CHEMISTRY LETTERS, pp. 229-230, 1981. © The Chemical Society of Japan 1981

THE ALKOXYALKYLATION OF 1,6-DIMETHYL-5-METHYLENE-3,4-BENZO-2-OXA-BICYCLO[4.1.0]HEPT-3-ENE WITH ORTHOFORMATES OR ACETALS

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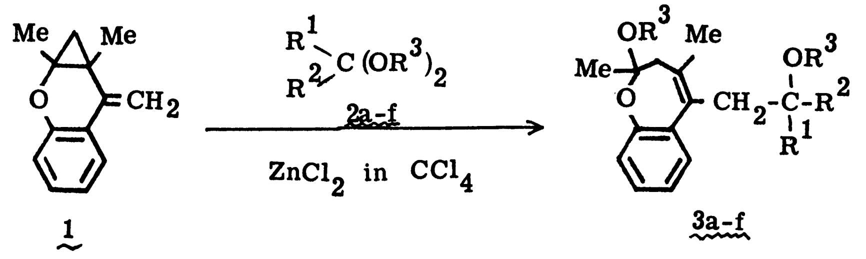
The reactions of the methylenehomochromene (titled compound) (**1**) with orthoformates (**2a,b**) or acetals (**2c-f**) easily took place in the presence of anhydrous zinc chloride to give 5-alkoxyethyl-2,3-dihydro-1-benzooxepin derivatives (**3a-f**) in moderate to good yields. Unusually high reactivity of **1** may be due to homoaromatic stabilization in the reaction intermediate.

Here we wish to report the reaction of 1,6-dimethyl-5-methylene-3,4-benzo-2-oxabicyclo-[4.1.0]hept-3-ene (methylenehomochromene) (**1**)$^{1)}$ with orthoformates (**2a,b**) or acetals (**2c-f**) catalyzed by anhydrous zinc chloride to form a new carbon-carbon single bond.

Treatment of **1** with ethyl orthoformate (**2a**) in carbon tetrachloride in the presence of anhydrous zinc chloride at room temperature for 4 h afforded 2,4-dimethyl-2-ethoxy-5-(2',2'-diethoxyethyl)-2,3-dihydro-1-benzooxepin (**3a**) in 54% isolated yield.$^{2,3)}$ The structural assignment of **3a** was based upon both elemental and spectroscopic analyses. Similarly, the reaction of **1** with methyl orthoformate (**2b**) or acetals (**2c-f**) gave the corresponding dihydrobenzooxepin derivatives (**3b** or **3c-f**), respectively. When **2c-e** were used, diastereoisomeric mixtures of **3c-e** were produced and each couple of isomers could be separated by the preparative TLC. Results are summarized in the Table.



	R^1	R^2	R^3
a :	H	OEt	Et
b :	H	OMe	Me
c :	H	Me	Et
d :	H	Ph	Me
e :	H	Cl-C_6H_4-	Me
f :	Me	Me	Me

In order to evaluate the relative reactivity of **1** to other related olefins, the reaction of **4a-c** with **2d** was carried out under the similar conditions as above. While the alkoxyalkylation of **1** was completed within 20 min, **4a-c** were recovered intact even after more than 48 h. Thus, the high reactivity of methylenehomochromene has been manifested in this alkoxyalkylation as well as previous reports.$^{1)}$ Such extremely high reactivity of **1** may be explained by the homoaromatic stabilization of the benzohomopyrylium ion in the reaction intermediate (**5**), and the significance of such stabilization as a driving force of the

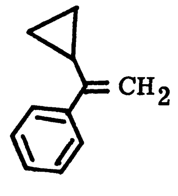
Table Reaction of Methylenehomochromene (**1**) with Orthoformates (**2a, b**) or Acetals (**2c-f**) in the Presence of $ZnCl_2$$^{a)}$ at Room Temperature$^{b)}$ and the PMR Data of the Alkoxyalkylated Products (**3a-f**)

2	Reaction	Product$^{c,d)}$		PMR Chemical Shifts (δ in ppm) in Carbon Tetrachloride				
R^1 R^2 R^3	Time$^{b)}$	(yield/%)		Allylic Methylene	Ring Methyl	R^1	R^2	R^3
H OEt Et	4 h	**3a**	(54)	2.03, 2.30;$^{g)}$ 2.70-2.92$^{i)}$	1.56, 2.03	4.27$^{j)}$	1.09, 1.14, 1.22, 3.14-4.10	
H OMe Me	1 h	**3b**	(72)$^{f)}$	2.04, 2.30;$^{g)}$ 2.70-2.93$^{i)}$	1.55, 2.04	4.20$^{k)}$	3.24, 3.30, 3.52	
H Me Et	20 min	**3c**$^{e)}$	(24)*	2.03, 2.33;$^{g)}$ 2.34-2.94$^{i)}$	1.58, 2.05	4.27$^{l)}$	1.08$^{q)}$	1.13, 1.25, 3.00-4.2
			(16)°	2.00, 2.30;$^{h)}$ 2.32-2.96$^{i)}$	1.57, 2.03	4.13$^{l)}$	1.00$^{r)}$	1.12, 1.23, 3.00-4.1
H Ph Me	20 min	**3d**$^{e)}$	(37)*	1.91, 2.22;$^{h)}$ 2.5-3.1$^{i)}$	1.53, 1.97	3.87$^{m)}$	6.6-7.3	3.07, 3.43
			(40)°	1.73, 2.12;$^{h)}$ 2.5-3.1$^{i)}$	1.19, 1.36	3.77$^{n)}$	6.7-7.4	3.08, 3.43
H ClC_6H_4 Me	75 min	**3e**$^{e)}$	(21)*	1.90, 2.22;$^{h)}$ 2.5-3.1$^{i)}$	1.52, 1.97	3.83$^{o)}$	6.6-7.2	3.07, 3.43
			(40)°	1.73, 2.10;$^{h)}$ 2.5-3.1$^{i)}$	1.12, 1.40	3.73$^{p)}$	6.7-7.4	3.07, 3.40
Me Me Me	30 h	**3f**	(28)	1.98, 2.27;$^{h)}$ 2.62, 2.85$^{h)}$	1.55, 2.03	0.78, 1.08		3.15, 3.50

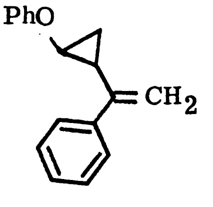
* More polar isomer by means of TLC. ° Less polar isomer by means of TLC. a) Molar ratio; **1**: **2**: $ZnCl_2$ = 1.0: 2.0-5.0: 1.0-5.0. b) Reaction was monitored by means of either PMR spectroscopy or TLC. Carbon tetrachloride was used as the solvent unless otherwise stated. c) Yields are based upon analytically pure samples which were obtained by TLC. In every entry **3** was obtained in good yields as the crude material. d) Mps of the products: **3a**, oil; **3b**, 63-63.5°C; **3c***, oil; **3c°**, oil; **3d***, 81-84°C; **3d°**, 89-90°C; **3e***, oil; **3e°**, 108-110°C; **3f**, 71-72°C. e) Production of a couple of diastereoisomers. f) In dichloromethane. g) 2H, ABq, J=13Hz. h) 2H, ABq, J=14Hz. i) 2H, m. j) 1H, dd, J=6.5, 5Hz. k) 1H, t like, J=5Hz. l) 1H, m. m) 1H, dd, J=8, 4Hz. n) 1H, dd, J=10, 4Hz. o) 1H, dd, J=8, 5Hz. p) 1H, dd, J=10, 5Hz. q) 3H, d, J=7Hz. r) 3H, d, J=6Hz.

reaction has also been demonstrated in solvolysis and cycloaddition.$^{1,4)}$

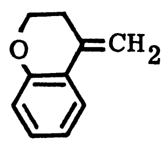
Although **1** lacks any hetero atoms adjacent to its olefin moiety, the reactivity of **1** toward **2** was found to be as high as ethyl vinyl ether in our preliminary experiments.$^{2)}$ Now, a new prototype of alkoxyalkylation is shown using an extraordinarily stabilized cationic intermediate in the whole molecule.



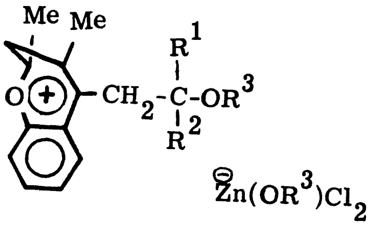
4a



4b



4c



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This work was partly supported by a Grant-in-Aid for Scientific Research (447022) from the Ministry of Education to which we are grateful.

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(Received November 25, 1980)