Organic Sulfur Compounds. XX. Free-Radical Addition of Thiols to Substituted β-Mercaptoacrylic Acid Methyl Esters

WOLFGANG H. MUELLER

Central Basic Research Laboratory, Esso Research and Engineering Company, Linden, New Jersey

Received December 15, 1965

The orientation of free-radical additions of methyl and of ethyl mercaptan to substituted β-mercaptoacrylic acid methyl esters, $RSCH{=}CHCO_2CH_3$, depends strongly on the nature of R. The electronic character of the R group rather than its steric requirement governs the attack of a thiyl radical at the α or β carbon. A reinvestigation of the addition of thiolacetic acid to methyl propiolate showed that in this case ionic Michael addition is strongly preferred, thus affording the β,β diadduct instead of the earlier reported α,β diadduct.[1]

The earlier reported orientation of diadduct formation obtained by the addition of thiols to propiolic acid or propiolates is not consistent with a single mechanism. A β,β diadduct would be expected to result from an ionic Michael addition, while α,β diadducts are more likely the result of a free-radical addition. The addition of thiolacetic acid to methyl propiolate at elevated temperature has been claimed to afford the α,β diadduct,[1] while that of cyclohexyl mercaptan to propiolic acid under similar conditions yielded the β,β diadduct.[2] From the ultraviolet light initiated reaction of ethyl mercaptan with propiolic acid, the α,β diadduct has been reported.[3]

The reported absence of β,β diadducts from thiolacetic acid was surprising, since this addend was felt to be especially prone to undergo ionic addition. Therefore, a reinvestigation of this particular reaction was carried out as the initial part of this study. The results of this first part of the investigation led to a study of the possible steric or electronic effects governing the orientation of free-radical thiol additions to substituted β-mercaptoacrylates. Additions of methyl- or ethyl mercaptan to acetylmercapto-, methylmercapto-, and phenylmercaptoacrylates were carried out.

Results and Discussion

Ionic Addition of Thiolacetic Acid to Methyl Propiolate.—Earlier workers[1] reported the following yield of *cis* and *trans* monoadducts together with the α,β-diacetylthiopropionic acid methyl ester.

$$CH_3COSH + HC{\equiv}CCO_2CH_3 \longrightarrow \underset{\substack{8\%\ cis\\ 18\%\ trans}}{CH_3COSCH{=}CHCO_2CH_3} + \underset{\displaystyle SOCCH_3}{CH_3COSCH_2CHCO_2CH_3} \quad 17\%$$

The lack of stereoselectivity[4] and the orientation of the diadduct[3] suggested a free-radical mechanism for this reaction. Since this addition had not been carried out previously with a free-radical initiator, but simply at elevated temperature, we set out to use ultraviolet light initiation at a controlled temperature of 17 ± 2°. However, a considerable quantity of polymeric by-product was obtained. On irradiation of a saturated ethereal solution of the pure *cis* monoadduct photolysis occurred. Very little of a *cis–trans* mixture of the starting material was recovered. The product, a viscous oil, may stem from photolytic rearrangement and subsequent polymerization.[5]

With the use of azobisisobutyronitrile (AIBN) at 60° as an initiator the formation of polymers was avoided, and *ca.* 60% of the monoadduct (42% *cis*, 58% *trans*) together with *ca.* 20% of a diadduct were obtained. Reactions without any catalyst or in the presence of a tertiary amine at ambient temperature afforded a similar ratio of mono- *vs.* diadduct. However, at least 95% of the monoadduct was of *cis* configuration. This stereospecificity is in agreement with earlier reported nucleophilic thiol additions to propiolic acid.[6] The stereochemistry of the monoadduct was readily deduced from its nmr spectrum (Table I).

TABLE I

SIGNIFICANT NMR PARAMETERS OF THIOLACETIC ACID–METHYL PROPIOLATE ADDUCTS AND THEIR CORRESPONDING DEUTERIO ADDUCTS

$CH_3COSCH{=}CHCO_2CH_3$ (β α) *cis* (and *trans*) — $(CH_3COS)_2CHCH_2CO_2CH_3$ (β α)

Proton	δ, ppm	$J_{\alpha-\beta}$, cps	Proton	δ, ppm	$J_{\alpha-\beta}$, cps
H_α	d 6.07 (6.01)	10 (16)	H_α	d 2.97	6
H_β	d 7.77 (8.00)	10 (16)	H_β	t 5.30	6
$H_\alpha(H_\beta = D)$	s 6.07		H_α (H_β = D)	s 2.97	

The larger coupling constant of the *trans* protons (*vs.* that of the *cis* protons) provides a simple determination of structure.[7,8] Nmr and glpc analysis supplied the *cis/trans* isomer ratio. The same diadduct was obtained under both free-radical and ionic reaction conditions. This diadduct had physical data (boiling point, n_D) in good agreement with those reported for the α,β diadduct.[1] However, a triplet at 5.3 and a doublet at 2.96 ppm in its nmr spectrum suggested rather the β,β-diadduct structure. Since no closely related nmr parameters were found in the literature, the β-deuterium-labeled diadduct was prepared.

(1) L. N. Owen and M. U. S. Sultanbawa, *J. Chem. Soc.*, 3109 (1949).
(2) B. Weibull, *Arkiv Kemi*, **3**, 225 (1951).
(3) A. T. Blomquist and J. Wolinsby, *J. Org. Chem.*, **23**, 551 (1958).
(4) J. A. Kampmeier and G. Chen, *ibid.*, **87**, 2608 (1965).
(5) A. Yogev, M. Gorodetsky, and Y. Mazur [*J. Am. Chem. Soc.*, **86**, 5208 (1964)] reported the photolytic rearrangement of isopropenyl acetate to acetyl acetone. A similar rearrangement, shown below, may have occurred.

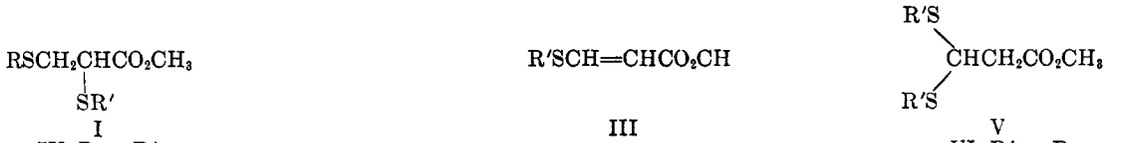
$$CH_3COSCH{=}CHCO_2CH_3 \longrightarrow \left[HSCH{=}C\begin{matrix}CO_2CH_3\\ \diagdown\\ \diagup\\ COCH_3\end{matrix}\right]^- \longrightarrow \text{polymer}$$

The nmr spectrum of the polymer shows a singlet at 1.98 ppm which is in the region for acetyl protons.

(6) W. E. Truce, D. L. Goldhamer, and R. B. Kruse, *ibid.*, **81**, 4931 (1959).
(7) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press Inc., New York, N. Y., 1959, pp 85–87.
(8) H. Hogeveen, G. Maccagani, and F. Taddei, *Rec. Trav. Chim.*, **83**, 937 (1964).

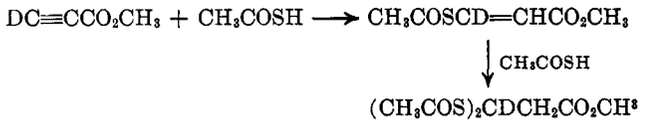
TABLE II

PRODUCT DISTRIBUTION FROM THE ADDITION OF THIOLS TO β-SUBSTITUTED THIOACRYLIC ACID METHYL ESTERS



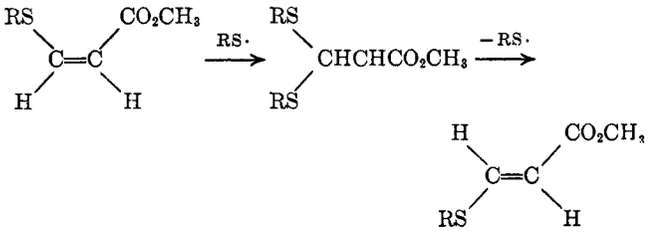
Reactants (equimolar)		Products, glpc area %						
RSCH=CHCO₂CH₃ R	Thiol R′	Starting acrylate	I	III	IV	V	VI	α/β[a]
CH_3CO-	CH_3-	0	39.5	25	10	1	24.5	1.1
CH_3-	C_2H_5-	25.8	52	6.2	6.1	0	9.9[b]	4.2
C_6H_5-	CH_3-	46	53	1	1	0		53

[a] Ratio of products derived from α attack over those from β attack. [b] Structure I, R′ = R.



The nmr parameters for the labeled compounds are summarized in Table I. Confirmation of the β,β-diadduct structure was obtained from the collapse of the doublet at 2.97 ppm for the α protons into a singlet and the disappearance of the triplet at 5.30 ppm for the β proton with the β-deuterio compound.

A free-radical mechanism for the diadduct formation could be ruled out by the lack of rate enhancement in the thiolacetic acid addition to the pure *cis* monoadduct in the presence of AIBN. In contrast to the parallel experiment without catalyst, the unreacted *cis* starting material had been partly isomerized to the *trans* compound. This isomerization may occur through the reversible formation of a diadduct radical.

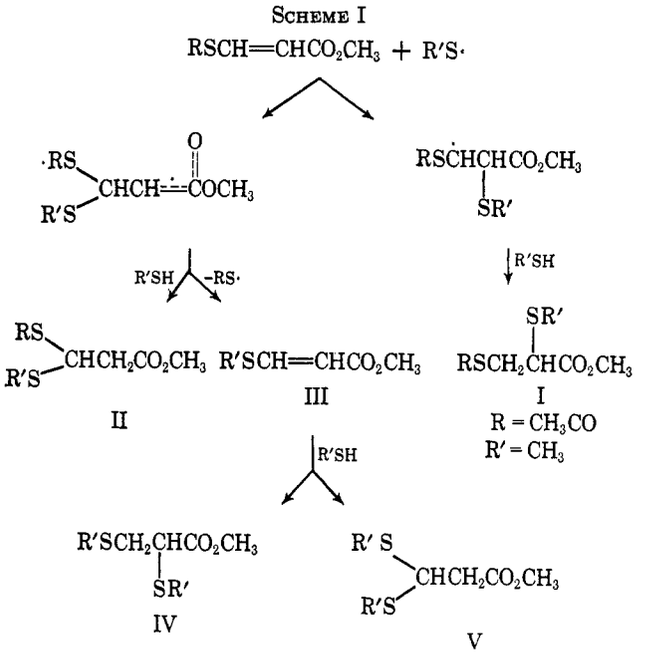


Complete reversibility of such an addition was observed in the reaction of methyl mercaptan with β-acetylthioacrylate as discussed below.

Free-Radical Additions.—The above results did not allow any conclusions as to the possible factors governing the course of free-radical thiol additions to the monoadducts. Therefore, β-acetylmercapto-, β-phenylmercapto-, and β-methylmercaptoacrylic acid methyl esters were selected as model substrates. Methyl or ethyl mercaptan was used in equimolar amounts as a free-radical addend. Their possible competitive ionic addition could be ruled out, since no reaction occurred in the dark. In order to avoid photolysis of the β-acetylmercaptoacrylate, AIBN was used as an initiator. With β-phenylmercaptoacrylate and β-methylmercaptoacrylate ultraviolet initiation was used since it did not cause undesired side reactions. Glpc analysis of the crude product mixtures served for the determination of the product distribution (Table II), and glpc retention time comparison of admixtures with independently synthesized and characterized mono- and diadducts was used for product identification. Some physical data and the methods used for the preparation of the starting substrates and reference adducts are summarized in Table III. Nmr parameters are given in Table IV.

β-Acetylmercaptoacrylic Acid Methyl Ester.—The addition of methyl mercaptan to β-acetylmercaptoacrylic acid methyl ester afforded five products (Table II). The formation of products I, III, IV, and V can be readily explained by the reactions in Scheme I. Elimination of the more stable radical from the β,β-disubstituted adduct radical may lead to a new olefinic substrate III which accounts in turn for the adducts IV and V. The thiolacetic acid generated during this reversal adds ionically to the starting acrylate to form the β,β adduct VI. The formation of VI can be largely suppressed by using an excess of methyl mercaptan in the reaction. From the product distribution, I:III + IV + V = 1.1 (α/β attack), it becomes apparent that the two possible adduct radicals lead to nearly equal amounts of product.

SCHEME I



β-Methylmercaptoacrylic Acid Methyl Ester.—The addition of ethyl mercaptan to β-methylmercaptoacrylate yielded essentially four products (Table II). Again the reactions in Scheme I account for compounds I, III, and IV. The complete absence of adduct II in this case, however, is surprising. Therefore, it appears that the reversibility of the β,β-adduct radical

TABLE III

THIOLMETHYL PROPIOLATE MONO- AND DIADDITIONS AND SOME PHYSICAL ANALYTICAL DATA OF THE PRODUCTS

RSCH=CHCO$_2$CH$_3$ (I) → RS–CHCH$_2$CO$_2$CH$_3$ (II) → RSCH$_2$CH(SR')CO$_2$CH$_3$ (III)

Starting materials											Elemental compn, %					
											Calcd			Found		
Unsaturate	Mercaptan	Mole ratio of unsaturate/mercaptan	General procedure	Reaction time, hr	Structure[a] (*trans*/*cis*)	R	R'	Summary formula	Yield, %	Bp, °C, uncor (mm)	C	H	S	C	H	S
HC≡CCO$_2$CH$_3$	CH$_3$SH	1:5	Ultraviolet	18	I (10:1)	CH$_3$		C$_5$H$_8$O$_2$S	34.5	35.5–38 (0.25)	45.45	6.06	24.24	45.73	6.12	24.20
					III	CH$_3$	CH$_3$	C$_6$H$_{12}$O$_2$S$_2$	15.5	64–65 (0.25)	40.00	6.67	35.56	40.35	6.73	35.51
CH$_3$SCH=CHCO$_2$CH$_3$	CH$_3$SH	1:7	Base	24	II	CH$_3$	CH$_3$	C$_6$H$_{12}$O$_2$S$_2$	54	63–64 (0.40)	40.00	6.67	35.56	40.35	6.59	35.60
HC≡CO$_2$CH$_3$	C$_2$H$_5$SH	1:1	Ultraviolet	47	I (4:1)	C$_2$H$_5$		C$_6$H$_{10}$O$_2$S	21	50–51 (0.15)	49.31	6.85	21.92	49.07	6.89	22.09
C$_2$H$_5$SCH=CHCO$_2$CH$_3$	C$_2$H$_5$SH	1:5	Ultraviolet	44	III	C$_2$H$_5$	C$_2$H$_5$	C$_8$H$_{16}$O$_2$S$_2$	25[c]	56–59 (0.03)	46.15	7.69	30.77	45.73	7.37	31.05
CH$_3$SCH=CHCO$_2$CH$_3$	C$_2$H$_5$SH	1:10	Ultraviolet	15	III	CH$_3$	C$_2$H$_5$	C$_7$H$_{14}$O$_2$S$_2$	53	69–70 (0.10)	43.30	7.22	33.00	42.97	7.46	32.52
		1:5	Base	24	II	CH$_3$	C$_2$H$_5$	C$_7$H$_{14}$O$_2$S$_2$	83[c]	57.5–59 (0.06)	43.30	7.22	33.00	43.21	7.26	33.28
HC≡CCO$_2$CH$_3$	C$_6$H$_5$SH	1:1	Ultraviolet	24	I (3:2)	C$_6$H$_5$		C$_{10}$H$_{10}$O$_2$S	44	158–161 (0.10)	61.85	5.15	16.49	61.46	5.17	17.00
C$_6$H$_5$SCH=CHCO$_2$CH$_3$	CH$_3$SH	1:1	Ultraviolet	65	III	C$_6$H$_5$	C$_2$H$_5$	C$_{11}$H$_{14}$O$_2$S$_2$	54	113–115 (0.07)	54.54	5.78	26.45	54.71	5.77	26.40
CH$_3$COSCH=CHCO$_2$CH$_3$	CH$_3$SH	1:5	*b*	14	III	CH$_3$COS	CH$_3$	C$_7$H$_{12}$O$_3$S$_2$	70[c]	69–73 (0.01)	40.38	5.77	30.77	40.40	5.79	30.88

[a] Based on semiquantitative nmr and glpc analysis. [b] Azobisisobutyronitrile as initiator.

is little influenced by the stability of the leaving radical. Based on earlier reported observations on free-radical additions to allylthio ethers,[9,10] a marked difference in the leaving ability of the resonance-stabilized acetylthiyl radical and the methylthiyl radical would have been anticipated. Adduct VI then results from addition of the expelled methylthiyl radical to the starting acrylate. The product ratio, I:III + IV = 4.2 (α/β attack), demonstrates the increased orienting effect of the β-methylmercapto substituent over that of the acetylthio group.

β-Phenylmercaptoacrylic Acid Methyl Ester.—The addition of methyl mercaptan to β-phenylmercaptoacrylate resulted essentially in α,β adduct I (Table II). If the methylthiyl radical attacks to a significant degree at the β carbon, the adduct radical formation would be expected to be highly reversible. Predominant expulsion of the phenylthiyl radical[9] should then lead to an adduct isomeric with I, which might

not be detectable by the analytical methods used. This possibility, however, could be excluded since phenyl mercaptan did not add (<2%) to β-methylmercaptoacrylate under the conditions in question. Apparently the adduct radical formation is extremely reversible which is in agreement with earlier reported observations.[9]

An examination of models of the β-substituted acrylates under consideration indicated steric hindrance by the β substituent of the incoming thiyl radical at the β position to be of the following order. Since this order

is not reflected in the orientation of adduct formation with the substrates examined above, significant steric effects may be ruled out.

Thus, from the observed ratio of α *vs.* β attack (Table II) it may be concluded that the withdrawing effect of the acyl group destabilizes the radical inter-

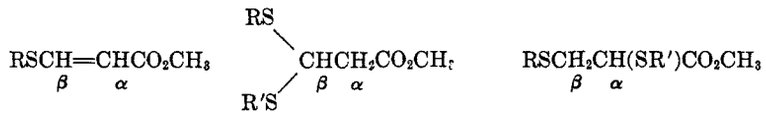
mediate, while the phenyl group confers an unexpectedly strong stabilization to the intermediate radical by resonance of the unpaired electron through the sulfur orbitals with the benzene π system (Scheme II).

(9) D. N. Hall, A. A. Oswald, and K. Griesbaum, *J. Org. Chem.*, **30**, 3929 (1965).

(10) E. S. Huyser and R. M. Kellogg, *ibid.*, **30**, 2867 (1965).

TABLE IV

NMR PARAMETERS OF THIOLMETHYL PROPIOLATE MONO- AND DIADDUCTS

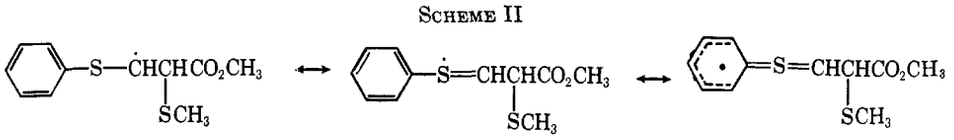


I II III

			Group chemical shift[a]											
			R					R'			Chemical shift			$J_{H\alpha-\beta}$
Structure	R	R'	C_6H_5	CH_3	CH_3	CH_2	CH_3COS	CH_3	CH_3	CH_2	CO_2CH_3	H_α	H_β	cps
I (*cis*)	CH_3			s 2.12							s 3.73	d 5.78	d 7.06	10.3
I (*trans*)	CH_3			s 2.35							s 3.68	d 5.62	d 7.71	15
I (*cis*)	C_2H_5				t 1.33[b]	q 2.82[b]					s 3.63	d 5.76	d 7.12	10.5
I (*trans*)	C_2H_5				t 1.33[b]	q 2.82[b]					s 3.63	d 5.68	d 7.67	15.3
I (*cis*)	C_6H_5		m ~7.3								s 3.68	d 5.88	*c*	10
I (*trans*)	C_6H_5		m ~7.3								s 3.60	d 5.67	d 7.74	15
II	CH_3	CH_3		s 2.10				s 2.10			s 3.68	d 2.72	t 4.09	7.5
II	CH_3	C_2H_5		s 2.08					t 1.25[b]	q 2.61[b]	s 3.66	d 2.70	t 4.14	7.5
III	CH_3	CH_3		s 2.14				s 2.14			s 3.43	dd 3.42	2.95[d]	9.2[f]
													2.66	5.8
III	C_2H_5	C_2H_5			t 1.23[b]	q 2.53[b]			t 1.23[b]	q 2.62	s 3.72	dd 3.39	2.98[d]	10.5[f]
													2.69	6.2
III	CH_3	C_2H_5		s 2.10					t 1.23[b]	q 2.66[b]	s 3.73	dd 3.43	2.97[d]	9.3[f]
													2.65	5.9
III	C_6H_5	CH_3	m ~7.25					s 2.06			s 3.64	m ~3.2[e]	m ~3.2[e]	
III	CH_3COS	CH_3					s 2.31	s 2.15			s 3.72	m ~3.2[e]	m ~3.2[e]	

[a] In parts per million downfield from tetramethylsilane as an internal standard using carbon tetrachloride as solvent. [b] $J_{CH_2CH_3}$ = 7.5 cps. [c] Signal coincides with phenyl protons. [d] ABX spin system, pair of overlapping quartets. [e] Multiplets for H_α and H_β coincide. [f] J_{gem} = 13.0 cps. Notation: s = singlet, d = doublet, dd = double doublet, t = triplet, q = quartet, m = mutliplet.

SCHEME II



Experimental Section

Methods of Analyses.—In general, the adduct mixtures were analyzed with an F & M Model 500 linear programmed gas chromatograph on a 3-ft column packed with 3% Dowfax 9N40 (an ethylene oxide–*p*-nonylphenol polyether of a 40:1 molar ratio) on 60–80 mesh Gas Chromosorb P. Operation conditions were as follows: detector, 250°; injector, 170°; flow rate, 60 cc/min; column heating rate, 5.6°/min; starting temperature, 50°; final temperature, 240°. The isomeric *cis–trans* monoadducts from thiolacetic acid were separated by capillary gc, using a temperature-programmed Barber–Coleman IDS, Model 20, chromatograph. The column of 200 ft, 0.02-in. i.d., was packed with 50% DCSSO (a phenylsilicone) and 50% XF-1105 (a nitrile silicone). Operating conditions were as follows: detector, 155°; injector, 160°; flow rate, 60 cc/min; column heating rate, 10°/min; starting temperature, 50°; final temperature, 150°.

A Varian A-60 proton spectrometer was used for the recording of the nmr spectra. All chemical shifts are measured in parts per million *vs.* tetramethylsilane as internal reference standard. The spectra were taken on 50% solutions in carbon tetrachloride.

Materials.—Methyl propiolate was obtained from the Farchan Laboratories and used as such. Thiolacetic acid and phenyl mercaptan from Matheson Coleman and Bell Co. were distilled prior to their use. The methyl and ethyl mercaptan, Eastman Organic Chemicals products of CP grade, were used without further purification.

Addition of Thiolacetic Acid to Methyl Propiolate. Without Catalysis.—A mixture of 2.1 g (0.025 mole) of methyl propiolate and 2.65 g (0.035 mole) of thiolacetic acid and 55 mg of hydroquinone was kept for *ca.* 48 hr at ambient temperature. White crystals formed on standing which were filtered off and recrystallized from methanol to give 2.63 g (66% yield) of *cis*-β-acetylthioacrylic acid methyl ester: mp 59–59.5° (lit. 58–58.5°). For nmr parameters, see Table I. *Anal.* Calcd for $C_6H_8O_3S$: C, 45.00; H, 5.00; S, 20.00. Found: C, 44.98; H, 4.83; S, 20.30. The filtrate afforded upon removal of the starting materials on a rotary evaporator 380 mg of a viscous oil. Semiquantitative nmr analysis of this residue indicated 68% of monoadduct in a *cis/trans* ratio of 3:1, and 32% β,β-diacetylthiopropionic acid methyl ester.

Base Catalysis.—To a solution of 3.8 g (0.05 mole) of thiolacetic acid, 56 mg (1 mole %) of triethylenediamine, and 60 mg (1 mole %) of hydroquinone in 50 ml of tetrahydrofuran (THF), 4.2 g (0.105 mole) of methyl propiolate was slowly added. The reaction mixture was kept under nitrogen and stirred for 15 hr at room temperature. Removal of the THF and unreacted starting material *in vacuo* afforded a semisolid. Crystallization and recrystallization of this residue from methanol yielded 5.36 g (67% yield) of *cis*-β-acetylthioacrylic acid methyl ester: mp 58.5–59°. Semiquantitative analysis of the combined mother liquors (1.83 g) showed small amounts of *cis* and *trans* monoadduct in admixture with β,β-diacetylthiopropionic acid methyl ester (*ca.* 15% yield).

With a 2 *M* excess of thiolacetic acid, 59% of the *cis* monoadduct and 36% of the diadduct, bp 108–111° (0.001 mm), $n^{22}D$ 1.5204 [lit.[1] bp 83–84° (0.001 mm), $n^{22}D$ 1.5201], was obtained. For nmr parameters, see Table I. *Anal.* Calcd for $C_8H_{12}O_4S$: C, 40.68; H, 5.08; S, 27.12. Found: C, 40.85; H, 5.04; S, 26.80.

AIBN Initiation.—A mixture of 2.1 g (0.025 mole) of methyl propiolate 1.9 g (0.025 mole) of thiolacetic acid, and 75 mg of azobisisobutyronitrile (AIBN) was heated at 55° for 12 hr in a magnetically stirred and sealed Pyrex tube. Upon work-up as described in the previous examples, 2.68 g (67%) of an isomeric monoadduct mixture, mp 41–52°, was obtained. Nmr and glpc analysis showed 42% *cis* and 58% *trans* adduct. In addition, 235 mg (4%) of β,β-diacetylthiopropionic acid methyl ester was isolated.

With an excess thiolacetic acid (1:1.5 molar reactant ratio) 20% of the diadduct was obtained, which was identical with that obtained during base-catalyzed additions.

Two parallel runs, one without AIBN otherwise under the same conditions as described above, showed similar rates and product distribution. The reaction progress was followed by nmr analysis.

β-Deuterio-β,β-diacetylthiopropionic Acid Methyl Ester.—β-Deuteriomethyl propiolate of 90% deuterium incorporation (nmr) was obtained by shaking a heterogeneous mixture of methyl propiolate and D_2O with a trace of sodium methoxide for 24 hr. Base-catalyzed addition of thiolacetic acid as described above afforded *cis*-β-deuterio-β-acetylthioacrylic acid methyl ester, mp 58.5–59.5, and β-deuterio-β,β-diacetylthiopropionic acid

methyl ester, bp 106–108° (0.001 mm), $n^{22}D$ 1.5198. Nmr analysis of both compounds showed *ca.* 90% deuterium incorporation; the nmr parameters are summarized in Table I. Deuterium exchange with thiolacetic acid prior to its addition can be excluded from the nmr spectrum of the monoadduct and the fact that identical diadducts were obtained from either thiolacetic acid addition to deuteriomethyl propiolate or to β-deuterio-β-acetylthioacrylic acid methyl ester.

AIBN-Initiated Addition of Methyl Mercaptan to β-Acetylthioacrylic Acid Methyl Ester.—Methyl mercaptan (4.8 g, 0.1 mole), β-acetylthioacrylic acid methyl ester (16.8 g, 0.1 mole), and 2 mole % of AIBN were heated in a sealed tube at 60° for 16 hr. The unreacted methyl mercaptan was released at ambient temperature, and the reaction mixture was analyzed by glpc. The product distribution is tabulated in Table II. All products were identified by glpc retention time comparison with authentic samples. β,β-Diacetylthiopropionic acid methyl ester was isolated by fractional distillation. The distillation residue contained a little polymeric material, presumably due to oligomer formation during the reaction.

All other adducts were synthesized by one of the following general procedures. The reactant ratios, reaction times, yield, and some of the purified products' physical and analytical data are summarized in Table III. Nmr parameters are recorded in Table IV.

Ultraviolet Initiation.—Unsaturate and mercaptan were sealed into a magnetically stirred quartz tube. The tube was irradiated with a 70-w high-pressure mercury arc Hanau immersion lamp in a temperature-controlled water bath at 17 ± 2°. The crude product mixture was sampled for nmr and glpc analysis. Pure products were obtained by fractional distillation *in vacuo*.

Base Catalysis.—Hydroquinone (1 mole %) as a free-radical inhibitor and 1–2 mole % of triethylene diamine were dissolved in the unsaturate and mercaptan. This reactant mixture was heated in a magnetically stirred and sealed Pyrex tube at 70°. Product analysis and purification was carried out as above.

Acknowledgment.—The author thanks Mr. W. C. Whitlock for excellent technical assistance.

Alicyclic Carbohydrates. XXX.[1a] Synthesis of the Remaining Cyclohexanetriols. Nuclear Magnetic Resonance Studies on the Nine Isomers[1b]

G. E. MCCASLAND,[2a] M. O. NAUMANN,[2b] AND LOIS J. DURHAM

Department of Chemistry and Institute of Chemical Biology, University of San Francisco, San Francisco, California 94117, and Department of Chemistry, Stanford University, Stanford, California 94305

Received April 1, 1966

The last remaining isomers of cyclohexanetriol, which have the 1,2,4 structure, have now been prepared. Nuclear magnetic resonance (nmr) spectroscopy has been used to establish configurations of the four diastereomers with this structure, and to confirm previously assigned configurations for the three 1,2,3 diastereomers and the two 1,3,5 diastereomers. The two 1,2,4 diastereomers of 1,2-*cis* configuration were prepared from 3-cyclohexen-1-ol benzoate by the "wet Prévost" reaction, also by reaction of the free cyclohexenol with silver chlorate–osmium tetroxide. The configurations of these triols of mp 161° (tri-*p*-toluenesulfonate 110°) and 138° (tri-*p*-toluenesulfonate 140°) were shown to be DL(1,2/4) and all-*cis*, respectively. From the reaction of 3-cyclohexen-1-ol benzoate with silver chlorate–osmium tetroxide in aqueous acetone, followed by benzoylation, there was surprisingly obtained *trans*-2,5-dihydroxycyclohexanone dibenzoate, mp 186°, instead of the expected triol tribenzoate. The two 1,2,4 diastereomers of 1,2-*trans* configuration were prepared by reaction of 3-cyclohexen-1-ol with peroxyformic acid, or of its benzoate with the (dry) Prévost reagent. The configurations of these triols of mp 138° (tribenzoate 116°) and 150° (tribenzoate 154°) were shown to be DL(1,4/2) and DL(2,4/1), respectively. From the Prévost reaction there was isolated a small amount of the intermediate 2-iodo-1,4-cyclohexanediol dibenzoate, mp 176°, having the configuration DL(2,4/1). The nmr spectra of the triols in deuterium oxide were recorded. Assignments of configuration and conformation were based on first approximation methods and on a study of the shielding–deshielding effects arising from anisotropy of the C–O bonds. The configurational assignments were consistent with chemical evidence.

The polyhydroxy cyclohexanes containing from one to six hydroxyl groups (*cyclitols* in the original sense[3]) are of unique interest as model compounds for studies in carbohydrate and stereochemistry, and because of their relationship to the biologically important[3] cyclitol, myoinositol. Previous work[4] in numerous laboratories has included extensive studies on cyclohexanol and the cyclohexanediols; isolation or synthesis of all ten diastereomeric pentols (quercitols);[4e] and synthesis of all eight diastereomeric hexols (inositols). We now report synthesis of the remaining members of the series of nine isomeric cyclohexanetriols.[5] All but two of the numerous isomeric cyclohexanetetrols[4e] are known, and syntheses of these last two isomers are in progress.[6]

In recent publications[1a] we have emphasized the application of nmr spectroscopy to cyclitols. We have now extended this approach to cyclohexanetriols synthesized in our own and other laboratories. Excellent nmr studies on certain derivatives of the 1,2,3-triols have previously been reported,[7] but, so far as we know, there have not been any previous nmr studies on the free 1,2,3-triols, or on any of the 1,2,4- or 1,3,5-triols or their simple derivatives.

For a triol or other trisubstituted cyclohexane, three structures are possible: 1,2,3 or vicinal (**1**), 1,3,5 or symmetric (**2**), and 1,2,4 or asymmetric (**3**). For the 1,2,3 structure there are predicted one DL and two *meso* diastereomers (**13**, **14**, **15**), all previously re-

(1) (a) For preceding paper, see G. E. McCasland, S. Furuta, and L. J. Durham, *J. Org. Chem.*, **31**, 1516 (1966). (b) Presented by G. E. M. at the 152nd National Meeting of the American Chemical Society, New York, N. Y., Sept 1966.

(2) (a) To whom any correspondence should be addressed at the University of San Francisco. (b) University of San Francisco; Fellow of the U. S. Public Health Service, 1965–1967.

(3) G. E. McCasland, *J. Am. Chem. Soc.*, **85**, 2189 (1963).

(4) For reviews of previous work on cyclohexanetriols, see (a) T. Posternak, "Cyclitols," Eng. transl., Holden-Day, Inc., San Francisco, Calif., 1965, pp 122–127; (b) H. D. Orloff, *Chem. Rev.*, **54**, 379 (1954); (c) E. H. Rodd, "Chemistry of Carbon Compounds," Vol. II-A, Elsevier Publishing Co., New York, N. Y., 1953, pp 165, 166. For reviews on other cyclitols, see also (d) S. J. Angyal and L. Anderson, *Advan. Carbohydrate Chem.*, **14**, 135 (1959); (e) G. E. McCasland, *ibid.*, **20**, 11 (1965).

(5) There are 14 cyclohexanetriol isomers if the two enantiomers of each racemic pair are separately counted.

(6) G. E. McCasland, unpublished results.

(7) R. U. Lemieux, R. K. Kullnig, and R. Y. Moir, *J. Am. Chem. Soc.*, **80**, 2237 (1958).