Chem. Phys. Lipids 3 (1969) 185–189 © North-Holland Publ. Co., Amsterdam

LETTER TO THE EDITORS

ALDOLS AND 2,3-DIALKYLACROLEINS DERIVED FROM LONG-CHAIN ALDEHYDES

Condensation or addition products of long-chain aldehydes have received little attention although they can be found in lipid extracts[1]) containing free fatty aldehydes[2]) or aldehydogenic compounds[3]). We have shown recently[4]) that the condensation of aldehydes to 2,3-dialkylacroleins can occur under physiological conditions and is catalyzed by ethanolamine phosphatides. Aldols were not encountered in this reaction.

Syntheses of aldols from long-chain aldehydes have not been described[5]). Basic ion-exchange resins have been applied[6]) to effect formation of aldols from short-chain aldehydes, but the elevated temperatures necessary to react higher homologues led to dehydration of the aldols to 2,3-dialkylacroleins.

In the present communication we report the preparation of aldols and 2,3-dialkylacroleins from long-chain saturated and unsaturated aldehydes. The reaction proceeds in the presence of aluminum chloride in pyridine and, when carried out at 0°C, leads to aldols in excellent yields, whereas under reflux conditions 2,3-dialkylacroleins are obtained almost exclusively. Aluminum chloride has not been used before as a catalyst for aldol condensations although such condensations were observed[7]) as side reactions of Friedel-Crafts acylations.

The aldols are stable in hexane solution and melt without decomposition. They give yellow 2,4-dinitrophenylhydrazones which are not altered during chromatography on silicic acid, but undergo complete dehydration upon heating. The infrared spectra of the aldols show strong bands at 2925 and 2850 cm^{-1} for methylene stretching absorption, and for methylene deformation near 1470 cm^{-1} (s). The O–H stretching vibrations occur at 3580 and 3400 cm^{-1} (m). The stretching vibrations of the C=O are found at 1720 cm^{-1} (s) and C–H stretching of the aldehyde function occurs at 2700 cm^{-1} (w). Additional absorption bands are those for the C–H deformation of the methyl groups at 1375 cm^{-1} (m) and the rocking mode of the long carbon chains at 718 cm^{-1} (m). The spectra of unsaturated aldols (*6*,*7*) also show the bands characteristic of carbon-carbon double bonds at 2985, 1650 and 695 cm^{-1} (sh). Isomerization of double bonds of *cis*-mono- and diunsaturated aldehydes during the addition reaction was found to be negligible, as only a very weak absorption band for *trans*-double bonds was found in the IR-spectra of the respective aldols. The NMR spectrum of the aldol (*4*) shows a doublet centered at δ 9.81 ppm for $-CHO$. Multiplets at δ 5.25 and δ 3.97 ppm accounting for a total of two protons can be assigned to the hydrogens at C-2 and C-3. A single peak at δ 1.28 ppm is due to the internal methylene groups, and an unsymmetrical triplet at δ 0.90 ppm to the terminal methyl groups.

The 2,3-dialkylacroleins are stable in hexane solution, melt without decomposition and give reproducible critical solution temperatures with nitromethane. They show an ultraviolet absorption maximum at 227 mμ and give orange 2,4-dinitrophenylhydrazones[4]) which melt without decomposition. The infrared spectra of 2,3-dialkylacroleins are characterized by absorption bands at 1690 (s) and 1640 cm^{-1} (m) and are identical to those described[4]). The spectra of the 2,3-dialkylacroleins (*6a*, *7a*) derived from unsaturated aldehydes show additional bands at 2985 cm^{-1} and 695 cm^{-1} (sh) characteristic of *cis* double bonds. Isomerization of double bonds of *cis*-mono- and diunsaturated aldehydes during the condensation reaction was found to be negligible. The NMR spectrum of 2-tetradecyl-octadec-2-enal (*4a*) shows a singlet at δ 9.40 ppm for the proton of $-CHO$ in conjugation with a $C{=}C$ double bond, a triplet centered at δ 6.46 ppm for the olefinic proton, a multiplet centered at δ 2.30 ppm for the methylene groups next to the double bond, and the singlet at δ 1.28 for internal methylene groups and triplet at δ 0.90 ppm (CH_3) for terminal methyl groups.

Other physical characteristics of the aldols and 2,3-dialkylacroleins are listed in Table 1.

Experimental

Melting points and critical solution temperatures[8]) were determined on a Kofler heating stage and are corrected. Infrared spectra were recorded with a Perkin-Elmer spectrophotometer, Model 21, from carbon disulfide and tetrachloroethylene solutions, and from liquid films. Ultraviolet spectra were recorded with a Beckman DK-2 spectrophotometer using diethyl ether as solvent. Nuclear magnetic resonance spectra were recorded with a Varian A-60A spectrometer using $CDCl_3$ as solvent; tetramethylsilane served as internal standard.

The course of reactions and the purity of the products were checked by thin-layer chromatography (TLC) on Silica Gel G. The plates were developed with hexane-diethyl ether (80: 20, v/v for aldols, and 95: 5, v/v for 2,3-

TABLE 1

Aldols and 2,3-Dialkylacroleins

Starting Material	No.	Product*	Formula	Yield** %	M.P., °C	CST, °C	DNPH*** M.P., °C
Decanal	1.	2-octyl-3-hydroxy-dodecanal	$C_{20}H_{40}O_2$	65	29–31		
	1a.	2-octyl-dodec-2-enal	$C_{20}H_{38}O$	64		66	82–82.5
Dodecanal	2.	2-decyl-3-hydroxy-tetradecanal	$C_{24}H_{48}O_2$	67	49–51		
	2a.	2-decyl-tetradec-2-enal	$C_{24}H_{46}O$	65	8.5–9	94.5	82.5–83
Tetradecanal	3.	2-dodecyl-3-hydroxy-hexadecanal	$C_{28}H_{56}O_2$	63	59–60		
	3a.	2-dodecyl-hexadec-2-enal	$C_{28}H_{54}O$	68	24.5–25	116.5	83–83.5
Hexadecanal	4.	2-tetradecyl-3-hydroxy-octadecanal	$C_{32}H_{64}O_2$	67	65–66		
	4a.	2-tetradecyl-octadec-2-enal	$C_{32}H_{62}O$	68	37.5–38.5	133	87–87.5
Octadecanal	5.	2-hexadecyl-3-hydroxy-eicosanal	$C_{36}H_{72}O_2$	66	69–71		
	5a.	2-hexadecyl-eicosa-2-enal	$C_{36}H_{70}O$	65	44.5–45.5	150	90–90.5
cis-9-Octadecenal	6.	2-hexadec-7′-enyl-3-hydroxy-eicosa-11-enal	$C_{36}H_{70}O_2$	65			
	6a.	2-hexadec-7′-enyl-eicosa-2,11-dienal	$C_{36}H_{68}O$	64		128	
cis,*cis*-9,12-Octadecadienal	7.	2-hexadeca-7′,10′-dienyl-3-hydroxy-eicosa-11,14-dienal	$C_{36}H_{68}O_2$	63			
	7a.	2-hexadeca-7′,10′-dienyl-2,11,14-trienal	$C_{36}H_{66}O$	67		106	

* Each compound gave satisfactory C, H and direct O analyses.

** After purification by TLC.

*** 2, 4-Dinitrophenylhydrazone.

dialkylacroleins) and toluene (for 2, 4-dinitrophenylhydrazones of aldols and 2,3-dialkyl-acroleins). Fractions were made visible by spraying the plates with a saturated solution of 2,4-dinitrophenylhydrazine in ethanol containing 10% sulfuric acid, or by spraying with chromic sulfuric acid and subsequent charring at 180°C. Reaction products were purified by chromatography on layers of Silica Gel H, 0.5 mm thick.

Aldehydes were prepared by oxidation of the corresponding alkyl methanesulfonates[9]) with dimethyl sulfoxide[10]).

A. *Preparation of Aldols*

The synthesis of *2-tetradecyl-3-hydroxy-octadecanal* (*4*) is described in detail. All other aldols (table 1) were prepared under the same conditions.

In a 100 ml three-necked flask equipped with inlet and outlet tubes for purified nitrogen, 1.6 g (12 mmoles) of aluminum chloride is suspended in 15 ml of absolute pyridine, and the suspension is chilled in an ice bath. An ice-cold solution of 0.48 g (2 mmoles) of *n*-hexadecanal in 15 ml pyridine is added at a temperature of 0–3°C, and the mixture is stirred for 45 min. Cold diethyl ether (150 ml) and 5 ml of air-free water are added to the almost colorless reaction mixture, and stirring is continued for 5 min. The layers are separated, and the aqueous phase is extracted with another 100 ml of diethyl ether. The combined ether phases are brought to dryness under reduced pressure. The residue is taken up in a small amount of benzene which subsequently is evaporated *in vacuo*, a process which is repeated until pyridine has been removed. The residue is dissolved in hexane, and purification by TLC yields 0.32 g (67%) of 2-tetradecyl-3-hydroxy-octadecanal.

$C_{32}H_{64}O_2$ (480.77)		C	H	O
	Calc.	79.94	13.41	6.65
	Found	79.62	13.41	6.75

B. *Preparation of 2,3-Dialkylacroleins*

The synthesis of *2-tetradecyl-octadec-2-enal* (*4a*) is described as an example. All other 2, 3-dialkylacroleins (table 1) were prepared under the same conditions.

In a 100 ml three-necked flask equipped with a reflux condenser and inlet and outlet tubes for purified nitrogen, 1.06 g (8 mmoles) of aluminum chloride is suspended in a solution of 0.48 g (2 mmoles) of *n*-hexadecanal in 30 ml of absolute pyridine, and the mixture is stirred for 30 min at 110°C. The buff-colored mixture is cooled, 150 ml of diethyl ether and 5 ml of air-free water are added, and stirring is continued for 5 min. The layers are separated, and the aqueous phase is re-extracted as described above. After removing the pyridine from the combined ether phases by repeated azeotropic evaporation with benzene, the residue is dissolved in hexane and the 2-tetradecyl-octadec-2-enal is purified by TLC yielding 0.30 g (68%).

$C_{32}H_{62}O$ (462.8)		C	H	O
	Calc.	83.04	13.50	3.45
	Found	83.09	13.46	2.96

Acknowledgment

This investigation was supported in part by PHS research grants CA 10155 and HE 08214 from the National Institutes of Health, Public Health Service, and by The Hormel Foundation.

University of Minnesota
The Hormel Institute
Austin, Minnesota 55912, U.S.A.

T. TAKAHASHI
H. H. O. SCHMID

References

1) H. H. O. Schmid, L. L. Jones and H. K. Mangold, J. Lipid Res. **8** (1967) 692
2) J. R. Gilbertson, W. J. Ferrell and R. A. Gelman, J. Lipid Res. **8** (1967) 38
3) M. M. Rapport and W. T. Norton, Ann. Rev. Biochem. **31** (1962) 103
4) H. H. O. Schmid and T. Takahashi, Z. Physiol. Chem. *in press*
5) A. T. Nielsen and W. J. Houlihan, Org. Reactions **16** (1968)
6) M. J. Astle and J. A. Zaslowsky, Ind. Eng. Chem. **44** (1952) 2867
7) N. O. Calloway and L. O. Green, J. Am. Chem. Soc. **59** (1937) 809
8) H. H. O. Schmid, H. K. Mangold and W. O. Lundberg, J. Am. Oil Chemists' Soc. **42** (1965) 372
9) W. J. Baumann and H. K. Mangold, J. Org. Chem. **29** (1964) 3055
10) V. Mahadevan, F. Phillips and W. O. Lundberg, Lipids **1** (1966) 183