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Mechanism Study of the Base-Catalyzed Ether Formation Involving α-(Hydroxymethyl)acrylates

Ronald F. Colletti, Robert J. Halley, and Lon J. Mathias*

Department of Polymer Science, University of Southern Mississippi, Hattiesburg, Mississippi 39406-0076

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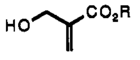
ABSTRACT: The formation of ethers from activated allyl alcohols under basic conditions is described. Tertiary amine is necessary for catalysis probably through O–H bond polarization and/or a proton relay mechanism. The latter would most likely involve a six-membered transition state in which Michael-like oxygen attack at the β-vinyl carbon occurs more-or-less simultaneously with loss of the allyl OH to generate the vinyl group at the allyl CH_2. Deuterium labeling, carbon-13 labeling, transetherification, and mixed ether formation all confirm the proposed mechanism. A similar process involving attack of an intermediate carbanion (from attack of DABCO on trifluoroethyl acrylate) leads to a 1,4-diene in which two acrylate groups are linked by a single methylene. Carbon-13 labeling shows intermediate formation of the α-(hydroxymethyl)acrylate and its ether before their conversion to the 1,4-diene. Synthetically these two processes make available new families of ether-linked diacrylates, mixed esters of these diacrylates, α-ether-substituted methacrylate esters, and diacrylates with a 1,4-diene structure.

During the synthesis of α-(hydroxymethyl)acrylate esters 1 using the diazabicyclo[2.2.2]octane (DABCO) catalyzed addition of formaldehyde to the corresponding acrylate,[1] it was observed that ether 2 and acetal products 3 and 4 were formed.[2,3] The diacrylate ether was subsequently investigated as a cross-linking agent,[4] a monomer for cyclopolymerization,[5,6] and a comonomer with dithiols for Michael polymerization.[7] An ene-type mechanism for ether formation was proposed[2] (Figure 1) involving a six-membered ring transition state with essentially simultaneous transfer of a proton, loss of water, and ether bond formation. It has been determined that base is needed to catalyze the ether-forming reaction. This mechanism was questioned by referees, who suggested alternative pathways be considered. We present here evidence from separate deuterium- and carbon-13 labeling experiments that confirms the overall mechanism.



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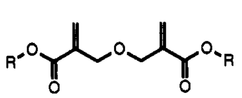

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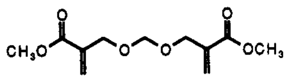

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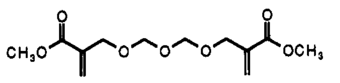

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Experimental Section

Methyl acrylate, ethyl acrylate, trifluoroethyl acrylate, and DABCO were purchased from Aldrich Chemical Co. (Milwaukee, WI) and used as received. ^2H- and ^{13}C-labeled paraformaldehyde were obtained from MSD Isotopes (Montreal, Canada). Carbon NMR spectra were acquired on a Bruker AC-300 at a frequency of 75.47 MHz. Deuterium NMR spectra were acquired on a Bruker MSL-200 at a frequency of 30.72 MHz. Gas chromatography was performed on an HP 5890 with a fused silica column coated with 5% phenylmethylsilicon (J & W Scientific Column DB5).

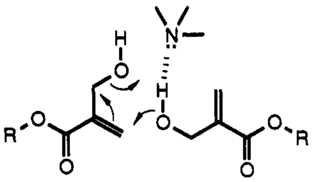

Figure 1. Proposed ene-type mechanism leading to ether formation.

Figure 2. Synthesis of the ^2H-labeled ethers from the α-(hydroxymethyl)acrylate.

Reactions were carried out in a 5-mm NMR tube. The acrylate and paraformaldehyde (mole ratio of 5:1) were introduced into an NMR tube, and 3 wt % DABCO was added along with a DMSO-d_6 capillary insert as the lock and reference. The NMR tube was placed in an oil bath maintained at 70 °C. At selected intervals the NMR tube was removed from the oil bath and allowed to cool to room temperature and an NMR spectrum acquired. A GC chromatograph was obtained at the same time to monitor reaction progress in correlation with each NMR spectrum.

Results and Discussion

Deuterated paraformaldehyde was used in the synthesis to produce the α-hydroxymethyl-α-d_2 adducts of the methyl and ethyl acrylates. In situ conversion of these alcohols to the corresponding ethers-d_4 occurred readily in the presence of DABCO with mild heating (Figure 2). Initial characterization of the labeled ethers gave proton NMR integration values that did not correspond exactly to products predicted by the proposed mechanism (Table I). That is, if only the ether-forming process in Figure 2 was occurring, ^2H incorporation should be equal at the α-CH_2 and vinyl CH_2 positions. Figure 3 gives the ^2H NMR spectrum of the ether of the methyl ester compound showing ^2H integration values that complement those reported in Table I based on ^1H integration.

Less-than-expected ^2H integration values at the vinyl positions are ascribed to a scrambling reaction involving

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Table I
Proton NMR Integration Results for Isolated Deuterium-Labeled Ethers of MHMA and EHMA

		theoret		exptl	
		ppm	H's	ppm	H's
methyl ester	ester CH_3	3.69	6	3.69	6.0
	α-CH_2	4.18	2	4.18	1.4
	vinyl CH	5.80	1	5.80	1.3
	vinyl CH	6.24	1	6.24	1.3
ethyl ester	ester CH_3	1.09	6	1.09	6.0
	ester CH_2	4.07	4	4.07	4.0
	α-CH_2	4.22	1	4.22	1.4
	vinyl CH	5.84	1	5.84	1.3
	vinyl CH	6.28	1	6.28	1.4

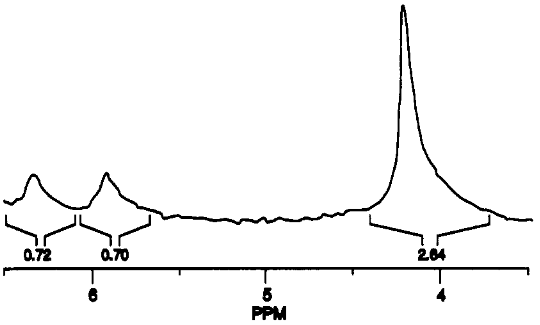


Figure 3. Solution ^2H NMR spectrum of 2-d_4 of MHMA; integration values correlate to ^1H NMR data, indicating rearrangement is occurring.

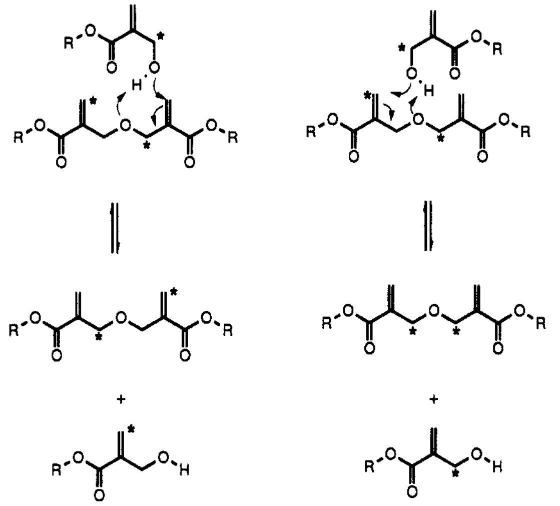


Figure 4. Proposed rearrangement reactions of the α-(hydroxymethyl)acrylate ethers.

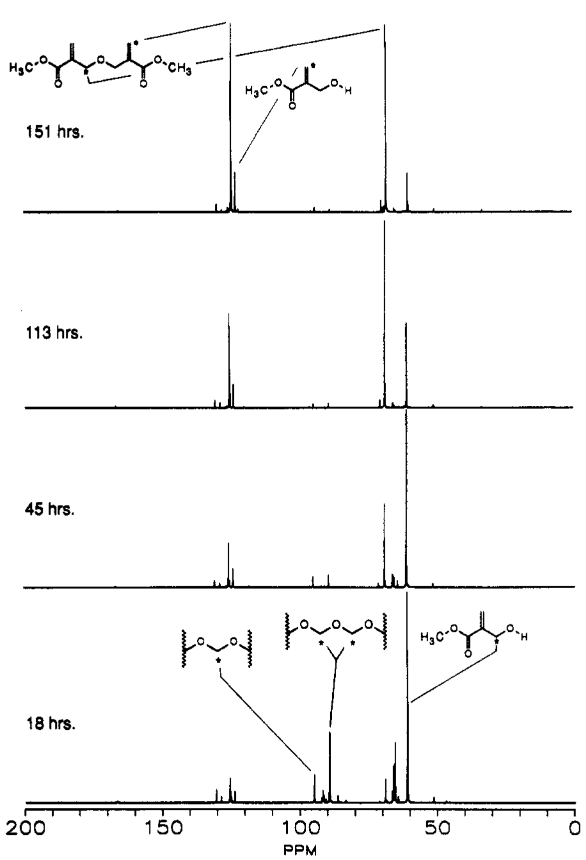


Figure 5. Solution ^{13}C NMR spectra of methyl α-(hydroxymethyl)acrylate reaction mixture at various reaction times.

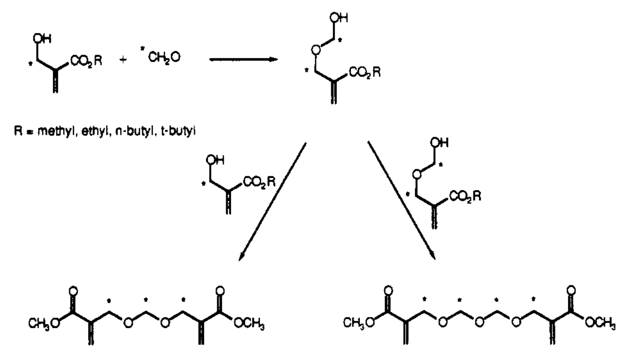


Figure 6. Overall process leading to the labeled acetals.

the same mechanism as in Figure 2 but with the *ether* as the coreactant. Two possibilities are given in Figure 4, although additional reaction of the products of these reactions can lead to further positional isotope equilibration, but always in *pairs* of ^2H atoms. In fact, no evidence was obtained by ^1H, ^2H, or ^{13}C NMR analysis of random ^1H–^2H exchange; all positions contained either two or no ^2H labels.

^{13}C-labeled paraformaldehyde was used to produce the ^{13}C-labeled products in a manner analogous to that used for deuterium labeling. Early in the reaction the NMR spectra contain intense peaks due to the CH_2OH (61.2 ppm) of the initially formed methyl α-(hydroxymethyl)acrylate (MHMA) plus its acetal products and oligomers of paraformaldehyde at 85–95 ppm (Figure 5). Figure 6 shows the formation (no mechanism implied) of the acetal products and positions of the ^{13}C-labeled carbons. The GC data confirm the NMR results in Figure 5, indicating that dimer ether formation (with the labeled vinyl carbon peak at 125.3 ppm and the carbon α to the oxygen at 69.1 ppm) occurs after the acetal products are observed; that is, the latter occurs much faster than the former. Peaks at 89.4 and 94.9 ppm correspond to the acetal methylene carbons of previously identified compound 3 and 4. After an additional 8-h heating, a peak at 124.7 ppm due to the ^{13}C-labeled vinyl CH_2 of MHMA begins to grow in and becomes more intense as the reaction proceeds. Labeling at this position can arise only due to a rearrangement reaction such as those proposed in Figure 4 to explain the deuterium labeling results. This "scrambling" reaction begins immediately after the diacrylate ether is formed and occurs at a comparable rate. Gradual conversion of the acetal products and the alcohol to ether continues throughout the reaction, leading to formation of the ether as the major product with higher content of the labeled carbon at the CH_2O group than at the vinyl CH_2. After ca. 120 h, however, the peak intensities of the labeled carbons of 2 become equal, indicating that isotopic equilibration has occurred at the two labeled carbon positions. This requires continued transetherification as the reaction goes to final equilibrium in the presence of

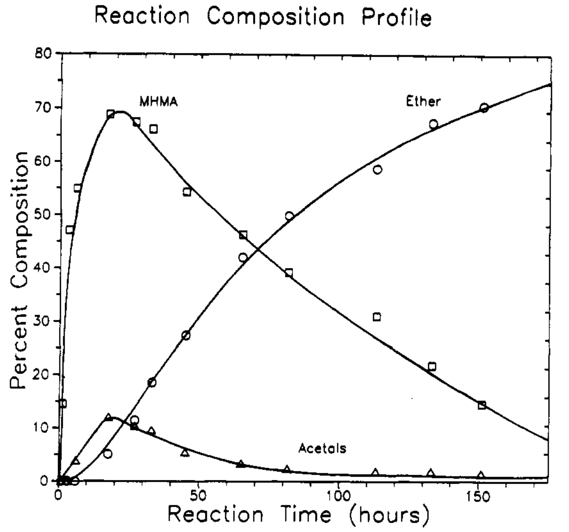
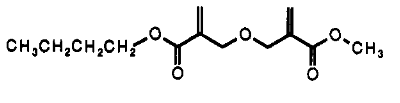


Figure 7. Plot of reaction composition with time (not including starting acrylate) for ^{13}C-labeled MHMA dimerization.

MHMA and water liberated by the ether-forming reaction. It should be pointed out that even at long reaction times, residual RHMA remains, presumably due to water in equilibrium with the ether.

At longer reaction times, a second phase formed in the bottom of the NMR tube (above reaction). This was likely due to the increased concentration of diacrylate ether (which is not miscible with the water-miscible MHMA in the presence of water). At ca. 160 h, the bottom phase spontaneously polymerized despite the presence of DABCO, which is an excellent radical inhibitor. Further work is underway to characterize this polymer.

Both the NMR and GC data confirm that MHMA and acetal products are formed initially and, as the reaction proceeds, these products decrease in concentration while the diacrylate ether concentration increases (Figure 7). The question of relative rates of the initial ether-forming reaction and the scrambling process arises. Allowing a mixture of purified ether 2 with methyl ester groups to react with the *n*-butyl ester acrylates (1, R = *n*-butyl) in the presence of DABCO lead to formation of *mixed* ester ether 5, over a somewhat longer time period than needed for formation of an ether directly from 1 (process monitored by GC and ^{13}C NMR). A statistical 1:2:1 mixture of the three possible ethers eventually formed.



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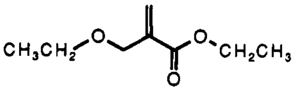
Additional support for the proposed mechanism was provided by the reaction of the ethyl ester 1 (EHMA) with ethanol in the presence of DABCO at 60 °C. Formation of the ethyl ester 6 took place over a substantially longer time period (several weeks) than required for synthesis of 2 under comparable conditions. Compound 6 was also synthesized from 1 by using H_2SO_4-catalyzed dehydration; GC and NMR analyses confirmed an identical composition for products produced by the two methods. Slower ether formation in this system may be due to lower ethanol acidity or decreased association of the two different alcohol moieties prior to transition-state formation catalyzed by the base. The EHMA molecules could plausibly associate more strongly or be closer to the transition-state structure than ethanol plus EHMA due to two possible sets of hydrogen bonds involving alcohols and ester groups for the paired EHMA molecules.



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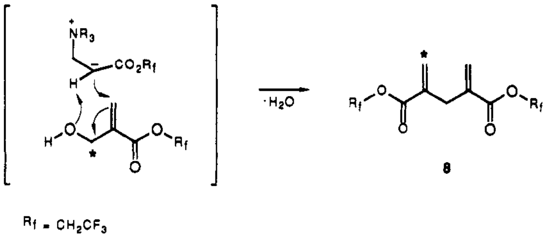
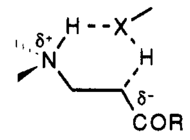


Figure 8. Proposed mechanism leading to 1,4-diene acrylate showing synthesis of ^{13}C-labeled 1,4-diene acrylate (from ref 3).

A base was shown to be a necessary component in these reactions. For example, without DABCO, no ether formation occurs with 1 in 7 days at 60 °C, whereas over 60% conversion was observed with the catalyst. Other tertiary amines such as triethylamine and tributylamine also catalyze the reaction, although rates of reaction were somewhat lower than with DABCO. (These bases do *not* catalyze initial formation of α-(hydroxymethyl)acrylates.) Base catalysis of Michael reactions that are analogous to this ether-forming reaction have been described.[8] Secondary amine addition to acrylates was found to be second order in amine and first order in olefin in aprotic solvents, while in protic solvents the reaction was first order in each. A proton relay process was proposed that involved either solvent or a second amine as shown for 7. In our process, the base probably functions as a polarizing agent for the alcohol O–H bond (Figure 1). This polarization facilitates the attack of the oxygen on the terminal methylene group and aids in the transfer of the hydrogen atom to the departing oxygen of water (Figure 2) or alcohol (Figure 4).



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The synthesis of fluoroalkyl esters of α-(hydroxymethyl)acrylate has been attempted by others with surprising results.[3] In contrast to alkyl acrylates, fluoroalkyl acrylates undergo reaction to give 1,4-diene bisacrylate 8 as the major product along with the α-(hydroxymethyl)acrylate and the 1,6-diene ether as byproducts. A mechanism has been postulated[3] (similar to that for the 1,6-diene ether acrylates) that accounts for the formation of the 1,4-diene acrylate (Figure 8). The reaction of trifluoroethyl acrylate with ^{13}C-labeled and natural-abundance paraformaldehyde was examined as a model for this system, with ^{13}C NMR spectroscopy and gas chromatography to monitor the progress. Figure 8 shows the expected placement of the ^{13}C label in the formation of the 1,4-diene moiety.

The GC results indicate that the 1,6-diene is formed rapidly after the α-(hydroxymethyl)acrylate is generated. The 1,4-diene is formed more slowly but quickly becomes the major product by a 2:1 ratio to the 1,6-diene ether. The NMR data confirm the GC results (Figure 9). The ^{13}C label gives an intense peak for the CH_2OH group (61.2 ppm) of the initially formed trifluoroethyl α-(hydroxymethyl)acrylate (TFEHMA) with a weak vinyl CH_2 at

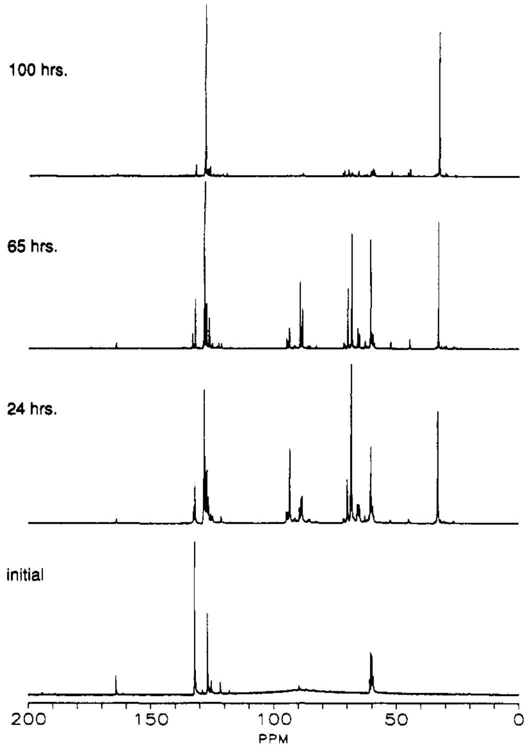

Figure 9. Solution ^{13}C NMR spectra of trifluoroethyl α-(hydroxymethyl)acrylate reaction mixture with labeled formaldehyde at various reaction times.

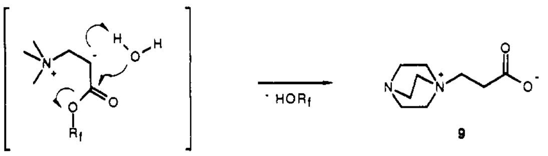

Figure 10. Mechanism of ester hydrolysis giving zwitterion **9**.

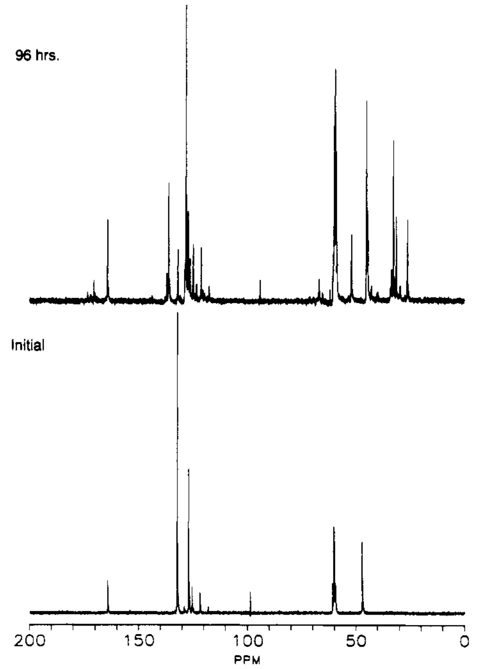

Figure 11. Solution ^{13}C NMR spectra of trifluoroethyl α-(hydroxymethyl)acrylate reaction mixture with unlabeled formaldehyde at various reaction times.

127.5 ppm. The acetal products and oligomers of paraformaldehyde appear at 85–95 ppm. The labeled vinyl carbon peak at 125.3 ppm and the carbon α to the oxygen at 69.1 ppm of the 1,6-diene ether gradually grow in. Peaks at 89.4 and 94.9 ppm correspond to the acetal methylene carbons of the acetal products of TFEHMA (Figure 9).

Most interesting is the peak that gradually grows in at 130 ppm. Figure 8 shows the proposed formation of the 1,4-diene product with this peak corresponding to the expected *sole* position of ^{13}C labeling. If this mechanism is occurring, then additional analogous "scrambling" reactions must also be occurring at a rate faster than the reaction originally forming the 1,4-diene; otherwise the vinyl carbon peak would be the most intense initially and throughout.

After ca. 70 h, additional DABCO was added to both the labeled and unlabeled reaction mixtures since it had been depleted. The subsequent GC results showed no significant amount of TFEHMA remaining, a decrease in the amount of the 1,6-diene ether product, and an increase in the 1,4-diene product. These results confirm that the 1,6-diene ether is also converted to the 1,4-diene, presumably in a manner analogous to that from TFEHMA directly. In fact, this is the best explanation of the appearance of the ^{13}C label at the allyl methylene carbon of 8 faster then at the vinyl position.

At longer reaction times after additional DABCO was added, the NMR spectrum gives *only* equally intense labeled peaks at 130 ppm due to the vinyl position and at 33 ppm for the methylene carbon between the acrylate groups of the 1,4-diene. The disappearance of the 1,6-diene under these conditions clearly indicates that, first, attack of the DABCO–acrylate adduct can occur on the ether vinylmethylene, and second, that all steps must be reversible, leading to the thermodynamic, all-carbon-bonded 1,4-diene as final product. The reaction conditions used here are markedly different from those previously employed[3] in which 1:1 mole ratios of the acrylate and formaldehyde were used. The excess acrylate and addition of DABCO during the course of the reaction both were important in determining the outcome.

First, the added DABCO is needed to replenish catalyst consumed during the reaction by a side reaction (Figure 10) leading to formation of the zwitterion **9**. The same electron-withdrawing ability of the trifluoroethyl moiety, which allows formation and reaction of the carbanion intermediate, also makes this group an excellent leaving group. A two- or three-step addition–elimination–proton transfer process results in overall formation of trifluoroethanol and **9**. Peaks are observed in the NMR spectra in Figure 11 (from the unlabeled experiment) for the zwitterion at 31, 46 (two peaks overlapping), 52, and 178 ppm. Identification of these peaks as belonging to **9** has been confirmed by mixing fluoroethyl acrylate with only DABCO plus water and observing the NMR spectrum of the rapidly formed **9**. The peak at 63 ppm is due to the hydrolysis product of **9**, β-hydroxypropionic acid. We have previously obtained **9** as a stable, white, crystalline salt from DABCO-catalyzed reactions of other activated-ester acrylates, especially when formalin rather than paraformaldehyde was used as the formaldehyde source. It should be noted that the loss of DABCO in forming **9** is a gradual process occurring as water is liberated from paraformaldehyde (end groups) and especially from 1,6-diene formation, which generates 1 equiv of water.

The second condition required for formation of 8 as the major product is excess acrylate starting material. As long as both DABCO and acrylate are present in the reaction mixture, reversible formation of the carbanion intermediate needed to give 8 will occur. Attack of the carbanion on the 1,6-diene vinylmethylene will continue to deplete its concentration. "Scrambling" of the labeled positions of 8 will also continue as part of the ether conversion process and as a result of the reversible formation of 8. The latter is required to explain the ca. 1:1 ratio of labeled carbons eventually obtained in the product, since less than an equivalent of label would develop at the allylmethylene through attack of the carbanion at the equally labeled and unlabeled vinylmethylenes of the 1,6-diene.

Summary

The labeling and additional experiments described here support the proposed ether-forming mechanism to give the 1,6-diene of most acrylates and the 1,4-diene of the fluoroalkyl acrylates. More importantly, the base-catalyzed ether formation has applicability beyond generation of the dimer acrylates **2**. While the latter compounds are desirable as crosslinking agents in vinyl polymerization[4] and for the formation of cyclopolymers,[2,3] the family of derivatives analogous to **6** have potential as monomers themselves to give novel polymers. In addition, they can also be used in cycloaddition reactions with dienes and should have application in natural products syntheses in which such compounds can serve as multifunctional Michael acceptors with further reaction possible at the ester moieties. The ^{13}C-labeling experiments with the fluoroacrylate indicate that the 1,4-diene is formed as the major (thermodynamic) product at long reaction times. These experiments also suggest that the steps leading to the 1,4-diene involve further scrambling of the vinyl and methylene positions similar to what is observed for 1,6-diene formation.

Conclusions

Understanding the mechanism of formation of all the intermediates, products, and byproducts of the DABCO-catalyzed reaction of formaldehyde with acrylates makes available a menage of synthetically useful procedures and compounds. Specifically, we note the following:

Knowing when ether dimerization begins to play a competitive role in the formation of the α-(hydroxymethyl)acrylates allows facile scaleup and isolation of the latter.

Ether dimers can be obtained as the major thermodynamic products for *unactivated* acrylates by pushing the reaction; water removal during synthesis should further enhance ether formation.

1,4-Diene formation can be similarly forced to good conversion by use of excess acrylate and added DABCO.

The above reactions can be extended to other derivatives such as the mixed acrylate ethers from two different α-(hydroxymethyl)acrylates, or one and a simple alcohol. Similarly, conversion of the allylic OH to better leaving groups (such as the Cl) facilitates mixed ether formation through essentially the same mechanism.

Overall, the synthesis and derivatization reactions now possible with the α-(hydroxymethyl)acrylates makes these monomers (and their polymers) some of the most useful and versatile functional materials available today.

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References and Notes

(1) Mathias, L. J.; Kusefoglu, S. H.; Kress, A. O. *Macromolecules* **1987**, *20*, 2039.

(2) Mathias, L. J.; Kusefoglu, S. H. *Macromolecules* **1987**, *20*, 2039; U.S. Patent 4,889,948, Dec 26, 1989.

(3) Antonucci, J. M.; Stansbury, J. W.; Cheng, G. W. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1990**, *31*, 320.

(4) Mathias, L. J.; Kusefoglu, S. H. *J. Polym. Sci., Polym. Lett. Ed.* **1987**, *25*, 451.

(5) Mathias, L. J.; Kusefoglu, S. H.; Ingram, J. E. *Macromolecules* **1988**, *21*, 545.

(6) Stansbury, J. W. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1990**, *31*, 530.

(7) Mathias, L. J.; Kress, A. O. *Polym. Commun.* **1988**, *29*, 302.

(8) Johnson, M. R. *J. Org. Chem.* **1986**, *51*, 833.