Tetrahedron Letters No.33, pp. 3679-3682, 1968. Pergamon Press. Printed in Great Britain.

THE RATIO OF C- AND O-ISOMERS IN THE ETHYLATION OF ALKALI ENOLATES OF ETHYL ACETOACETATE IN HEXAMETHYLPHOSPHORAMIDE AND DIMETHYL SULFOXIDE

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(Received in UK 26 March 1968; accepted for publication 22 May 1968)

A series of publications has appeared recently which point out the formation of significant quantities of O-isomer in the alkylation of the alkali enolates of β-ketoesters and β-diketones /1-4/.

However, in the above referred works /2, 3/, the reactions were carried out with the use of carbonates or tert-butylates of alkali metals as bases. As a result, in the reaction mixtures there was always a certain amount of water or alcohol.

It seemed worthwhile to us to carry out the ethylation reaction in the absence of hydroxylic compounds, since it is well known that the latter bring about the screening of the oxygen center due to selective solvation /5, 6/.

The reactions were carried out in a dry argon atmosphere. The products were identified by means of thin-layer chromatography (Al_2O_3 IV; hexane-ethyl acetate 13:1).

Quantitative analysis of the mixtures was carried out by GLPC using a flame-ionisation detector chromatograph. The length of the column was 2 m; the diameter 4 mm; the stationary phase was polysiloxane (1%) placed on NaCl (0.15 - 0.25 mm). The column temperature was 120°C with nitrogen carrier gas flow rate at 70 ml per min.

Samples of C-ethyl compound /7/ and ethyl α,α-diethylacetoacetate /8/ were obtained by standard methods; ethyl β-ethoxycrotonate obtained in experiment N° 1 (TABLE 2) was freed of impurities of C-isomer and ethyl α,α-diethylacetoacetate by means of preparative chromatography (Al_2O_3 IV; hexane-ethyl acetate 13:1). The IR-spectrum shows two strong bands at 1632 cm^{-1} and 1718 cm^{-1}.

The results obtained are presented in tables 1, 2 and 3.

In all cases, the yields in per cents were calculated for the ethyl acetoacetate entering in the reaction.

Practically, complete alkylation was achieved in the experiments with $(EtO)_2SO_2$ and EtI.

TABLE 1*

Ethylation of Li-, Na- and Cs-ethyl acetoacetate in HMPA, C=1 mol/l, t=20°C

N°	Metal derivatives	Alkylation agent	Time (hrs.)	% O-isomer	% C-isomer	% ethyl α,α-diethylacetoacetate
1	Li	$(EtO)_2SO_2$	214	62	31	7
2	Li	Et_3OBF_4	20	37	61	2
3	Na	$(EtO)_2SO_2$	23	69	24	7
4	Na	Et_3OBF_4	40	61	35	4
5	Na	EtCl	138	60	28	12
6	Na	EtBr	22	38	52	10
7	Na	EtI	24	17	71	12
8	Cs	$(EtO)_2SO_2$	4	81	19	<1

TABLE 2**

Ethylation of K-ethyl acetoacetate by $(EtO)_2SO_2$, t=20°C

N°	Metal derivatives	Solvent	Concentration (mol/l)	Time (hrs.)	% O-isomer	% C-isomer	% ethyl α,α-diethylacetoacetate
1	K	HMPA	1	23	83	15	2
2	K (in presence of equimolar amount of t-BuOH)	"	1	23	60	36	4
3	K (in presence of equimolar amount of H_2O)	"	1	120	71	24	5
4	K	"	0.1	120	86	14	<1
5	K + Bu_4NClO_4 (1:1)	"	0.1	50	91	9	<1
6	K	DMSO	1	74	69	24	7
7	K	"	0.2	120	74	18	8

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* Li-, Na-enolates were obtained in the reaction of LiH and NaH with ethyl acetoacetate, respectively. Cs-derivative was obtained in the reaction of Cs_2CO_3 with ethyl acetoacetate at 95°C.

** For tables 2 and 3: K-ethyl acetoacetate was obtained from ethyl acetoacetate and tert-BuOK in ether with subsequent extraction and drying at 70°C / 1 mm Hg during 24 hours.

TABLE 3

Ethylation of K-ethyl acetoacetate, t=20°C

N°	Metal derivatives	Alkylation agent	Solvent	Concentration (mol/1)	Time (hrs)	% O-isomer	% C-isomer	% ethyl α,α-diethylacetoacetate
1	K	Et_3OBF_4	HMPA	1	98	71	18	11
2	K (t+70°C)	"	"	1	1	77	21	2
3	K	"	HMPA-CH_2Cl_2 (1:1)	2	53	82	18	<1
4	K (t-10°C)	"	"	2	19	65	31	4
5	K	"	HMPA-CH_2Cl_2 (2:1)	1	16	69	27	4
6	K+Et_4NClO_4 (1:1)	"	HMPA-CH_2Cl_2 (4:1)	0.5	16	75	23	2
7	K	EtCl	HMPA	1	115	60	32	8
8	K	EtBr	"	1	54	39	38	23
9	K	EtI	"	1	120	13	71	16
10	K	Et_3OBF_4	DMSO	1	72	67	28	5
11	K	"	"	0.2	120	65	30	5

The yields of O-isomer increase with electronegativity of X in the series $RI < RBr < RCl < (RO)_2SO_2$. The apparent exception is that of Et_3OBF_4. On the basis of data concerning the ratio of isomers, in the experiments in binary mixtures of HMPA-CH_2Cl_2, it is obvious that the alkylating agent is a complex of Et_3OBF_4 with HMPA, whose electrophility is less than that of $(EtO)_2SO_2$.

The yields of the O-isomer increase in the series $Li < Na < K < Cs < NR_4$ in correspondence with the increase of the ionic character of the bond.

The greatest yield of the product of O-ethylation (91%) was obtained for the reaction of K-ethyl acetoacetate with $(EtO)_2SO_2$ in HMPA, in which an equimolar amount of Bu_4NClO_4 is present.

From data in Table 2 it is seen that even equimolecular additions of protonic solvents diminish appreciably the yield of ethyl β-ethoxycrotonate.

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