Journal of Labelled Compounds and Radiopharmaceuticals - Vol.XII, No.2

THERMAL TRANSCARBOXYLATION REACTIONS
VIII.* A STUDY ON THE PROCESS OF ANOMALOUS CARBOXYL GROUP – CO_2 EXCHANGE

J.Szammer, A.Szabolcs
Central Research Institute for Chemistry of the
Hungarian Academy of Sciences, Budapest, Hungary

Received on September 22, 1975

SUMMARY

The anomalous course of $^{14}CO_2$ incorporation observed in the thermal transformation of disodium adipate was studied. It has been established that the thermal transformation of butane-1,1,4-tricarboxylic acid trisodium salt is accompanied by intramolecular 1-4 transfer of carboxyl groups. The results of ^{14}C incorporation and carboxyl group exchange suggest that disodium adipate α-carbanion is present and participates in the reaction in cyclic form.

As reported earlier (1), the thermal transformation of disodium adipate (ANa) in the presence of $^{14}CO_2$ results in substantially higher ^{14}C concentration in cyclopentanone formed than in the adipate recovered. In our interpretation, α-carboxylated ANa, formed as the intermediate of carboxyl group exchange, is converted mainly into cyclopentanone and not back into adipate. This assumption has been confirmed by the experimental data of thermal transformation of ^{14}C labeled and unlabeled butane-1,1,4-tricarboxylic acid trisodium salts

---

*Part VII.: J.Szammer, L.Noszkó: Acta Chim.Acad.Sci.Hung. in press.

(BNa). At the same time, it may be justly assumed that BNa decomposition starts with decarboxylation of the malonate moiety (Fig.1), thus, the labeled carboxyl group and carbanion in the ANa molecule are in a position where the ^{14}C atom cannot be incorporated into the carbonyl group of cyclopentanone by cyclisation. This is in contradiction with the above observation, and the reaction mechanisms of cyclopentanone formation through carbanion (2) and carboxyl group exchange through malonate (1,3,4) become also questionable.

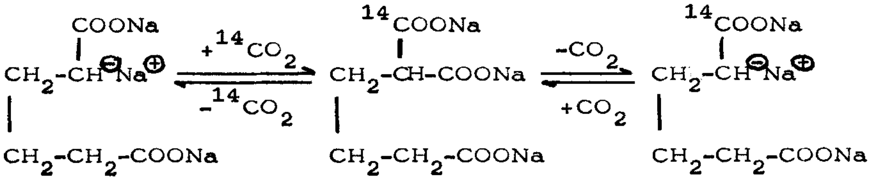


Fig. 1

In order to elucidate the problem, we studied the change in radioactivity of the cyclopentanone formed in the course of the thermal decomposition of butane-1,1,4-tricarboxylic acid (1,1-carboxy-$^{14}C_1$) trisodium salt (BNa-1,1-$^{14}C_1$). The undecomposed butane tricarboxylic acid has been prepared from the solid residue of partial decomposition, and distribution of the ^{14}C-labeled carboxyl group in the molecule has been determined by decarboxylation.

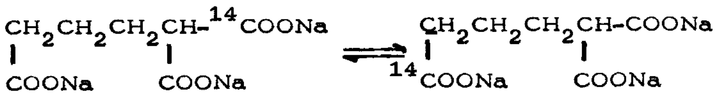
According to the experimental results given in Table I., quasi radioinactive cyclopentanone is formed in the initial stage of the thermal transformation of BNa-1,1-$^{14}C_1$ in good agreement with cyclisation through α-carbanion. At the same time, the higher incorporation detected in the advanced stage of the reaction is due to a fast carboxyl group exchange: on 38 % completion of the reaction the concentration of ^{14}C-labeled carboxyl groups is nearly equal in both positions. In other words, in a relatively quick exchange reaction, the carboxyl groups are transferred from position 1 to position 4 (Fig.2).

Table I.

Data of carboxyl group incorporation and exchange of BNa-1,1,4-${}^{14}C_1$[a] at 420°C

Reaction time (min)	Conversion (%)	Radioactivity 10^6 dpm/mmole cyclopentanone	distribution in positions 1	4
0-10	-	0.19	-	-
10-25	-	0.80	-	-
25-35	38	1.20	4.00	1.70

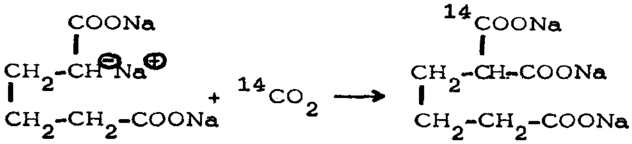
[a] Abbreviation: BNa-1,1-${}^{14}C_1$: Butane-1,1,4-tricarboxylic acid (1,1-carboxy-${}^{14}C_1$) trisodium salt (spec.act.: 5.7×10^6 dpm/mmole)



$$\underset{\mathrm{COONa}}{\mathrm{CH_2}}\mathrm{CH_2CH_2}\underset{\mathrm{COONa}}{\mathrm{CH}}\mathrm{-{}^{14}COONa} \rightleftharpoons \underset{\mathrm{{}^{14}COONa}}{\mathrm{CH_2}}\mathrm{CH_2CH_2}\underset{\mathrm{COONa}}{\mathrm{CH}}\mathrm{-COONa}$$

Fig. 2

If this 1-4 carboxyl group exchange is due to an intermolecular transcarboxylation process, carboxylation of the ANa-α-carbanion can lead only to BNa-1,1-${}^{14}C$ (Fig.3).



$$\begin{array}{l}\mathrm{CH_2-\overset{COONa}{CH^{\ominus}}Na^{\oplus}} \\ \mathrm{CH_2-CH_2-COONa}\end{array} + \mathrm{{}^{14}CO_2} \longrightarrow \begin{array}{l}\mathrm{CH_2-\overset{{}^{14}COONa}{CH}-COONa} \\ \mathrm{CH_2-CH_2-COONa}\end{array}$$

Fig. 3

This assumption can be controlled by studying the exchange reaction between BNa carboxyl groups and ${}^{14}CO_2$: after partial completion of the reaction, the labeled carboxyl group of the butane tricarboxylic acid recovered is to be found in the malonate moiety of the molecule. For comparison, the position of the incorporating $^{14}CO_2$ has also been determined with some other aliphatic tricarboxylic acid trisodium salts. The results depicted in Table II show the exchange of BNa carboxyl groups with $^{14}CO_2$ to be a much slower process than described above, and that ^{14}C incorporation occurs with nearly identical frequency in both positions. At the same time, in the case of the other tricarboxylates, $^{14}CO_2$ incorporation took place in the malonate part of the molecules, as was expected. The $^{14}CO_2$ exchange data of BNa carboxyl groups also suggest that the 1-4 carboxyl group transfer is not the result of on intermolecular transcarboxylation reaction, discussed earlier (1,3).

The specificity of ANa-α-anion is very probably responsible for the anomalous reaction observed in the thermal transformation of ANa and BNa. This special feature of the ANa-α-anion is that it is also a δ-anion, which is significant in the formation of some cyclic structure. In our opinion, the most probable structure of this cyclic anion (Fig.4) can be deduced from the (the basis of condensation) mechanism proposed by Neunhoeffer and Paschke (2).

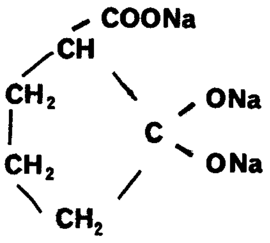


Fig. 4

We presume that the answer to the above questions can be found in the stability conditions of open chain carbanions with cyclic structure: The α-carbanion derived from ANa is

Table II

Data of $^{14}CO_2$ incorporation

Salt + $^{14}CO_2$ [a,b]	Temp. (^{o}C)	Time (min.)	Conversion (%)	Radioactivity x10^6 dpm/mmole [c]						Exchange (%)
				f_o	f_1	f_2	f_a	distribution in positions 1	4	
ETNa	350	40	28	9.82	1.51	2.62	0.82	1.45	0.06	29.1
PRNa	370	60	39	11.36	1.50	2.65	0.84	1.38	0.12	33.7
BNa	410	60	27	8.63	1.34	2.32	0.91	0.90	0.44	25.6
PTNa	400	20	29	10.73	1.61	2.80	0.90	1.48	0.13	31.8

[a] Abbreviations: ETNa: Ethane-1,1,2-tricarboxylic acid trisodium salt
PRNa: Propane-1,1,3-tricarboxylic acid trisodium salt
BNa : Butane-1,1,4-tricarboxylic acid trisodium salt
PTNa: Pentane-1,1,5-tricarboxylic acid trisodium salt

[b] Composition of reaction mixture: 5 mmole salt + 1 mmole $^{14}CO_2$ (spec.act. 1.8x10^8 dpm/mmole)

[c] Designation and calculation see in "Experimental"

more stable in the cyclic form and takes part in thermal transformation processes mainly in this form. Before conversion into cyclopentanone, the cyclic anion may be carboxylated with $^{14}CO_2$ into tricarboxylate containing a labeled carboxyl group both on the first and fourth carbon atom (Fig.5).

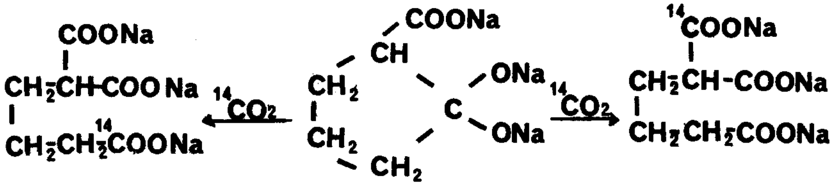


Fig. 5

One of the conversions also involves intramolecular carboxyl group transfer.

Accordingly, the anomalous $^{14}CO_2$ incorporation observed in the thermal transformation of ANa (1) may be interpreted as follows: the considerable cyclopentanone-^{14}C formation may be due to fast carboxylation and decarboxylation processes with participation of cyclic anion while only relatively few disodium adipate-^{14}C α-carbanions in the reaction mixture produce disodium adipate-^{14}C in a hydrogen abstraction reaction.

EXPERIMENTAL

MATERIALS

Preparation of the carboxylic acid salts, as well as ethane-1,1,2-tricarboxylic acid, propane-1,1,3-tricarboxylic acid, butane-1,1,4-tricarboxylic acid, pentane-1,1,5-tricarboxylic acid (2), and the synthesis of butane-1,1,4-tricarboxylic 1,1-carboxy-$^{14}C_1$ had been reported earlier (1).

EXPERIMENTAL METHOD

The reaction conditions of thermal transformations have been chosen on the basis of thermogravimetric data (2).

The experiments were performed in a metal bath thermostat. The accuracy of thermostating in the temperature range applied was ± 1°C. The temperature of the thermostat was measured with a platinum resistance thermometer.

Butane-1,1,4-tricarboxylic acid (1,1-carboxy-$^{14}C_1$) trisodium salt (10 mmoles) was placed into the reaction vessel and subjected to thermal decomposition in nitrogen flow (8 liter/hr). The cyclopentanone formed in the course of decomposition was collected in a receiver cooled with liquid air. The receiver was exchanged at intervals depicted in Table I. The crude cyclopentanone fractions accummulated in the receiver were purified by lyophylization and prepared in the form of semicarbazone. The cyclopentanone semicarbazone samples were recrystallized from aqueous ethanol and the radioactivity was counted. The solid residue was dissolved in water and 20 mmole of radioinactive BNa was added. The aqueous solution was acidified by hydrochloric acid, the butane-1,1,4-tricarboxylic acid was separated (2) and the radioactivity was measured. The conversion in the thermal decomposition was calculated from the amount of initial and diluting salt (a_o, a_1) and the radioactivity of initial and diluted samples (f_o, f_1).

The position of the labeled carboxyl group was determined by decarboxylation of the tricarboxylic acid recovered, with the following formula

$$F: 2.10\ (f_1 - f_a)$$

where F: radioactivity in the malonate moiety (dpm/mmole)

f_1: radioactivity of diluted tricarboxylic acid recovered (dpm/mmole)

f_a : radioactivity of dicarboxylic acid formed by decarboxylation of tricarboxylic acid (dpm/mmole);

owing to the isotope effect in similar reactions (5), a correction of + 0,05 $(f_1 - f_a)$ has been made.

The carboxyl group-$^{14}CO_2$ exchange reaction was studied in a closed system. To tricarboxylic acid (5 mmoles) placed in a glass tube, $^{14}CO_2$ (1 mmole) was distilled in vacuo with liquid air. The tube was sealed, heated in a thermostat at an appropriate temperature for a period required for partial exchange. After removal from the thermostat, the reaction vessel was allowed to cool and then frozen with liquid air. The system was opened and $^{14}CO_2$ was recovered in the form of $BaCO_3$. In order to facilitate recovery of the undecomposed tricarboxylic acid and to determine the conversion, we applied a double dilution: the solid residue was dissolved in water and the aqueous salt solution was divided into two equal parts. To one portion we added a_1 (10 mmoles) and to the other portion a_2 (15 mmoles) of the radioinactive tricarboxylic acid Na salt. The aqueous salt solutions were acidified with HCl, dried in vacuo and the solid residue was extracted with alcohol. After evaporation of the alcoholic extracts, the tricarboxylic acids were repeatedly recrystallized from an appropriate solvent (2), purity was checked by m.p. and radioactivity was counted.

The amount $(2a_x)$ and the radioactivity (f_o) of tricarboxylic acid recovered were calculated from the isotope dilutions of the samples:

$$f_o a_x = f_1 \ (a_x + a_1)$$

$$f_o a_x = f_2 \ (a_x + a_2)$$

$$a_x = \frac{a_1 f_1 - a_2 f_2}{f_2 - f_1} \quad ; \quad f_o = f_1 \ (1 + \frac{a_1}{a_x})$$

where f_1 and f_2 represent radioactivities in dpm/mmole of residual sodium tricarboxylate diluted with a_1 and a_2 mmoles of radioinactive salt.

The conversions were calculated from the expressions obtained for a_x:

$$\text{Conversion } (\%) = 100 \left(1 - \frac{2a_x}{a_o}\right)$$

The exchange between carboxyl groups and $^{14}CO_2$ (radioactivity: 1.8×10^8 dpm/mmole) was characterised by the extent of equilibrium ^{14}C distribution. In the case of a reaction mixture containing 5 mmoles of tricarboxylate and 1 mmole of $^{14}CO_2$ it can be calculated from f_o with the following formula:

$$\text{Exchange } (\%) = 100 \frac{16\ f_o}{3\text{x}1.8\text{x}10^8}$$

The radioactivity of the samples was counted in dioxane solution on a Packard Tri-Carb liquid scintillation spectrometer.

REFERENCES

1. Szammer J., Szabolcs,A., Noszkó L.- J.Lab.Compounds 10: 451 (1974).
2. Neunhoeffer O., Paschke P.- Ber. 72: 919 (1939).
3. Szabolcs A., Szammer J.- J.Lab.Compounds 10: 113 (1974).
4. Szammer J., Szabolcs A., Noszkó L.- Radiochem.Radioanal.Letters 21: 241 (1975).
5. Raaen V.F., Ropp G.A., Raaen H.P.- Carbon-14, McGraw - Hill, New York, 1968, p. 86.