

ETHYL FORMATE ANION - A NEW CARBANION

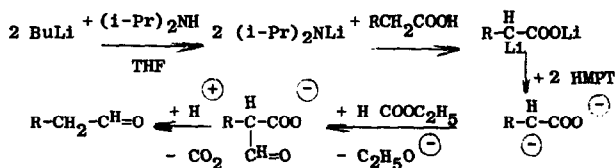
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During studies on the synthesis of  $^{14}\text{C}$ -labelled aldehydes by reaction of 2-lithio carboxylic acids with  $\text{H}^{14}\text{COOC}_2\text{H}_5$  according to Pfeffer and Silbert<sup>1</sup> a remarkable barrier to yield improvement was observed.

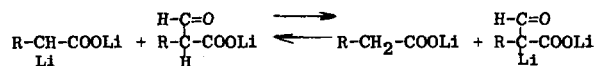
In this reaction the dianion of a carboxylic acid is formed by reaction with the Li-derivative of diisopropylamine,  $(i\text{-Pr})_2\text{NLi}$ , in anhydrous tetrahydrofuran (THF), containing equivalent amounts of hexamethylphosphorous triamide (HMPT). In our studies ethyl formate was added at  $-70^\circ\text{C}$ , the reaction was completed at the desired temperature and the aldehyde was obtained by acidification and decarboxylation with 10% aqueous HCl at  $-40^\circ\text{C}$ . In some experiments decomposition of excess Li-compounds was achieved with  $^3\text{H}_2\text{O}$ -10% HCl and acidification was completed with inactive HCl. The composition of the reaction product was determined by GLC (10% PEGA on Chromosorb W at  $150^\circ\text{--}200^\circ\text{C}$ ), using methyl nonanoate as the internal standard.



Under the conditions used by Pfeffer and Silbert overall yields vary from 65% for heptanal to 30% for oleoylaldehyde, with decreasing values with increasing chain length of the aldehydes. Since these yields are not attractive for the preparation of labelled compounds on a mmole scale, the formation of other products and the influence of different reaction conditions were studied.

The observation of Pfeffer and Silbert, that the only other detectable component is the starting acid, was confirmed. Their suggestion that the yield of aldehyde is

lowered by the contribution of an exchange reaction



is contradictory to the finding that excess of Li-compound does not increase the yield of aldehyde<sup>1</sup>. This is confirmed by the data in Table 1. By using <sup>14</sup>C-formate it was shown that <sup>14</sup>C was incorporated into the aldehyde, but that no labelled acid was formed, which means that the low yields of aldehyde are not due to oxidation to acid during recovery.

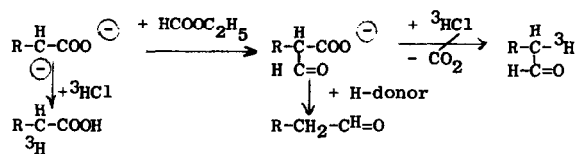
A possible explanation may be that the formation of  $\alpha$ -anions of the acid is already quantitative with equivalent amounts of Li-reagent, when only equivalent amounts of HMPT are also present in the medium. This is in agreement with the almost quantitative formation of alkylation products with alkyl bromides<sup>2</sup>.

Table 1

The influence of Li-reagent on the yield of nonanal from equivalent amounts of nonanoic acid and ethyl formate (23 mmole); temperature of the reaction with ethyl formate 0-10°C; decomposition with 1 ml 10% aq. <sup>3</sup>HCl at -40°C, followed by further acidification with non-labelled HCl

Equivalent amounts			Nonanoic acid	Yield nonanal (%)	Unconverted nonanoic acid (%)	% Incorporation of <sup>3</sup> H
BuLi	(i-Pr) <sub>2</sub> NH	HMPT				
2	2	2	1	56-65	27-28	0.4
4	4	4	1	41-46	44-49	35-40
4	4	6	1	44	31	21
4	4	2	1	20	50	28

Another indication that the formation of  $\alpha$ -anions is probably not the critical factor in the reaction, was obtained by decomposition of the reaction product with tritiated HCl. Whereas almost no <sup>3</sup>H is found in the organic layer when equivalent amounts of reactants are used, a considerable residual activity is present when an excess of Li-compounds is applied. It was shown by radio-GLC that this activity is present in the unconverted acid. This also shows that decarboxylation of the reaction product occurs already at 0°C in the reaction medium before addition of HCl, and that no  $\alpha$ -anion of the acid is left after reaction with an equivalent amount of ethyl formate:



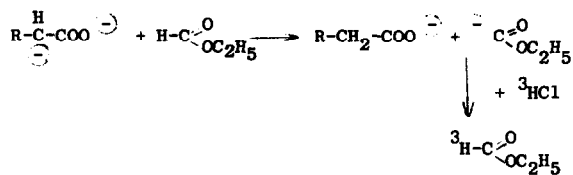
From Table 2 it is seen that an increase in the amount of ethyl formate only slightly improves the yield of aldehyde. Better results are obtained by raising the temperature of the reaction with formate from  $-40^\circ\text{C}$  to  $0-10^\circ\text{C}$ . Under these conditions no influence of chain length was observed anymore; from oleic acid 72% oleoylaldehyde was obtained.

Table 2

The influence of temperature and excess of formate on the efficiency of the reaction of ethyl formate with 2-lithio-carboxylic acid (1 equivalent of nonanoic acid is treated with 2 eq. BuLi, 2 eq. (i-Pr)<sub>2</sub>NH and 2 eq. HMPT)

Temp. of reaction (°C)	Equivalent amounts		Unconverted nonanoic acid (%)	Yield nonanal (%)	Yield nonanal with respect to ethyl formate (%)	% Incorporation of <sup>3</sup> H
	Nonanoic acid	Ethyl formate				
-40	1	2	36-46	50-51	25	
	1	3	29	57	19	
-20	1	2	35	61	30	
0	1	2	25	70	35	
	1	1	27-28	56-65	60	0.4
	1	0.6		44	73	21

All data point to a side reaction by which  $\alpha$ -lithio acid and ethyl formate are consumed simultaneously. Apparently this reaction is less favoured by an increase in temperature than is the formation of aldehyde. Moreover, this side reaction must be due to a characteristic feature of ethyl formate, since it is absent in the alkylation with alkyl bromides. Participation of the alcohol group in the reaction of esters with Li-reagent has never been observed<sup>3,4</sup> and the side reaction was also found to be absent in the reaction with diethyl carbonate instead of ethyl formate. The only possible reaction, which can explain the anomalous behaviour is the removal of the hydrogen atom of the formic acid moiety:



To check this supposition the reaction mixture was treated at 0°C with an equivalent amount of  $^3\text{HCl}$ , followed by fractionation of the solution. By radio-GLC (20% Carbowax on Chromosorb W at 55°C) labelled ethyl formate was shown to be present in the distillate with the expected specific activity. This means that the hitherto unknown formate anion is actually formed during the reaction. Its formation may be favoured by resonance stabilization. Excess of Li-compounds favours both the formation of ethyl formate anion and the conversion into aldehyde. Excess of formate increases the yield of aldehyde to some extent, but simultaneously depletes the  $\alpha$ -anion of the acid.

#### REFERENCES

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