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ORGANIC SYNTHESIS AND INDUSTRIAL ORGANIC CHEMISTRY

Synthesis of Bicyclo[2.2.1]Hept-5-Enyl Methyl Esters of Haloacetic Acids

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Abstract—Synthesis of norbornenyl methyl esters of a number of haloacetic acids via [4+2] cycloaddition of cyclopentadiene to allyl esters of these acids was examined. The yield and isomer composition of the synthesized compounds were examined in relation to the reaction conditions, and the best conditions for their preparation were found.

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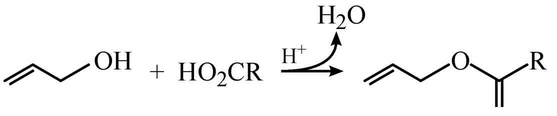
The structure of bicyclo[2.2.1]heptane, or norbornane, is a basis of many important natural compounds like borneal, camphor, etc. [1]. Similarly to norbornane and adamantane moieties, the norbornene moiety is a part of amines, many of which are medical preparations [2].

Significant interest in norbornene compounds also stems from their availability increased due to improvement of diene synthesis techniques. In most cases, this reaction does not involve side processes, which makes it possible to reveal factors governing the rate, direction, and equilibrium of the process with and without catalysts [3].

Halogenated functionally substituted norbornenes are good synthons for preparation of important intermediate halogenated sterically hindered phenols [4–8]. These compounds are also suitable as stanting materials for preparation of α-diketones and γ-lactones [9–12].

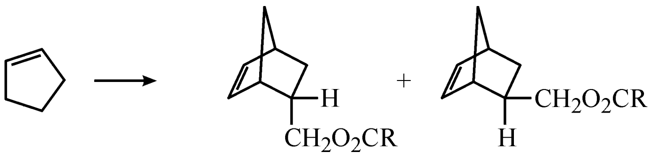
This study continues a series dedicated to synthesis of halogen-containing esters of norbornene compounds [13–16]. Here, we prepared bicyclo[2.2.1]-hept-5-enylmethyl esters of a number of haloacetic acids by the reaction of cyclopentadiene (CPD) with allyl esters of haloacetic acids **11–19**. The allyl esters **10–18** were synthesized by the well-known technique of esterification of corresponding acids **1–9** with allyl alcohol



R = CH_2Cl (**1**, **10**); $CHCl_2$ (**2**, **11**); CCl_3 (**3**, **12**); CH_2Br (**4**, **13**); $CHBr_2$ (**5**, **14**); CBr_3 (**6**, **15**); CF_3 (**7**, **16**); CH_3–CHCl (**8**, **17**); CH_2Cl–CH_2 (**9**, **18**).

Table 1 lists the physicochemical parameters of the starting allyl esters (**10–18**).

The target products (**19–27**) were prepared by [4+2] cycloaddition of CPD to allyl esters of haloacetic acids (**10–18**) by the scheme



R = CH_2Cl (**19**), $CHCl_2$ (**20**), CCl_3 (**21**), CH_2Br (**22**), $CHBr_2$ (**23**), CBr_3 (**24**), CF_3 (**25**), CH_3–CHCl (**26**), CH_2Cl–CH_2 (**27**).

The reaction was carried out at temperatures within 100–180°C in the course of 6–10 h at the diene-to-dienophile molar ratio of 1 : (1–4).

Table 1. Constants of allyl esters of haloacetic acids **10–18**

Compound	Ester	bp, °C (*P*, mm Hg)	n_D^{20}	d_D^{20}	Yield, %
10	Allyl monochloroacetate	43–44 (5)	1.4460	1.1469	85
11	Allyl dichloroacetate	63–64 (10)	1.4544	1.3496	70
12	Allyl trichloroacetate	68–69 (10)	1.4632	1.4648	75
13	Allyl monobromoacetate	73 (10)	1.4729	1.4329	65
14	Allyl dibromoacetate	66–67 (10)	1.4704	1.4500	60
15	Allyl tribromoacetate	80–82 (1)	1.5470	2.0061	45
16	Allyl trifluoroacetate	78–79	1.3364	1.1765	60
17	Allyl α-chloropropionate	81–82 (40)	1.4468	1.0868	75
18	Allyl β-chloropropionate	80–81 (40)	1.4385	1.0806	80

Table 2. Properties of bicyclo[2.2.1]hept-5-enyl methyl esters of haloacetic acids **19–27**

Compound	bp, °C (*P*, mm Hg)	n_D^{20}	d_D^{20}	Found, %			Formula	Calculated, %		
				C	H	halogen		C	H	halogen
19	91 (1)	1.4930	1.1723	59.67	6.24	17.43	$C_{10}H_{13}O_2Cl$	59.95	6.48	17.71
20	111 (2)	1.5004	1.2492	50.92	5.02	29.86	$C_{10}H_{12}O_2Cl_2$	51.06	5.11	30.21
21	107–108 (1)	1.5029	1.3243	44.14	3.88	39.08	$C_{10}H_{11}O_2Cl_3$	44.53	4.08	39.52
22	87–89 (1)	1.5077	1.3443	48.65	5.15	32.24	$C_{10}H_{13}O_2Br$	48.98	5.31	32.65
23	107–108 (2)	1.5105	1.5871	36.23	3.63	49.51	$C_{10}H_{12}O_2Br_2$	37.03	3.07	49.07
24	125–128 (3)	1.5531	1.8910	29.53	2.52	59.12	$C_{10}H_{11}O_2Br_3$	29.77	2.72	59.55
25	61–62 (10)	1.4205	1.2249	54.17	4.86	25.68	$C_{10}H_{11}O_2F_3$	54.55	5.10	25.91
26	90–91 (1)	1.4821	1.2575	61.05	6.52	14.26	$C_{11}H_{15}O_2Cl$	61.54	6.99	16.55
27	89–90 (1)	1.4852	1.2614	61.14	6.73	14.7	$C_{11}H_{15}O_2Cl$	61.54	6.99	16.55

Table 2 lists the physicochemical characteristics of the compounds synthesized.

The yield and isomer composition of adducts **19–27** were examined in relation to various reaction parameters (temperature, time, addend ratio). The results are presented in Table 3.

It is seen from Table 3 that, as the temperature increases from 100 to 160°C, the yield of adduct **19** grows from 7.4 to 56.65%. Further increase in temperature (to 180°C) causes a decrease in the yield. A possible reason is formation of a bis-adduct based on compound **19**.

The best conditions for formation of adduct **19** are as follows: temperature 140°C, reaction time 6 h, and diene : dienophile ratio 1:1.5. With increasing temperature, the *endo* selectivity of the reaction of synthesis of adduct **19** decreases from 85 to 61%, which can be associated with conversion of the *endo* isomer to a thermodynamically more advantageous *exo* isomer at a high temperature.

Under similar optimal conditions, we carried out diene condensation of CPD with other allyl esters of haloacetic acids. The yield of the adducts varied within 50.92–87.6%; the highest yield was observed for allyl tri-

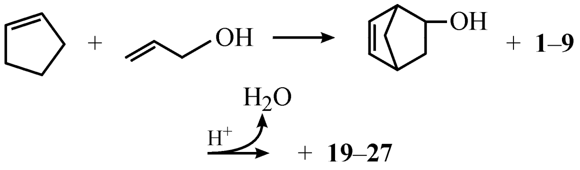
Table 3. Yield and isomer composition of esters **19–27** in relation to the conditions of the reactions of CPD with allyl esters of haloacetic acids **10–18**

Temperature	Dienophile	Diene : dienophile molar ratio	Time, h	Yield of **19–27**	Isomer ratio, %	
					endo	*exo*
100	**10**	1 : 1.5	6	7.14	95	5
120	**10**	1 : 1.5	6	19.17	85	15
140	**10**	1 : 1.5	6	55.35	79	21
160	**10**	1 : 1.5	6	56.65	71	29
180	**10**	1 : 1.5	6	52.21	61	39
140	**10**	1 : 1	6	51.41	80	20
	10	1 : 2	6	55.75	82	18
	10	1 : 3	6	56.11	81.5	18.5
	10	1 : 4	6	56.91	82	18
	10	1 : 1.5	6	55.89	78	22
	10	1 : 1.5	10	56.35	78	22
	11	1 : 1.5	6	50.92	83	17
	12	1 : 1.5	6	44.14	85	15
	13	1 : 1.5	6	48.55	83	16
	14	1 : 1.5	6	39.23	85	15
	15	1 : 1.5	6	29.67	87	13
	16	1 : 1.5	6	87.6	82	18
	17	1 : 1.5	6	61.05	78	22
	18	1 : 1.5	6	61.14	78	22

fluoroacetate **16** (87.6%), and the lowest, for allyl ester of tribromoacetic acid **15** (29.63%).

Comparative examination showed that the highest *endo* selectivity was observed in the reaction of CPD with allyl ester of tribromoacetic acid **15** (87%).

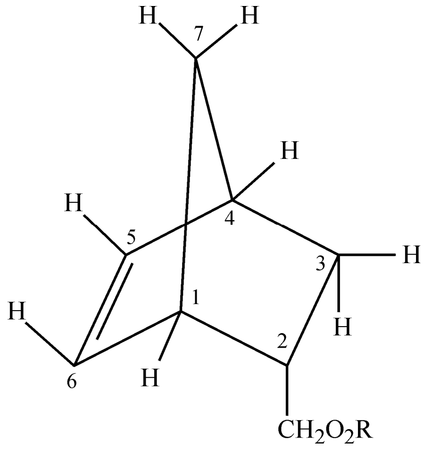
The composition and structure of the synthesized compounds **19–27** were proven by counter synthesis. First, by the technique described in [17] we carried out condensation of CPD with allyl alcohol into 2-hydroxymethylbicyclo[2.2.1]hept-5-ene **28** whose esterification with haloacetic acids by the well-known technique yielded the corresponding esters **19–27**:



All the physicochemical data obtained by both techniques for compounds **19–27** are identical.

The composition and structure of adducts **19–27** were confirmed by IR and ^{1}H NMR spectra. The IR spectra of the bicyclic esters synthesized contain characteristic signals of the C=O-group at 1730–1750 cm^{-1} and of the C–O ester group at 1000–1275 cm^{-1}. The bands of the carbon–chlorine bond are observed for chlorine-containing compounds in low-frequency spectral regions: 750, 760, 780, 760, and 770 cm^{-1} for compounds **19–21**, **7**, and **27**, respectively. The IR spectra of bromine-containing esters **22–24** contain intense bands associated with C–Br vibrations at 650–600 cm^{-1}. The ν_{C-F} band of ester **25** is observed near 1050 cm^{-1}. The absorption bands of the ethylene moiety in the norbornene ring lie at 1570–1555 and 3060–3045 cm^{-1} ($\nu_{C=C}$, ν_{C-H}).

The ^{1}H NMR spectra of esters **19–27** contain signals from protons of the double bond in the norbornene ring (H^5, H^6), manifested at 6–6.25 ppm as a multiplet, and are characterized by spin-spin coupling constants $J_{5,6}$ of 7.0 Hz. The H^3 (2H) protons give multiplet signals at high fields with a chemical shift δ of 0.7–1.2 ppm. The multiplet associated with the H^2 proton is observed at δ of 2.5 ppm and is characterized by the constant of spin-spin coupling with the H^3 proton, $J_{2,3}$ of 9.6 Hz. The H^1 and H^4 protons are chemically equivalent and give multiplet signals at δ of 2.70–2.85 ppm. The methylene protons H^8 (CH_2O group) give multiplet signals at δ of 4.15–3.95 ppm:



The isomer composition of esters **19–27** was determined by gas–liquid chromatography.

EXPERIMENTAL

The IR spectra were recorded on a UR-20 spectrophotometer at 4000–400 cm^{-1} for thin films or KBr pellets. The ^{1}H NMR spectra were measured on a BS-487B Tesla radiospectrometer (working frequency 80 MHz) for solutions in CCl_4, with HMDS as internal standard. The chromatographic analysis, as well as determination of the purity of the compounds synthesized, were carried out on an LKhM-8 MD chromatograph with a thermal-conductivity detector on a 300×0.3 cm column packed with 5% PEGS on Dinokhrom; carrier gas helium; flow rate 40 cm^3 min^{-1}; column temperature 155, and evaporator temperature 240°C.

The initial allyl esters of halogenated acetic acids **10–18** were obtained by a well-known technique via esterification in the presence of 5% H_2SO_4 as the catalyst. Upon completion of the reaction, the reaction mixture was washed with water, dried over $MgSO_4$, and distilled.

Bicyclo[2.2.1]hept-5-enyl methyl monochloroacetate 19. A mixture of 14.17 g (0.15 mole) of allyl monochloroacetate **10** and 6.6 g (0.1 mole) of freshly distilled CPD in the presence of hydroquinone was heated at 140°C for 6 h in a sealed ampule. Vacuum distillation yielded 12.69 g (55.25%) of adduct **19**, bp 95°C (1 mm Hg), n_D^{20} 1.4930, d_D^{20} 1.1723. IR spectrum, ν, cm^{-1}: 1735 (C=O), 1100 (C–O), 750 (C–Cl), 1755 (C=C). Elemental analysis:

Found, %: C 59.67; H 6.24; Cl 17.43.
Calculated, %: C 59.95; H 6.48; Cl 17.71.

2-Hydroxymethylbicyclo[2.2.1]hept-5-ene **28** was prepared by condensation of CPD with allyl alcohol by the technique described in [17]. A counter synthesis of esters **19–27** was carried out by esterficiation of bicyclic alcohol **28** with corresponding carboxylic acids **1–9** by the known technique. All the physicochemical characteristics of esters **19–27** prepared by counter synthesis are identical to the data of the same compounds obtained by condensation of CPD with esters **10–18**.

CONCLUSION

Norbornenyl methyl esters of a number of haloacetic acids were synthesized by [4+2] cycloaddition of cyclopentadiene to allyl esters of these acids. With increasing temperature, the total yield of the adducts tends to grow, and the stereoselectivity, to decrease. The best conditions for preparation of the compounds synthesized were found.

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