Reaction behaviour of monomeric β-ketoesters

2. Synthesis, characterization and polymerization of methacrylate group containing enamines

Norbert Moszner*, Ulrich Salz, and Volker Rheinberger

Ivoclar AG, Bendererstrasse 2, FL-9494 Schaan, Liechtenstein

Summary

Polymerizable enamines were synthesized by the reaction of 2-acetoacetoxy-ethyl methacrylate (AAEMA) with various aliphatic mono- and diamines. The enamines were characterized by elemental analyses, IR, ^{1}H NMR and ^{13}C NMR spectroscopy. Radical polymerization of synthesized enamines yielded polymers with pendant enamine groups which were also prepared by the reaction of poly(AAEMA) with the corresponding amines.

Introduction

Enamines are usually available by condensation of aldehydes or ketones with secondary amines and have been utilized as starting compounds in many syntheses [1,2]. In case of the preparation of heterocycles the like synthesis of cocaine according Willstätter [3] or the Nenitzescu reaction [4], enamines from β–dicarbonyl compounds and primary amines are important.

Ethyl acetoacetate reacts with ammonia, primary or secondary amines exothermically at room temperature yielding β-aminocrotonates or the tautomeric β-iminobutanoates [5]. Starting from β-dicarbonyl compounds the enamine tautomer is thermodynamically favored over the imino form [6].

Enamine formation as a method of crosslinking of acetoacetylated polymers with diamines was investigated [7,8]. The use of enamine formation to crosslink acetoacetylated resins appear to be a attractive alternative to the use of isocyanate or aldehyde crosslinking reagents, because it provides ambient-temperature curing and can be used in both water- and solvent-borne applications.

Previously, model studies on enamine formation with acetoacetates were carried out and the results were used to make qualitative correlations with pot-life and cure speed of coating systems [9].

In this paper the synthesis, characterization and polymerization of various enamines formed by the reaction of AAEMA with aliphatic mono- (N-substituted methacryloyloxyethyl 3-aminocrotonates **1a-h**) and diamines (dimethacryloyloxyethyl 3-aminocrotonates **2a-f**) is presented. In addition, the reaction of poly(AAEMA) with primary amines is also described.
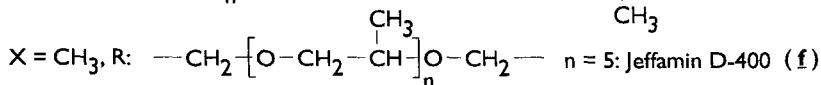
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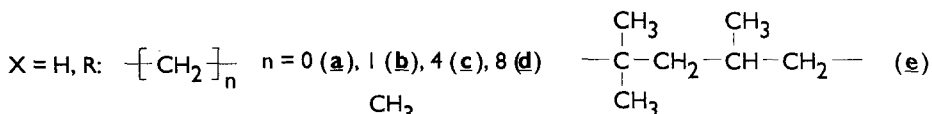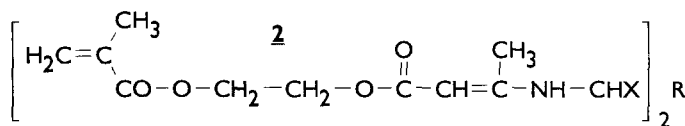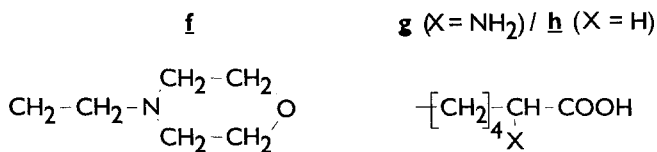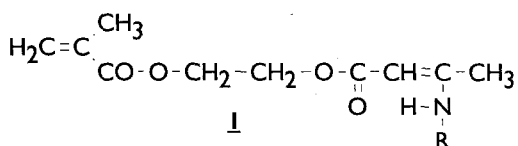
Experimental

Materials

AAEMA (Lonza) was used with purity of about 96% and contained 2-hydroxyethyl methacrylate (HEMA, about 3.0%) and methacrylic acid (about 0.5%). 2,2,4-trimethylhexamethylene diamine (Hüls), poly(oxypropylen)diamine (Jeffamine D-400, Texaco) and the other primary mono- and diamines or amino acids (Fluka) were of analytical grade and were used without further purification.

Dimethylformamide (DMF), and 2,2-azobisisobutyronitrile (AIBN) were purified as described previously [10]. Methylethylketone (MEK) was dried by refluxing over P_2O_5 and distilled before use. Camphorquinone (CQ), N,N-(2-cyanoethyl)methylaniline (CEMA), 2,6-di-tert.-butyl-4-methylphenole (BHT), anhydrous tetrahydrofuran (THF, Fluka) and dioxane (Fluka) were used in analytical grade without further purification.

Synthesis
Monomeric enamines

In a typical enamine formation, 50 mmol amine or 25 mmol diamine dissolved in 40 ml THF were added to a solution of 50 mmol AAEMA in 20 ml THF under

$$H_2C=C \overset{CH_3}{\underset{CO-O-CH_2-CH_2-O-\underset{\underset{O}{\|}}{C}-CH=\underset{\underset{R}{\overset{H-N}{|}}}{C}-CH_3}{}}$$

1

a	**b**	**c**	**d**	**e**
C_4H_9	C_6H_{13}	C_8H_{17}	$C_{12}H_{25}$	$CH_2-CH_2-CH_2-OH$

f   **g** (X = NH_2)/ **h** (X = H)

$$CH_2-CH_2-N\overset{CH_2-CH_2}{\underset{CH_2-CH_2}{\diagdown}}O \qquad \underset{4}{[CH_2]}-\underset{X}{CH}-COOH$$

$$\left[H_2C=C\overset{CH_3}{\underset{CO-O-CH_2-CH_2-O-\overset{\overset{O}{\|}}{C}-CH=\overset{CH_3}{\underset{}{C}}-NH-CHX}{}} \right]_2 R$$

2

X = H, R: $[CH_2]_n$ n = 0 (**a**), 1 (**b**), 4 (**c**), 8 (**d**) $-\underset{CH_3}{\overset{CH_3}{\underset{|}{\overset{|}{C}}}}-CH_2-\overset{CH_3}{\underset{}{CH}}-CH_2-$ (**e**)

X = CH_3, R: $-CH_2-[O-CH_2-\underset{n}{\overset{CH_3}{\underset{|}{CH}}}]-O-CH_2-$ n = 5: Jeffamin D-400 (**f**)

stirring at room temperature. After 6h the reaction mixture was extracted with ether. The extract was washed twice with 20 ml 1.0 M cold NaOH, then with water, and dried over anhydrous sodium sulfate. Evaporation of ether and drying to constant weight in vacuo yielded pure product. Starting from amino acids methanol was used as solvent and the washing with NaOH was omitted. Products were stabilized with 100 ppm BHT. The liquid enamines were characterized without further purification, while solids were recrystallized from water/ethanol mixture.

1a: Viscous liquid, yield: 79%; $C_{14}H_{23}NO_4$ (269.3 g/mol): found: C: 62.21 (calculated: 62.43), H: 8.52 (8.60), N: 5.13 (5.20); IR (film, cm^{-1}): 3288 (NH), 1721 (C=O), 1654 (C=O), 1607 (C=C).

1b: Viscous liquid, yield: 81%; $C_{16}H_{27}NO_4$ (297.4 g/mol): C: 64.46 (64.62), H: 9.21 (9.15), N: 4.59 (4.71); IR (film, cm^{-1}): 3289 (NH), 1721 (C=O), 1654 (C=O), 1606 (C=C).

1c: Viscous liquid, yield: 85%; $C_{18}H_{31}NO_4$ (325.5 g/mol): C: 66.22 (66.43), H: 9.54 (9.60), N: 4.29 (4.03); IR (film, cm^{-1}): 3288 (NH), 1721 (C=O), 1654 (C=O), 1608 (C=C).

1d. Viscous liquid, yield: 87%; $C_{22}H_{39}NO_4$ (381.6 g/mol): C: 69.12 (69.25), H: 10.14 (10.30), N: 3.63 (3.67); IR (film, cm^{-1}): 3284 (NH), 1722 (C=O), 1655 (C=O), 1608 (C=C).

1e: Viscous liquid, yield: 74%, IR (film, cm^{-1}): 3391 (OH), 3311 (NH), 1720 (C=O), 1652 (C=O), 1605 (C=C).

1f: Viscous liquid, yield: 81%; IR (film, cm^{-1}): 3287 (NH), 1719 (C=O), 1655 (C=O), 1601 (C=C).

1g: Viscous liquid, yield: 58%; IR (film, cm^{-1}): 3395 (OH), 3288 (NH), 1720 (C=O), 1650 (C=O), 1601 (C=C).

1h: High viscous liquid, yield: 62%,; IR (film, cm^{-1}): 3400 (OH), 3289 (NH), 1718 (C=O), 1656 (C=O), 1633 (C=C), 1603 (C=C).

2a: Solid, m.p.: 112 °C, yield 78%; $C_{22}H_{32}N_2O_8$ (452.5 g/mol): C: 58.40 (58.40), H: 7.06 (7.13), N: 6.17 (6.19); IR (KBr, cm^{-1}): (NH), 1709 (C=O), 1675 (C=O), 1630 (C=C), 1592 (C=C).

2b: Solid, m.p.: 88 °C, yield: 79%; $C_{23}H_{34}N_2O_8$ (466.5 g/mol): C: 59.14 (59.21), H: 7.27 (7.35), N: 5.98 (6.02); IR (KBr, cm^{-1}): 3300 (NH), 1713 (C=O), 1667 (C=O), 1597 (C=C)).

2c: Solid, m.p.: 67 °C, yield 84%; $C_{26}H_{40}N_2O_8$ (508.6 g/mol): C: 61.33 (61.41), H: 7.91 (7.93), N: 5.44 (5.51); IR (KBr, cm^{-1}): 3300 (NH), 1713 (C=O), 1655 (C=O), 1639 (C=C), 1596 (C=C)).

2d: Solid, m.p.: 38 °C; yield 81%; $C_{30}H_{48}N_2O_8$ (564.7 g/mol): C: 63.66 (63.81), H: 8.42 (8.57), N: 5.06 (4.96); IR (KBr, cm^{-1}): 3284 (NH), 1722 (C=O), 1653 (C=O), 1603 (C=C).

2e: High viscous liquid, yield: 86%; IR (film, cm^{-1}): 3280 (NH), 1720 (C=O), 1651 (C=O), 1610 (C=C).

2f: Viscous liquid, yield: 79%; IR (film, cm^{-1}): 3284 (NH), 1721 (C=O), 1655 (C=O), 1606 (C=C).

AAEMA: ^{1}H NMR (CDCl$_3$, δ (ppm)): 1.95 (s, =C-CH$_3$, =C(OH)-C$\underline{H}_3$), 2.27 (s, -CO-C$\underline{H}_3$), 3.49 (s,-CO-CH$_2$-CO-),4.40 (4H,s,-CH$_2$-CH$_2$-), 5.05 (s,-C$\underline{H}$=C(OH)-), 5.68 (1H,s) and 6.13 (1H,s,CH$_2$=); from the ^{1}H NMR spectra results the enol content is about 10%; IR (film, cm^{-1}): 1740 (C=O), 1720 (C=O), 1737 (C=C).

Modification of poly(AAEMA)

1.07 g poly(AAEMA) (5.0 mmol, M_n (GPC) = 78300 g/mol) were swollen in 19.5 ml dioxane at 30 minutes. 0.55 ml (5.5 mmol) n-butyl amine were added to the mixture with stirring at 30 °C. After the appropriate time, the formed polymer solution was precipitated in excess n-hexane. The polymer was filtered and dried in vacuo to constant weight. The purification of the crude product was carried out by twice precipitating from dioxane/methanol. Analogously the reaction of poly(AAEMA) was carried through with other NH_2-group containing compounds.

Polymerization

The polymerization reactions of enamines were carried out in sealed glass tubes containing a given amount of AIBN dissolved in THF. Subsequently, the monomer was introduced. The tubes were degassed through three freeze-thaw cycles (liquid nitrogen) before they were placed in a constant-temperature bath (60 °C). After a certain time, homopolymerizations were terminated by the addition of excess methanol. The monomer conversion were calculated from the gravimetrically determined yields of the dried polymers. The polymer were repricipitated from THF/hexane or THF/methanol (poly(**1d**)) and dried under vacuo to constant weight.

Poly(**1a**): $(C_{14}H_{23}NO_4)_n$:C: 62.21 (62.43), H: 8.54 (8.60), N: 5.11 (5.20); ^{1}H-NMR (CDCl$_3$, δ (ppm)): 8.60 (1H,t,-NH-), 4.52 (1H,s,-CO-CH=), 4.18 (4H,m,-O-CH$_2$-CH$_2$-O-), 3.23 (2H,q,-NH-CH$_2$-), 1.93 (3H,s,=C(NH)-CH$_3$), 1.48 (6H,m, -CH$_2$-C(CH$_3$,CO)-,-CH$_2$-CH$_2$-CH$_2$-CH$_3$) and 0.95 (6H,m,-C(CO)-CH$_3$,Alk-CH$_3$); IR (KBr, cm^{-1}): 3291 (NH), 1734 (C=O), 1654 (C=O), 1605 (C=C).

Radical homopolymerization of AAEMA (2.0 mol/l) was carried out in the presence of AIBN (0.05 mol/l) in MEK. The polymer formed after 4 h was separated and purified as described above. Monomer conversion was 82% and a number-average molecular weight of poly(AAEMA) of 78300 g/mol were determined by GPC.

Poly(AAEMA): ^{1}H-NMR (DMSO-d$_6$, δ (ppm)): 4.28 (4H,-CH$_2$-CH$_2$-), 3.69 (2H, -CO-CH$_2$-CO-), 2.24 (3H,-CO-CH$_3$), 1.85 (2H,-CH$_2$-), 0.92 (3H,-C(CH$_3$)-); IR (KBr, cm^{-1}): 1730 (C=O);

Measurements

^{1}H NMR measurements were recorded on an EM 390 (Perkin-Elmer, 90 MHz) using hexamethyldisilane (HMDS) as the standard. ^{13}C NMR spectroscopic measurements were performed with a AC 300F spectrometer (Bruker, 300 MHz) using CDCl$_3$ or dimethylsulfoxide-d$_6$ as a solvent. An FT-IR spectrometer 1600 (Perkin-Elmer) was used to record IR spectra.

The number-average molecular weights of polymers were determined by GPC using a isocratic pump IsoChrom (Spectra-Physics) and THF as eluent, an detector RI-4 (Varian) and colums calibrated with polystyrene standards. Differential scanning calorimetry (DSC) measurements were performed by using a Perkin-Elmer DSC-7 thermal analyzer. Scanning rates of 10 °C/min were used.

Results and Discusion

The aliphatic mono- and diamines reacted relatively quickly and uniform with AAEMA in absence of catalyst at room temperature. In the most cases the reaction was complete within 3 h. In contrast to compounds **1a-d**, **1f** , **2a-d** and **2f** functionalized enamines **1e**, **1g,h** and the dienamine **2e** showed a strong tendency to polymerize and it was very difficult to isolate them pure. The reactivity of aromatic amines against AAEMA was lower. For example, in the reaction of 4-aminoacetophenone about 20% of AAEMA was consumed. The reaction of AAEMA with such amino compounds which are insoluble in THF or methanol like glycine or taurine was not successful.

Characterization of enamines was carried out by ^{1}H NMR and IR spectroscopy and partially by ^{13}C NMR spectroscopy and elemental analysis, respectively. The ^{1}H NMR spectra of prepared enamines show the expected signals of protons of methacrylate or -CH_2-CH_2- group analogous to AAEMA at 5.6 (1H,s) and 6.1 (1H,s) or 4.3 ppm (4H,m) (Tab. 1). The protons of both methyl groups of AAEMA give two singlets at 1.95 (3H, =$C(CH_3)$-) and 2.27 ppm (3H, -CO-CH_3). In contrast, signals of methyl groups of enamines are overlaped in the region of 1.90-1.98 ppm, consistent with calculated values according [11]. Furthermore, the signals of NH protons are displaced to down field. They appear at about 8.6 ppm and confirm the z-configuration of enamines, which is stabilized by the formation of an internal hydrogen bond. An analogous down field displacement of NH protons was found by DUDEK et al. [11,12] in the case of various α,β-unsaturated β-ketoamines or bis(acetylacetone)-alkylenimines.

Table 1: ^{1}H NMR spectroscopic data of AAEMA and enamines **1a-d** and **2a-d**

Compound	-NH-	CH_2=	-CH=	CH_2-CH_2	=C-CH_3	N-CH_2-
			Chemical shifts (intensity, multiplicity)[1]			
AAEMA	-	6.13 (1H,s) 5.68 (1H,s)	-	4.40 (4H,m)	1.95 (3H,s)[2]	-[3]
1a	8.58 (1H,t)	6.12 (1H,s) 5.57 (1H,s)	4.45 (1H,s)	4.28 (4H,m)	1.93 (6H,s)	3.23 (2H,q)
1b	8.60 (1H,t)	6.13 (1H,s) 5.58 (1H,s)	4.45 (1H,s)	4.30 (4H,m)	1.94 (6H,s)	3.22 (2H,q)
1c	8.60 (1H,t)	6.13 (1H,s) 5.57 (1H,s)	4.45 (1H,s)	4.28 (4H,m)	1.93 (6H,s)	3.21 (2H,q)
1d	8.63 (1H,t)	6.17 (1H,s) 5.58 (1H,s)	4.50 (1H,s)	4.33 (4H,m)	1.95 (6H,s)	3.22 (2H,q)
2a	8.65 (2H,t)	6.15 (2H,s) 5.58 (2H,s)	4.53 (2H,s)	4.30 (8H,m)	1.93 (12H,s)	3.37 (4H,m)
2b	8.60 (2H,t)	6.15 (2H,s) 5.57 (2H,s)	4.52 (2H,s)	4.32 (8H,m)	1.92 (12H,s)	3.30 (4H,q)
2c	8.60 (2H,t)	6.17 (2H,s) 5.55 (2H,s)	4.50 (2H,s)	4.30 (8H,m)	1.93 (12H,s)	3.23 (4H,q)
2d	8.53 (2H,t)	6.11 (2H,s) 5.57 (2H,s)	4.60 (2H,s)	4.30 (8H,m)	1.94 (12H,s)	3.19 (4H,q)
4	8.72	-	4.48	-	-	3.30, 3.41

[1] Shift value in ppm down field from internal HMDS
[2] CH_3-CO-: 2.27 (3H,s); [3] -CO-CH_2-CO-: 3.49 (2H,s) bzw. -CH=C(OH)-: 5.05 (s);
[4] Diethyl-(ethylenbis-3-aminocrotonate) [11]

The ^{13}C NMR data of selected enamines (Tab. 2) also support the proposed structures. For assigment of the observed signals chemical shift increments compiled by Pretsch et al. [13], the DEPT (distortioness enhancement by polarization transfer) experiment [14] and data on cyclic β-ketoesteramines [15] were used. Thus as a result of enamine formation, chemical shifts of carbon atom 1, 2 and 3 were significantly changed in comparison to AAEMA, whereas the chemical shift changes of the other carbon atoms were only minimal.
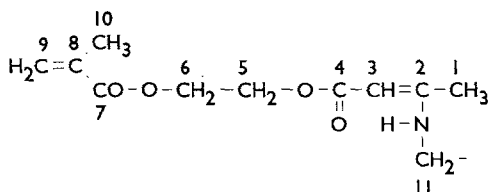
The IR spectra of the enamines confirm the formation of a hydrogen bond between the enamine nitrogen and the oxygen of the carbonyl group in β-position to it, which cause a displacement of the carbonyl absorption of 1740 cm^{-1} in case of AAEMA to values between 1650 and 1660 cm^{-1}. This has also been observed with other N-substituted 3-aminocrotonic acid derivatives [15-17]. In agreement with this, the absorption bands between 1592 and 1606 cm^{-1} can

Table 2 ^{13}C NMR spectroscopic data of enamines[1]

| Compound | Chemical shifts[2] | | | | | | | | | |
	1	2	3	4	5, 6	7	8	9	10	11
1a	19.4	162.5	81.3	170.1	63.3, 60.2	167.2	136.2	125.7	18.3	42.7
2a	19.3	161.8	83.2	170.0	63.0, 60.4	167.3	136.1	125.8	18.3	43.8
2b	19.4	162.3	82.4	170.1	63.1, 60.3	167.3	136.1	125.8	18.3	39.9
2c	19.4	162.5	81.5	170.1	63.2, 60.2	167.3	136.1	125.2	18.3	42.9
2d	19.4	162.5	81.4	170.1	63.2, 60.1	167.3	136.2	125.7	18.3	43.1
AAEMA	30.1	200.3[3]	49.8[4]	166.9	62.9, 62.2	167.1	136.0	126.1	18.2	-

[1] Shift value in ppm down field from internal HMDS
[2]

$$H_2C = \overset{\overset{\displaystyle 10}{\underset{}{9 \;\; 8 \;\; CH_3}}}{C} \quad \underset{7}{CO} - O - \overset{6}{CH_2} - \overset{5}{CH_2} - O - \overset{4}{\underset{\underset{O}{||}}{C}} - \overset{3}{CH} = \overset{2}{\underset{\underset{CH_2-}{\underset{||}{11}}}{\underset{H-N}{C}}} - \overset{1}{CH_3}$$

[3] C=O, C-OH (enol): 176.2; [4] CH_2, CH= (enol): 89.4

be assigned to stretching vibrations of the enamine double bonds. For most cases, the absorption band of the methacrylate double bond of enamines (AAEMA at 1637 cm^{-1}) is covered and only visible in case of **2a** or **2b**.

The synthesized enamines are radically polymerizable in THF, dioxane, DMF or MEK in the presence of AIBN. The results in Table 3 show, that the monomer

Table 3 Polymerization of various enamines (1.0 mol/l) in the presence of AIBN (0.05 mol/l) in THF at 60 °C

Monomer	[Monomer]	Time (min.)	Conversion (%)	M_n (g/mol)	T_G (°C)
1a	1.00	15	8.1	-	-
1a	1.00	30	18.8	-	-
1a	1.00	60	37.7	62800	-14
1a	1.00	120	46.5	-	-
1a	0.50	60	28.8	27300	9
1a	0.75	60	36.7	45000	-9
1a	1.50	60	39.2	78000	-26
1b	1.00	60	40.3	71100	-38
1c	1.00	60	41.9	-	-
1d	1.00	60	48.6	84200	-42
1f	1.00	60	43.2	-	-
1g	1.00	60	64.2	-	-

conversion increases with polymerization time. As expected from a normal radical polymerization [18], the number-average molecular weight of polymers increases with increasing concentration of monomeric enamine **1a**. The succesful polymerization was confirmed by spectroscopic investigation of the products. Thus in the ^{1}H NMR spectra of poly(**1a**) the signals of vinyl protons disappeared, whereas the signals of other protons like NH- (8.60), -CH= of enamine group (4.50) or -CH$_3$ (1.95 and 0.93 ppm) are visible. Also the IR spectra of poly(**1a**) shows an absorption band at 1606 cm^{-1} which can be assigned to stretching vibrations of enamine double bonds.

The glass transition temperature (T_G) of poly(**1a**) (27300 g/mol) determined by DSC analysis is 9 °C. Interestingly, T_G of polymeric enamines decreases with increasing number-average molecular weight and increasing length of the lateral alkyl group, respectively (Table 3).

The prepared enamines can also be polymerized in the presence of CQ/CEMA by irradiation with visible light yielding transparent elastic materials.

The polymeric enamines can also be obtained from the reaction of poly(AAEMA) with amines. For example polymers with a poly(**1a**) corresponding stucture can be prepared by the reaction of poly(AAEMA) with n-butyl amine in dioxane. This is supported by the fact that ^{1}H NMR and IR spectra of repricipated reaction products display all signals which are typical for polymerized AAEMA and **1a** units. In the case of other alkyl amines the extent of conversion decreases with increasing chain length. With glycine or 6-aminocaproic acid, which are poorly soluble in dioxane, no reaction takes place within 24h under the same reaction conditions.

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