Reactions of Salts of Aromatic Carboxylic Acids in an Atmosphere of $^{14}CO_2$ and Preparation of Some of these Acids Labelled with ^{14}C*

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SUMMARY

   The transcarboxylation reaction mechanisms of aromatic carboxylic acid salts in an atmosphere of $^{14}CO_2$ was studied. 2,6-Naphthalenedicarboxylic, 2,5-pyridine-dicarboxylic and 2,5-furanedicarboxylic acids, labelled with ^{14}C in the carboxylic groups were prepared.

INTRODUCTION

   Our earlier studies on the mechanism of transcarboxylation reactions of salts of benzenecarboxylic acids, performed in an atmosphere of $^{14}CO_2$, showed that the ^{14}C isotope is incorporated into carboxylic groups. This finding served as one argument in favour of an intermolecular course of these transcarboxylations. The amount of ^{14}C incorporated into the carboxylic groups reached equilibration values, so that the method can be used for preparation.

   Based on the incorporation of ^{14}C into molecules of carboxylic acids, and on the composition of the reaction mixtures in relation to the time course of the reaction, we have proposed a general scheme for transcarboxylation reactions of benzenecarboxylic acids (A, B) [1,2]. It was further shown that the reaction has an ionic character, consisting of multiple repeating cycles of several fundamentally simple decarboxylation and recarboxylation reactions (e.g. C-E). Potassium terephthalate, as the most stable reaction component, separates on in crystalline form from the mixture [1,3].

A

B

C

D*

E*
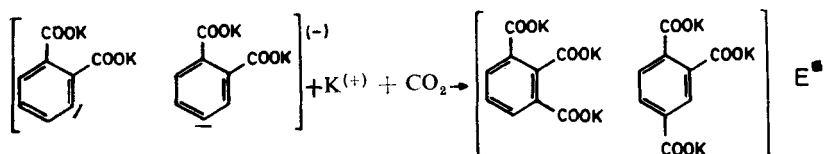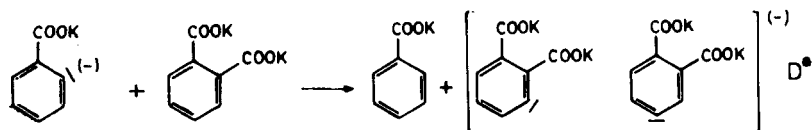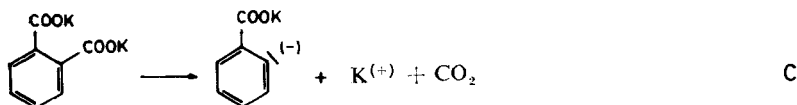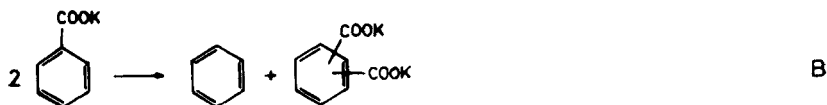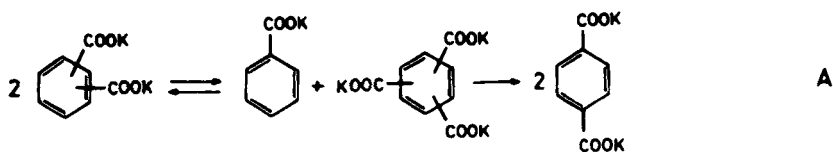
In the present paper we wish to show that the incorporation reaction is not limited to salts of benzenecarboxylic acids. It proceeds in the same manner with other aromatic carboxylic acids. It was possible to prepare terephthalic acid-^{14}C as well as ^{14}C-labelled 2,6-naphthalenedicarboxylic, 2,5-pyridine-dicarboxylic and 2,5-furandicarboxylic acids. It can be seen from Tables I and II that for preparation purposes the incorporated amount of ^{14}C in the carboxylic groups depends on : 1) the molar ratio of $^{14}CO_2$ to carboxylate in salts of aromatic carboxylic acids and 2) the contact area between the solid salts of the acids and gaseous $^{14}CO_2$.

RESULTS AND DISCUSSION.

The mecanism of incorporation in the above mentioned acids is the same as with benzenecarboxylic acids [4]. Thus with naphthalenecarboxylic acids,

* D and E is included in every equation. The bracket stands for the equivalent and the formulae in brackets are position isomers formed in a mixture during the reaction.

TABLE I. Transcarboxylation Reactions of Salts of Naphthalenecarboxylic Acids in an Atmosphere of $^{14}CO_2$.

Expt. No.	Starting Compounds[a]	Reaction Temperature °C	Reaction Time min.	Products	Yield of Acid %	Radio-activity of Acid[b] %
1	2 α-Naph.K	400	15	2,6-Naph.H$_2$ + Naph.	75	65
2	2 β-Naph.K	400	15	2,6-Naph.H$_2$ + Naph.	76	65
3	2 α-Naph.K	400	15	2,6-Naph.H$_2$ + Naph.	79	96 (4.0)
4	2 β-Naph.K	400	15	2,6-Naph.H$_2$ + Naph.	75	95.5 (3.9)
5	1,8-Naph.K$_2$	420	20	2,6-Naph.H$_2$	60	67
6	2,3-Naph.K$_2$	425	20	2,6-Naph.H$_2$	63	64.5
7	1,8-Naph.K$_2$	420	20	2,6-NaphH$_2$.	58	95 (4.1)
8	2,3-Naph.K$_2$	425	20	2,6-Naph.H$_2$	64	94 (4,2)
9	2 α-Naph.K	400	1	mixture of Naph.-acids + Naph.		65
10	2 α-Naph.K	400	5	2 α-Naph. H		0
11	2 β-Naph.K	400	1	mixture of Naph.-acids + Naph.		64
12	2 β-Naph.K	400	5	2 β-Naph.H		0
13	1,8-Naph.K$_2$	420	2	mixture of Naph.-acids		64
14	1,8-Naph.K$_2$	420	5	1,8-Naph.H$_2$		0
15	2,3-Naph.K$_2$	425	2	mixture of Naph.-acids		63,5
16	2,3-Naph.K$_2$	425	5	2,3-Naph.H$_2$		0

ABBREVIATIONS : α-Naph.K — potassium α-naphthoate; β-Naph.K — potassium β-naphthoate; 1,8-Naph.K$_2$ — potassium naphthalene-1,8-dicarboxylate; 2,3-Naph.K$_2$ potassium naphthalene-2,3-dicarboxylate; Naph.— naphthalene; α-Naph.H — α-naphthoic acid; β-Naph.H — β-naphthoic acid; 2,6-Naph.H$_2$ — naphthalene-2,6-dicarboxylic acid; mixture of Naph. acids — mixture of naphthalenecarboxylic acids.

[a] The starting salts of acids were used in molar amounts indicated in the corresponding column; the molar ratio of carboxylic groups of salts of acids to $^{14}CO_2$ in experiments 3, 4, 7 and 8 was 1 : 25; in all other experiments 2 : 1. Experiments 10, 12, 14 and 16 were carried out without a catalyst, for the others we used 10 % CdI$_2$ (per weight of acid salts).

[b] Specific radioactivity of acids per mmole in per cent of specific radioactivity of $^{14}CO_2$ (mmole) used for the reaction. The values in parentheses indicate the percentage of ^{14}C incorporated into the acid carboxyls with reference to the starting amount of $^{14}CO_2$.

incorporation of ^{14}C into the molecules from an atmosphere of labelled carbon dioxide takes place during the initial stages of the transcarboxylation reaction, when reaction intermediates are formed (Table I, experiments 9, 11, 13 and 15). However, if transcarboxylation does not take place (e.g. in the absence of catalysts or at low temperatures) or if it proceeds very slowly, ^{14}C is incor-

porated into the molecule of naphthalenecarboxylic acids either not at all or at a very low rate (Table I, experiments 10, 12, 14 and 16). The course of incorporation of ^{14}C into acid molecules is in agreement with the mechanism determined from the composition of the reaction mixtures, in relation to the time of the reaction. In the case of salts of naphthalenecarboxylic acids (cf. Raecke [5] and McNelis [6]), there was a disproportionation in the formation of a mixture of salts of naphthalenemono- and tricarboxylic acids as with benzenecarboxylic acids. This mixture undergoes a further transcarboxylation with the formation of salts of naphthalenedicarboxylic acids. The complex reaction mixture finally deposits the salt of 2,6-naphthalenedicarboxylic acid as the most stable component, as in the case of separation of terephthalate mentioned above (Scheme F). Transcarboxylations of potassium α- and β-naphthoates are accompanied by an irreversible disproportionation of the naphthoate to naphthalene and naphthalene dicarboxylates (Scheme G).
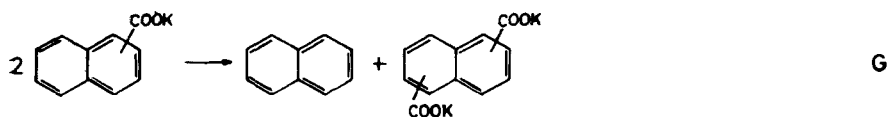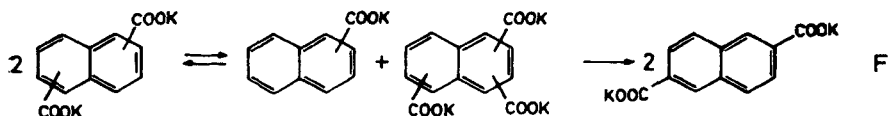

It can be seen from the nature of the naphthalene ring that the reaction mixture during transcarboxylations of salts of naphthalenecarboxylic acids is very complex. We could isolate from the reaction mixtures naphthoic acids, all the 10 possible isomeric naphthalenedicarboxylic acids and 6 of the 14 possible naphthalenetricarboxylic acids. The isolation of only 6 isomeric naphthalenetricarboxylic acids is due to the difficult separation of isomeric naphthalenetricarboxylic acids.

Our studies on the mechanism of transcarboxylation reactions of salts of benzenecarboxylic acids have shown that the course of formation of all bi- and tricarboxylic acids is analogous. Therefore, to understand the mechanism of transcarboxylation of salts of naphthalenecarboxylic acids it will suffice to estimate in the reaction mixture the starting acid plus the final 2,6-naphthalenedicarboxylic acid, and then the sum of all the other dicarboxylic, monocarboxylic and tricarboxylic acids [7]. However, it is necessary to choose a suitable starting acid (such as 1,8-isomer), which can be estimated in the reaction mixture as easily as the final product, e.g. 2,6-naphthalenedicarboxylic acid.

All the experimental data indicate that the transcarboxylation mechanism of salts of naphthalenecarboxylic acid is similar to that of salts of benzene-

carboxylic acids, i.e. decarboxylation for 1,8-naphthalenedicarboxylic acid :
e.g. Scheme H-K). These experimental results are also in agreement with
the conclusions of McNelis [6] on the ionic character of the transcarboxylation
reaction for naphthalenecarboxylic acids, except for his assumption of
reversibility of reaction G. This reaction is irreversible according to our
results, analogous to the reaction B of benzoate[10].
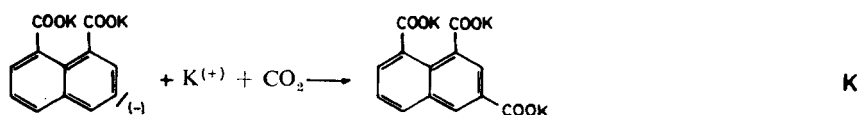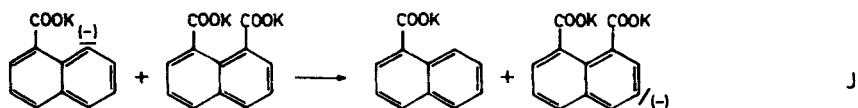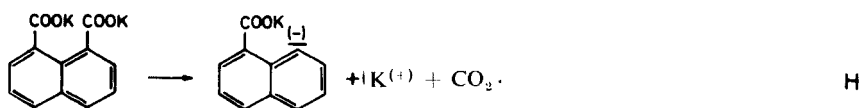
Similarly to benzenecarboxylic and naphthalenecarboxylic acids, ^{14}C
is incorporated from the $^{14}CO_2$ reaction atmosphere into carboxylic groups
of salts of heterocyclic, pyridinecarboxylic and furanecarboxylic acids (Table II).
It can be seen from experiments 12, 14 and 16 of Table II that incorporation
of ^{14}C into the molecules of these acids proceeds in the same manner as with
benzene- or naphthalenecarboxylic acids even in the initial stage of the reaction.
It can also be seen from Table II that if the salts of the acids are not trans-
carboxylated, no incorporation of ^{14}C takes place (experiments 11, 13 and 15).
The overall process of transcarboxylation of salts of pyridinecarboxylic acids
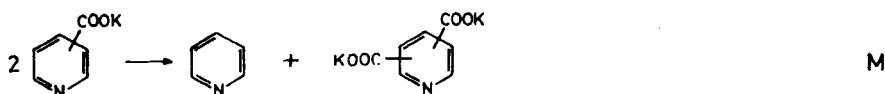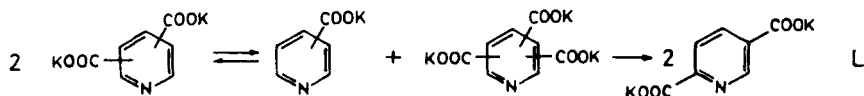is depicted in Schemes L and M.)

TABLE II. Transcarboxylation Reactions of Salts of Pyridine- and Furanecarboxylic Acids in an Atmosphere of $^{14}CO_2$.

Expt. No.	Starting Compounds[a]	Reaction Temperature °C	Reaction Time min.	Products	Yield of Acid %	Radioactivity of Acid[b] %
1	2 α-Pic.K	425	20	2,5-Pyr.H_2 + Pyr	46	65
2	2 α-Pic.K	425	20	2,5-Pyr.H_2 + Pyr	53	95 (4.1)
3	2 Nic.K	425	20	2,5-Pyr.H_2 + Pyr	50	65
4	2 Nic.K	425	20	2,5-Pyr.H_2 + Pyr	59	94 (4.0)
5	2 i-Nic.K	425	20	2,5-Pyr.H_2 + Pyr	47	65
6	2 i-Nic.K	425	20	2,5-Pyr.H_2 + Pyr	57	95 (4.1)
7	2,3-Pyr.K_2	430	25	2,5-Pyr.H_2	43	63
8	2,3-Pyr.K_2	430	25	2,5-Pyr.H_2	51	95,5(3.9)
9	2 α-Fur.K	420	20	2,5-Fur.H_2 + Fur	40	67
10	2 α-Fur.K	420	20	2,5-Fur.H_2 + Fur	59	94 (4.0)
11	2 α-Pic.K	420	5	2 α-Pic.H		0
12	2 α-Pic.K	425	1	Mixture of Pyr-acids + Pyr.		62
13	2 Nic.K	425	5	2 Nic.H		0
14	2 Nic.K	425	1	Mixture of Pyr-acids + Pyr.		63
15	2 α-Fur.K	420	5	2 α-Fur.H		0
16	2 α-Fur.K	420	1	Mixture of Fur-acids + Fur.		62

ABBREVIATIONS : α-Pic. K — potassium α-picolinate; Nic. K — potassium nicotinate; i-Nic. K — potassium isonicotinate; 2,3-Pyr. K_2 — potassium pyridine-2,3-dicarboxylate; α-Fur. K — potassium pyromucate; 2,5-Pyr. H_2 — pyridine-2,5-dicarboxylic acid; 2,5-Fur. H_2 — furane-2,5-dicarboxylic acid; α-Pic. H — α-picolinic acid; α-Fur. H — pyromucic acid; Fur. — furane; Pyr. — pyridine.

[a] The starting acid salts were used in molar amounts indicated in the appropriate column the molar ratio of carboxylic groups of acid salts to $^{14}CO_2$ in experiments 2, 4, 6, 8 and 10 was 1 : 25, in all other experiments it was 2 : 1. Experiments 11, 13 and 15 were conducted without catalysts, the other were done in the presence of 10 % CdI_2 (expressed per weight of acid).

[b] The same as in Table I.

For preparative purposes, such reactions are suitable only for such final products which are formed in high yield, and which are relatively easily isolated. Theoretically, incorporation of ^{14}C into carboxylate groups of aromatic carboxylic acids can be used as proof of an intermolecular mechanism of transcarboxylation reactions.

EXPERIMENTAL

Preparation of Samples.

Salts of aromatic carboxylic acids and the catalyst were placed in a thin layer on a carrier (sintered corundum SK 61/5, granulation 0.6-0.75 mm, porosity 32 %) [1]. The combination contained 7-9 % potassium salts of aromatic carboxylic acids and 0.15 % Cd salts of these acids (as catalyst) (expressed per weight of the carrier). The filling of the reaction ampoule with the corresponding volume of carbon dioxide, and determination of the gas activity, were carried out as reported previously [1,4], using an apparatus described by Tykva [8].

Reaction Technique.

The reactions were carried out in sealed glass ampoules in an electrically heated quartz tube. The content of the ampoule was thoroughly stirred by rotating the ampoule so that a vertical (pseudofluid) layer was formed. Thus, the acid salts on top of the carrier came into a sufficient contact with $^{14}CO_2$.

Treatment of the Reaction Mixture.

The radioactivity of the reaction atmosphere after reaction, and that incorporated into the carboxylic acids, was determined in an apparatus designed for filling internal gas counters [8] by previously described techniques employing a proportional counter [1,4]. To determine low radioactivity, we used a low-background arrangement [9]. All the determinations were referred to a standard with a standard deviation of the mean of less than $\pm$ 0.5 %. The specific radioactivity of the final product and of the reaction atmosphere after reaction is expressed both in Ci/mmole and in per cent of specific activity of $^{14}CO_2$ used for the reaction (to express more clearly the degree of equilibration).

2,6-Naphthalenedicarboxylic Acid-^{14}C.

The reaction mixture containing potassium α-naphthoate (1 mmole) and the CdI$_2$ catalyst (10 % of salt weight) was placed on the surface of a support and heated to 400 °C for 15 min in an atmosphere of $^{14}CO_2$ (0.5 mmole, specific radioactivity 87.8 nCi/mmole i.e. total activity 43.9 nCi) in a glass ampoule. After heating, the ampoule had one end extended into a sealed capillary and a loop. The reaction mass consisted of three components : solid salts of acids on the carrier surface, naphthalene which distilled and solidified in the capillary and gaseous $^{14}CO_2$. This was first gently heated to release napthalene from the capillary. Naphthalene flowed down and distilled into the ampoule, thus opening the capillary. The ampoule was then attached to the measuring unit, opened by breaking and the radioactivity of the reaction mixture was determined (13.8 nCi; I). The reaction material was extracted

with ether and the extracts evaporated to yield naphthalene. The salts were then extracted from the carrier with water in such an amount as to produce a 2-3 % solution, which was filtered while hot to remove impurities and the catalyst. The clear solution was acidified while hot with perchloric acid, and the radioactivity of the $^{14}CO_2$ released from potassium carbonate was determined as 0.7 nCi (II). The precipitated 2,6-naphthalenedicarboxylic acid was filtered while hot, washed with hot water, dried to constant weight (81 mg. i.e. 75 %) and the radioactivity measured (21.4 nCi; III). The naphthalenecarboxylic acids dissolved in the filtrate were isolated after alkalinisation, concentration and reacidification of the filtrate, by extraction with ether. After removing the ether by evaporation (28 mg) the radioactivity was determined as 7.0 nCi (IV). The sum of activities I-IV of the individual components of the reaction mixture was 42.9 nCi, i.e. 98 % of the radioactivity of $^{14}CO_2$ used for the reaction. The radioactivity of impurities filtered from the solution after dissolving the reaction mixture was negligible. The purity of the 2,6-naphthalenedicarboxylic acid was determined both by analysis per se during radioactivity determination, and analysis of the dimethyl ester (prepared with diazomethane) with a melting point at 191-192° C.

It can be seen from the results that the specific radioactivity of 2,6-naphthalenedicarboxylic acid was 57 nCi/mmole i.e. 65 % of the specific radioactivity of $^{14}CO_2$ used for the reaction. The specific radioactivity of the reaction atmosphere after the reaction was 27.6 nCi/mmole, i.e. 31 % of the initial activity.

2,5-Pyridinecarboxylic Acid-^{14}C.

The reaction mixture containing potassium nicotinate (1 mmole) and CdI_2 catalyst (10 % of the salt weight) was placed on the carrier in an atmosphere of $^{14}CO_2$ (0.5 mmole, specific activity 960 nCi/mmole) and processed in the same manner as with potassium α-naphthoate, except that a higher concentration of salts (about 10 %) was used. The amount of $^{14}CO_2$ incorporated into 2,5-pyridinedicarboxylic acid (40 mg, i.e. 50 %) corresponded to complete equilibration between $^{14}CO_2$ and the carboxylic groups of the acid : the $^{14}CO_2$ still contained 307 nCi/mmole (32%) and the acid after incorporation 623 nCi/mmole (65 %). The acid was identified by its melting point (246° C) and by the m.p. of its dimethyl ester (161° C).

2,5-Furanedicarboxylic Acid-^{14}C.

As starting material we used potassium pyromucinate (1 mmole) which was placed with CdI_2 (10 % of salt weight) on the carrier. The reaction was carried out in an ampoule in a $^{14}CO_2$ atmosphere (0.5 mmole specific radioactivity 92.1 nCi/mmole) as described above, at 415° C for 15 min. The isolated 2,5-furanedicarboxylic acid (35 mg, i.e. 40 %) was identified by its melting point, higher than 315° C, and that of its dimethyl ester (109° C).

The acid contained 62.2 nCi/mmole (67 %) incorporated activity, the $^{14}CO_2$ contained 29.6 nCi/mmole (32 %).

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