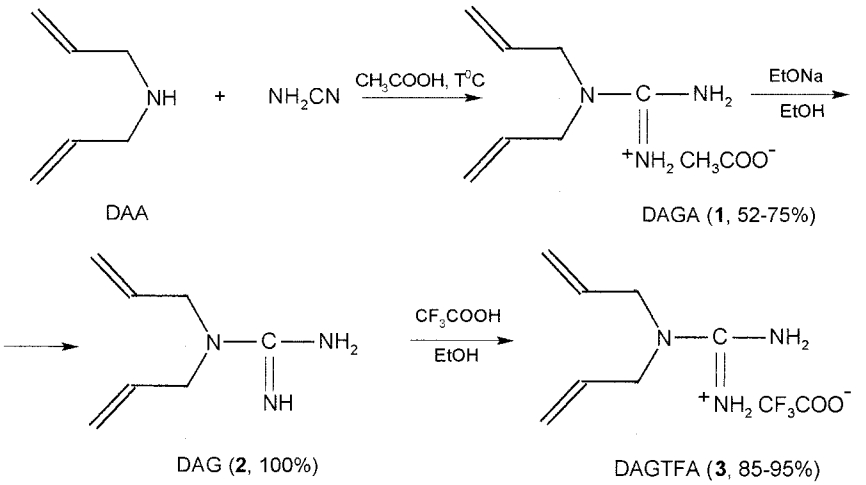
Syntheses of monomers

Diallylguanidine (DAG) derivatives were synthesized by reaction of DAA acetate and cyanamide in acetonitrile (Scheme 1) with the following transformation of obtained DAGA (**1**) into DAG (**2**) and DAGTFA (**3**).

TABLE II
Synthesis of Diallylguanidine Acetate (1)

Entry	DAA,[a] mL (g, mol)	AA,[b] mL (g, mol)	CA,[c] g (mol)	MeCN[d] (mL)	MeCN[e] (mL)	t[f] (min)	Yield (**1**)[g] (%)
1	127 (100.5, 1.034)	57 (59.9, 0.986)	41.4 (0.986)	50	25	100 + 110	52
2	169 (133.4, 1.375)	75 (78.6, 1.310)	55.8 (1.310)	65	170	120 + 90	67
3	134 (105.9, 1.070)	59 (62.0, 1.020)	43.9 (1.020)	50	250	100 + 90	75
4	150 (118.7, 1.224)	67 (69.9, 1.186)	49.0 (1.186)	60	250	105 + 105	73
5	157.5 (124.4, 1.280)	70 (73.5, 1.220)	51.3 (1.220)	60	250	105 + 105	75

[a] Quantity of diallylamine.
[b] Quantity of glacial acetic acid.
[c] Quantity of cyanamide.
[d] Volume of acetonitrile for preliminary dissolution of CA.
[e] Volume of refluxing acetonitrile for addition of the mixture of DAA acetate, DAA and CA.
[f] Reaction time: the first number is the drip time; the second number is the additional refluxing time.
[g] Yield was calculated on CA amount.



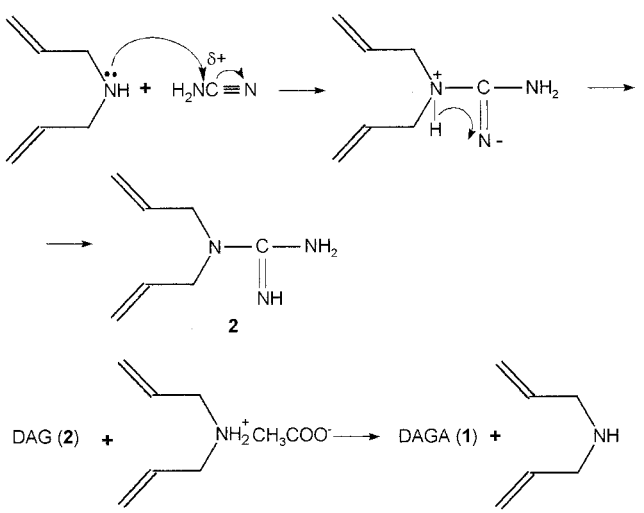
Scheme 1

This method is simple and convenient. A preliminarily prepared mixture of DAA acetate and DAA was added under cooling to a solution of cyanamide in acetonitrile. Amine is used with some excess because the nucleophilic addition of DAA to cyanamide's nitrile group takes place on the first stage of reaction (Scheme 2). The resulting mixture is added dropwise gradually to refluxing acetonitrile. The obtained DAG (**2**) is unstable at high temperature, but because of greater basicity compared with that of DAA, DAG entered into an exchange reaction with DAA acetate to form a stable salt, DAGA (**1**), eliminating DAA for the following transformation.

As investigation has shown the volume increase of refluxing acetonitrile (from 25 to 250 mL per 1 mol of cyanamide) raised the yield of DAGA from 52 to 75% (see Experimental section). Probably, the protonation reaction of base (**2**) in more dilute solutions occurs at a greater rate and yield of salt (**1**) (dilution will complicate isolation of product).

For the above-mentioned reasons DAG (**2**) was obtained quantitatively by salt (**1**) addition into ethanol solution of preliminarily prepared sodium ethylate (Scheme 1). After sodium acetate separation the ethanol solution of DAG (without its isolation) may be used to obtain other salts; accordingly, trifluoroacetate (**3**) was synthesized by the addition of trifluoroacetic acid (TFAA). In a wide range of DAG : TFAA ratios (up to threefold excess of acid) salts of equimolar composition were obtained. These were confirmed by data of elemental analysis and melting point measurements. For prepared monomers ^{1}H-NMR spectra were measured and solubility in water and some organic solvents were determined. Solubility of salts conformed to the following order:

1. DAGA: water > methanol > ethanol ≫ acetone
2. DAGTFA: methanol > ethanol > acetone > water



Scheme 2

Radical polymerization of DAG derivative monomers

Radical polymerization of DAGA (**1**) and DAGTFA (**3**) was studied in water, water–methanol, and methanol solutions at different temperatures (20–60°C). Ammonium persulfate (APS) and azobisisobutyronitrile (AIBN) ([I] = 10^{-2}–10^{-3} mol L^{-1}) were used as initiators. Polymerization was preliminarily shown not to occur without an initiator.

The prepared reaction solutions were degassed in ampoules *in vacuo* (10^{-3} mmHg) and then sealed and heated. In the case of initiator decay at low temperature (20°C, UV) the reaction solution was transferred to a quartz cuvette (*in vacuo*).

Scheme 3

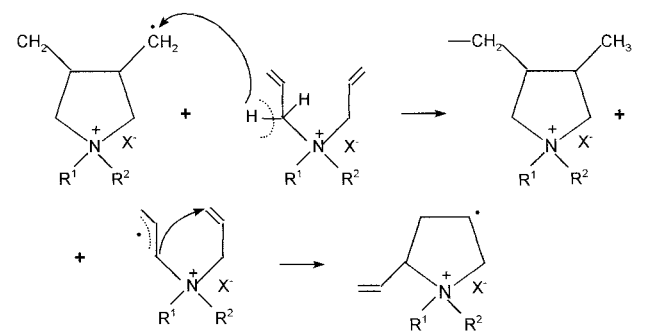
The polymerization process was controlled by spectra (^{1}H-NMR) or viscosity measurements of dialysis cleared and dried *in vacuo* polymeric products.

On the basis of experimental data we suggest that homopolymerization of monomer salts DAGA and DAGFTA is difficult under investigated conditions. So, for example, DAGA conversion in polymer in conditions of [DAGA] = 4 mol L^{-1}; water; [APS] = 4 $\times$ 10^{-3} mol L^{-1}; 60°C; and 72 h was about 125% ([η] $\approx$ 0.05 dL g^{-1}). All of these facts indicate the considerable contribution of degradative chain transfer on monomer (CTM) in the investigated systems.

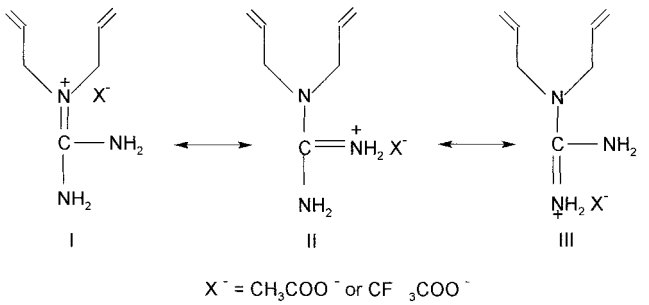
It is known[3–5] that reaction of degradative CTM is inherent just for allyl monomers. Because of the high mobility of α-protons of monomer's allyl groups the abstraction of α-protons by propagation radicals is facilitated to form stable (low active) radicals (Scheme 3).

The analogous processes are observed both for dyallylamine and for its *N*-alkyl derivatives. However, monomeric *N*-alkyl-*N*,*N*-diallyl derivatives in quaternized form polymerize easily under radical initiation to obtain cationic high molecular weight polyelectrolytes.[5–7] Zubov et al.[4] and Timofeeva et al.[7] have established that both protonation and quaternization of examined monomers result in an increase of activation energy of α-proton abstraction attributed to strengthening of α-proton bonds. Because of it, considerable inhibition of degradative CTM was observed, replaced by effective CTM.[7,8] This assumption is confirmed by the appearance of the end vinyl and methyl proton signals in ^{1}H-NMR spectra of corresponding polymers[9,10] (Scheme 4).

In the investigated systems cationogen monomer salts (**1** or **3**) may exist in aqueous solutions in three resonance structures (I–III) but the requirement for suppression of degradative CTM—charge on nitrogen



Scheme 4



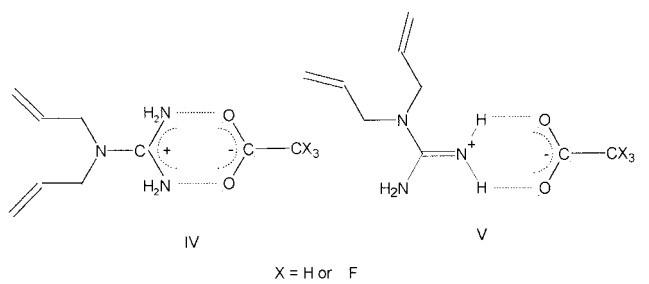
Scheme 5

atom bonded to allyl groups—is fulfilled only in structure I (Scheme 5).

Structures II and III form stable systems (including on steric factors) (Scheme 6). Structures of two nitrogen atoms (IV) and two hydrogen atoms of charged nitrogen (V) both generate delocalized structures with acetate (or trifluoroacetate) counterion.

The combined analysis of both IR and ^{1}H-NMR spectroscopy data confirmed that structure IV is inherent for DAGA and structure V, for DAGTFA. Thus, $\nu_{C=O}$ (DAGTFA) displays a signal at 1598 cm^{-1}, whereas the same signal for DAGA is at 1579 cm^{-1}; that is, in the second case the degree of delocalization in carboxylate ion is greater. The absence of an intensive band of C=N bond at 1660–1680 cm^{-1} in IR spectrum of DAGA also confirms structure IV for this substance (in the IR spectrum of DAGTFA this band is present). The same conclusions can be drawn in a comparison of chemical shifts of CH_2—N protons of these salts in ^{1}H-NMR spectra (see Experimental section).

On the basis of these assumptions it can be concluded that for polymerization of monomer salts (**1**) and (**3**) the degradative CTM will be kept to a considerable degree. For the case X = F (Scheme 6), the decrease of degradative CTM degree would be expected because the high inductive effect (–I) of the trifluoromethyl group would cause the decrease of structure V's stability. However, the expected effects and substantial rate of DAGTFA polymerization could not be achieved, probably because of the low mono-



Scheme 6

TABLE III
Dependency of Copolymer Composition on Initial Composition of Reaction Solution for Copolymerization of DADMAC (M_1) and DAGA (M_2)[a]

	Initial comonomer mixture		Copolymer		
Entry	$[M]_{sum}$ (mol L^{-1})	$M_1 : M_2$ (mol %)	$M_1 : M_2$ (mol %)[b]	Q (%)[c]	$[\eta]$[d]
1	4.00	20 : 80	30 : 70	2	0.14
2	4.00	40 : 60	56 : 44	3	0.19
3	4.00	50 : 50	68 : 32	6	0.21
4	4.26	70 : 30	93 : 7	18	0.39
5	4.17	80 : 20	97 : 2	31	0.48
6	4.12	90 : 10	98 : 2	52	0.64

[a] Conditions: [APS] = 4×10^{-3} mol L^{-1}; H_2O; 60°C; copolymerization 40 h.
[b] According to ^{1}H-NMR data.
[c] Conversion degree.
[d] In 1*N* NaCl aqueous solution at 30°C, dL g^{-1}.

mer solubility in the investigated systems (maximum solubility in water: 0.5 mol L^{-1} at 60°C).

Radical copolymerization of DAGA and DADMAC

Radical copolymerization of DAGA and DADMAC was carried out in ampoules *in vacuo* in aqueous media ([M] = 4.0–4.3 mol L^{-1}; initiators [APS], [AIBN] $\sim 4 \times 10^{-2}$–4×10^{-3} mol L^{-1}; 60°C). The comonomer reaction solutions with initiator were degassed (10^{-3} mmHg) and then sealed and heated. Precipitated copolymers were separated on glassy filter, dried *in vacuo*, and twice reprecipitated from methanol in diethyl ether. Copolymer composition was determined by ^{1}H-NMR data (spectra were measured in D_2O); intrinsic viscosity was measured on a Ubbelohde-type viscometer in 1*N* NaCl aqueous solution at 30°C.

As a result of completed investigations a broad series of copolymers of different compositions were obtained in sufficient quality for further physical–chemical and biological study. Copolymerization was carried out at different degrees of conversion (2–93%). (Investigation of copolymerization to high conversion degrees can produce important results for practical purposes.)

In all cases (including low conversion, $q \leq 5\%$) copolymers enriched with DADMAC links in comparison with initial mixture of comonomers were formed (Tables III and IV). This fact confirms the greater DADMAC reactivity in propagation reactions. It should be noted that polymerization in solution took place in the presence of radical initiator only; and it was completely suppressed by addition of effective radical inhibitors.

Thus, on the basis of the obtained data the conclusion was made about the comparative reactivity of the investigated comonomers. These facts give cause for elaboration of methods of synthesis of new cationogen polymer products with given characteristics (composition, molecular weight, hydrophilic–hydrophobic balance), which may be varied on a large scale.

More definite determinations about potential fields of practical usage of synthesized copolymers will certainly be made after additional investigation of physical–chemical properties and characteristics.

TABLE IV
Dependency of Copolymer Composition on Initial Composition of Reaction Solution for Copolymerization of DADMAC (M_1) and DAGA (M_2)[a]

	Initial comonomer mixture		Copolymer		
Entry	$[M]_{sum}$ (mol L^{-1})	$M_1 : M_2$, mol%	$M_1 : M_2$ (mol %)[b]	Q (%)[c]	$[\eta]$[d]
1	4.00	20 : 80	38 : 62	10	0.10
2	4.00	40 : 60	75 : 25	23	0.13
3	4.00	50 : 50	83 : 17	28	0.17
4	4.29	70 : 30	87 : 13	74	0.20
5	4.17	80 : 20	91 : 9	80	0.31
6	4.17	90 : 10	94 : 6	93	0.52

[a] Conditions: [APS] = 4×10^{-2} mol L^{-1}; H_2O; 60°C; copolymerization 33 h.
[b] According to ^{1}H-NMR data.
[c] Conversion degree.
[d] In 1*N* NaCl aqueous solution at 30°C, dL g^{-1}.

TABLE V
Biocide Activity of Some Monomers and Copolymers

Entry	Biocide	MSC (wt %)[a]	
		E coli.	*St. aureus*
1	DAGA	—[b]	—[b]
2	DAGTFA	1.5×10^{-2}	—[b]
3	Copolymer[c]	1.5×10^{-3}	4.0×10^{-3}
4	Copolymer[d]	3.5×10^{-4}	4.5×10^{-4}

[a] Minimum suppressing concentration of biocide.
[b] No active to corresponding test bacteria.
[c] DADMAC : DAGA = 94 : 6, $[\eta] = 0.52$ dL g^{-1} (Table 2, Entry 6).
[d] DADMAC : DAGA = 83 : 17, $[\eta] = 0.17$ dL g^{-1} (Table 2, Entry 3).

Nevertheless, expecting *a priori* considerable bactericidal activity of copolymers has been validated for a few compositions (Table V). The prepared copolymers demonstrate considerably greater biocidal activity than that of either polyDADMAC or polyhexamethyleneguanidine containing guanidine in each link, which is probably related to combined action: biocide function of guanidine-containing links and transport function of DADMAC segments of polycation.

CONCLUSIONS

The methods of synthesis of new cationogen monomers DAGA and DAGTFA were elaborated; their physical–chemical characteristics were investigated; the possibility of involvement of these monomer salts in reaction of radical copolymerization was shown; and polymer products of different composition and molecular weight were obtained. At the same time the presence of guanidine groups in the structures of homo- and copolymers provided the opportunity to carry out macromolecular design based on their analogous polymer structure and graft modification. Further investigations of copolymers by introducing groups with different properties will broaden the field of their practical use.

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