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TRITIUM ISOTOPE EFFECTS IN THE OXIDATION OF 1,2,3,4-TETRAHYDRO-(1-^3H)NAPHTHALENE TO (1-^3H)NAPHTHALENE BY 2,3-DICHLORO-5,6-DICYANO-QUINONE (DDQ)

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Abstract—The dehydrogenation of 1,2,3,4-tetrahydronaphthalene (tetralin) to naphthalene with 2,3-dichloro-5,6-dicyano-quinone (DDQ) involves 1,2-dihydronaphthalene as an intermediate. The kinetic, the secondary, and the intramolecular isotope effects in the conversion of (1-^3H)tetralin to 1,2-dihydro-(4-^3H)naphthalene and of 1,2-dihydro-(1-^3H)naphthalene to (1-^3H)naphthalene have been determined. The isotope effects involved in both conversions were of the same order of magnitude, the intramolecular effect being 10 and 23, the kinetic effect 2·1 and 2·4 and the secondary effect 0·9 and 0·8 in the first and second conversion, respectively. These data indicate the α-hydrogen abstraction as the rate determining step in accordance with the proposed hydride transfer mechanism.

DURING a previous investigation we found a fairly large isotope effect in the conversion of 1,2,3,4-tetrahydro-(1,4-^2H)naphthalene [(1,4-^2H)tetralin] to (1,4-^2H)-naphthalene by oxidation with DDQ. NMR and mass spectroscopic data indicated that (1,4-^2H)tetralin, containing 1·28 D-atom per molecule, produced naphthalene having 0·95 D-atom per molecule in the α-position.[1]

Isotope effects in quinone oxidations are already known. Lewis *et al.*[2] found in the quinone oxidation of deuterated leuco triphenylmethane dyes k_H/k_D-values ranging from 7 to 14. In their experiments the oxidation with DDQ was too fast to be measured directly and competitive measurements were carried out to obtain a k_H/k_D-value. It was therefore interesting to determine directly the tritium isotope effects in the DDQ-oxidation of (1,4-^3H)tetralin. Because of the magnitude of the isotope effects involved, (1,4-^3H)naphthalene with a high specific activity can be prepared if highly active (1,4-^3H)tetralin is used as starting material.* As expected, the conversion of (6-^3H)tetralin to (2-^3H)naphthalene did not show any isotope effect.

The tetralin oxidation was carried out as described by Braude *et al.*[3] We found that depending on the reaction time and the isolation technique, naphthalene and 1.2-dihydronaphthalene (DHN) could be isolated. The identity of DHN was established by comparison with an authentic sample in NMR spectroscopy and gas chromatographic analysis (GLC). The ratio of the amounts of napthalene and DHN produced seemed to depend on the isolation conditions. We used two methods for the analysis of the heterogeneous reaction mixture:

A. After adding THF to the heterogeneous reaction mixture the resulting solution was analysed by GLC.

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* Catalytic H-T-exchange between tetralin and tritium gas produces (1,4-^3H)tetralin with a specific activity much higher than that of the tritium gas used.[1]

B. The reaction mixture was first boiled with water[3] and afterwards THF was added and the solution was then extracted with light petroleum from an alkaline medium and the extract was analysed by GLC. If method A was used only traces of tetralin and DHN were present in addition to the main product naphthalene (Table 1).

TABLE 1. DDQ-OXIDATION OF TETRALIN

Exp. No.	Molar ratio DDQ/T	Reaction temp. °C	Reaction time	Solvent	Percent via method A N	Percent via method A DHN	Percent via method A T	Percent via method B N	Percent via method B DHN	Percent via method B T
1	2·70	80	5 min	benzene	75	0	0	33	32	14
2	2·76	80	7 min	benzene	84	0	0	55	24	2
3	2·72	80	10 min	benzene	82	<1	<1	44	36	<1
4	2·76	80	20 hr	benzene	80	0	0	85	0	0
5	2·80	20	20 hr	benzene	85	0	0	25	38	26

N = naphthalene, T = tetralin, DHN = 1,2-dihydronaphthalene.

We investigated the ratio of the reaction products in the two phases which can be isolated after the reaction. The solid phase was separated by centrifugation and each phase was analysed by method A and B. Analysis of both phases, isolated in experiment 2, gave the following results:

Phase	Method A N	Method A DHN	Method A T	Method B N	Method B DHN	Method B T
Liquid	43	0	0	32	9	2
Solid	41	0	0	23	15	0

Thus no dramatic differences were found.

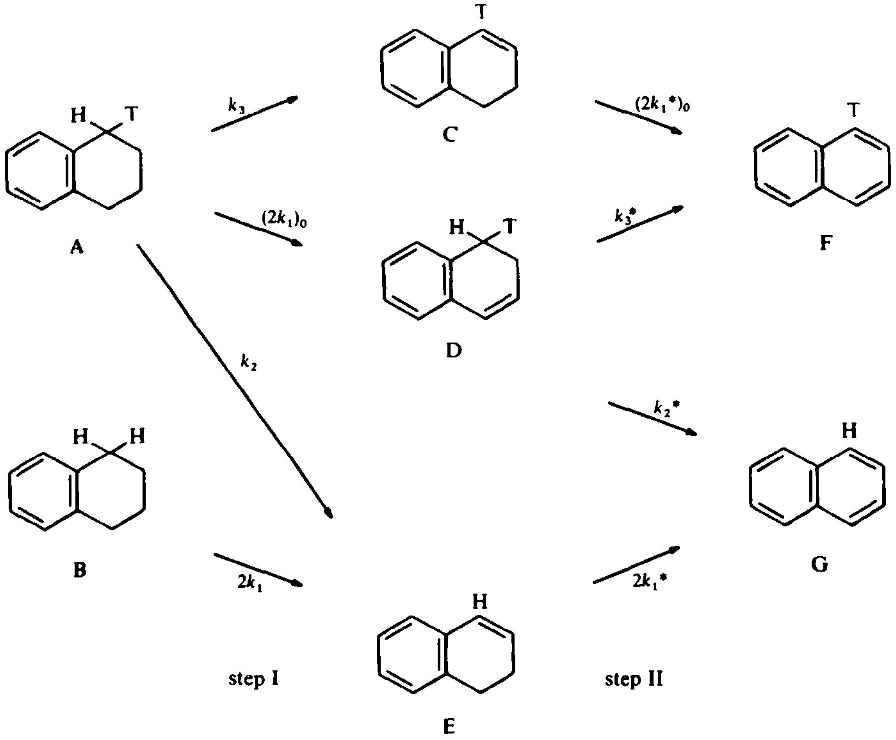
The yield of naphthalene obtained by method A was in all cases about equal to the sum of the yields of naphthalene, DHN and tetralin obtained by method B. If method A was used for the analysis of the reaction mixture, DHN and tetralin complexes with DDQ were still present and presumably these complexes were converted to naphthalene when subjected to our gas chromatographic conditions (column temps up to 160°). We found indeed that gas chromatographic analysis of a solution of DHN and DDQ in benzene–THF solvent showed the presence of naphthalene. Further experiments showed that in benzene as solvent, DHN is converted into naphthalene. A one minute reaction at 80° yielded 77% DHN and 14% naphthalene, and after a reaction time of 20 hr at 20° a yield of 98% naphthalene was obtained. The foregoing results indicate that 1,2-dihydronaphthalene is a likely intermediate in the DDQ-oxidation of tetralin to naphthalene.

We determined the overall tritium isotope effect of the oxidation during the most usual reaction conditions, e.g. in benzene as solvent at reflux temp and via isolation of the naphthalene produced by method B.[3] If the starting material tetralin is labeled by catalytic H-T-exchange with tritium gas with a low specific activity,[1] we expect as predominant species unlabeled tetralin and (1-^{3}*H*)tetralin. The rate constants for the conversion of these species into naphthalene are represented in Scheme I, assuming that DHN acts as an intermediate.

The isotope effects involved in the conversion to 1,2-dihydro-(4-^3H)naphthalene (step I) are the intramolecular isotope effect (i.I.E.) defined as k_3/k_2, the secondary isotope effect (s.I.E.) defined as k_3/k_1 and the kinetic isotope effect (k.I.E.) defined as $2k_1/k_2 + k_3$.[4] The same type of isotope effects are involved in the conversion of 1,2-dihydro-(1-^3H)naphthalene into (1-^3H)naphthalene (step II).

SCHEME I

Rate constants in the conversion of (1-^3H)tetralin into (1-^3H)naphthalene



If we assume that $(2k_1)_0 = 2k_1$ and $(2k_1^*)_0 = 2k_1^*$, we note that a conversion without isotope effect in step I is followed by a conversion with isotope effect in step II and that the same is true for the reverse. Thus the overall isotope effect in the conversion of (1-^3H)tetralin into (1-^3H)naphthalene originates partly from step I and for the other part from step II.

In order to determine the isotope effects involved, we first investigated the change in the ratio of the specific activities of naphthalene and tetralin as a function of the degree of conversion. In Table 2 some experimental results are summarized. The data given in Table 2 are insufficient for a calculation of the kinetic isotope effect by means of formula I:[5]

$$\frac{k_2 + k_3}{2k_1} = \frac{\ln \dfrac{x_0 - ys}{x_0(1 - s)}}{\ln(1 - s)} + 1$$

TABLE 2. ISOTOPE EFFECTS IN THE DDQ-OXIDATION OF (1-^3H)TETRALIN TO (1-^3H)NAPHTHALENE IN REFLUXING BENZENE

Exp. No.	Reaction time	$s \times 100$ = yield (%)	Specific activity (μC/mM) tetralin = x_0	Specific activity (μC/mM) naphthalene = y	y/x_0
6	0·5 min	1·4	2·93	1·92	0·655
6^a	1 min	15·4	1·82	1·27	0·697
7	1 min	24·3	2·93	2·10	0·717
8	5 min	16·6	2·93	2·17	0·741
9	10 min	44·7	1·98	1·55	0·783
10	30 min	71·5	1·98	1·67	0·843
11	60 min	74·8	1·98	1·76	0·889
12	17 hr	83·0	1·98	1·79	0·904

x_0 = specific activity of starting material before reaction; y = specific activity of the product; s = fraction of converted starting material.

The problem is finding the right value of s, as besides the product naphthalene. DHN is formed and the total recovery of material only amounts to about 80% (Table 1). If s is based on the ratio, mM product found/mM starting material used,[4] the data of Table 2 gives values of the k.I.E. between 1·26 and 1·47. A similar problem concerning s, is encountered in using formula II:[6]

$$\frac{k_2 + k_3}{2k_1} = \frac{\ln x/x_0}{\ln (1 - s)} + 1 \qquad \text{II}$$

with x = specific activity of the remaining starting material after the reaction.

For example, experiment 6a (Table 2) yielded 15·4% naphthalene and 18·4% DHN, while 44·5% of the tetralin could be recovered (total recovery of material 78·3%, compare Table 1). The specific activity of the recovered tetralin was 2·32 μC/mM. Application of formula II with $s = 0{\cdot}154$ (based on the yield of naphthalene) gave an impossible value for the k.I.E. ($-2{\cdot}28$), but the same value of s in formula I produced k.I.E. = 1·47. However, if s is based on the consumption of tetralin ($s = 0{\cdot}555$), formula I and II yield k.I.E. = 1·66 and 1·42, respectively.

These considerations indicate that the use of formula I and II for the calculation of the k.I.E. has to be based on reactions which can give a quantitative yield of one product. We tried therefore to determine the k.I.E. indirectly.

The most revealing relations between degree of conversion and the activity ratio y/x_0 are to be found at 0 and 100% yield. At 100% yield the ratio y/x_0 reflects only the influence of the i.I.E. of both steps, and at 0% yield only the influence of the s.I.E. of step I is effective.[6] By polynomial regression was found that the best fit for the experimental results presented in Table 2, is:

$$y/x_0 = 66{\cdot}69 + 0{\cdot}276\,(100 \times s)$$

From this relation we calculate at

$$100\%\ \text{yield}\ y/x_0 = 0{\cdot}943 \pm 0{\cdot}016$$

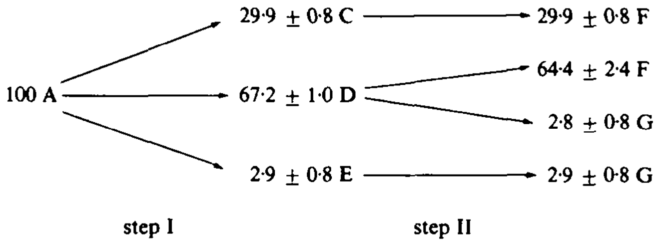
and

$$0\%\ \text{yield}\ y/x_0 = 0{\cdot}667 \pm 0{\cdot}016$$

The error was calculated from the experimental deviations from the linear relation. We thus notice in Scheme I that at a yield of 100% F + G, the activity loss from A is only 5·7%. If we assume that equal amounts of E and G are produced from A and D respectively, 97·1% of the activity of A has to be distributed over C and D. The distribution over C and D is determined by the ratio $k_3/(2k_1)_0 = k_3/2k_1$, thus by the s.I.E. of step I. Without any isotope effect the ratio of the specific activity of DHN and tetralin in step I should be 0·750. From this value and the extrapolation of y/x_0 to 0% yield we calculate that the secondary isotope effect in step I = 0·667/0·750 = 0·889 ± 0·021. From the value of the s.I.E. follows that the ratio of the number of molecules of C and D equals 889:2000. if A is 100% converted. Thus we find that 100 molecules of A produce 29·9 ± 0·8, 67·2 ± 1·0 and 2·9 ± 0·8 molecules of 1, D and E respectively. If we consider 100% conversion of the compounds C, D and E to F + G, we notice that C is completely converted into F. This means that the contribution of D to the total activity of F equals the difference between the activity value at 100% yield and the activity contribution from C. Thus D produces 94·3 − 29·9 = 64·4 molecules of F. The results of these calculations are summarized in Scheme II.

SCHEME II

Calculated reaction yields at 100% conversion, based on Scheme I



From the data in Scheme II the i.I.E. of step I and II can be calculated. According to Weygand *et al.*[4] the ratio k_3/k_2 equals

$$\frac{100 - \%\,\text{loss}}{\%\,\text{loss}}$$

at 100% conversion. This % loss indicates the decrease of the specific activity of the product in relation to the specific activity of the starting material at 100% conversion. We thus find

step I i.I.E. = 10·3 ± 3·1

and step II i.I.E. = 23·0 ± 7·2

By using the relation

$$\text{k.I.E.} = \frac{2\,\text{i.I.E.}}{\text{s.I.E.}\,(\text{i.I.E.} + 1)} \qquad \text{III}$$

and the value for the s.I.E. of step I, we obtain

step I k.I.E. = 2·05 ± 0·05

An experimental verification of the k.I.E. in step I directly from the change in the specific activity of the produced DHN or the remaining tetralin is impossible. The isolated DHN will always be a mixture of the compounds C, D and E and because of the through-reaction to F and G, the isotope effect in step II will affect the specific activity of (C + D + E). Moreover, the problem of estimating the degree of conversion has a profound influence on the magnitude of k.I.E. (*vide supra*).

We decided to investigate the isotope effects in step II, by using the pure compound D as starting material. In order to compare the results of such an experiment with the results of the previous experiments, it was necessary to carry out the reaction under the same conditions, e.g. in refluxing benzene, followed by isolation via method B. Owing to the speed of the reaction, only reactions yielding 60 to 90% of naphthalene could be studied. Some results are summarized in Table 3.

TABLE 3. ISOTOPE EFFECTS IN THE DDQ-OXIDATION OF 1,2-DIHYDRO-(1-^3H)NAPHTHALENE TO (1-^3H)NAPHTHALENE IN REFLUXING BENZENE

Exp. No.	Reaction time	Yield (%) DHN	Yield (%) naphthalene	Spec. act. (μC/mM) DHN	Spec. act. (μC/mM) naphthalene	k.I.E.
13	± 0·5 min	18	60	3·54	1·97	2·25
14	1 min	14	77	3·54	1·96	2·64
15	7 min	5	82	3·54	2·14	2·50
16	7 min	5	78	3·54	2·15	2·36
17	2 hr	0	90	3·54	2·44	2·38
18	3 hr	0	92	3·54	2·44	2·51

The k.I.E.'s presented in Table 3 were calculated by use of formula I. The differences between the separate values are mainly caused by the variation in the yield of naphthalene (e.g. Exp. 17 and 18). The fact that the total recovery of material varied between 80 and 90% had undoubtly its bearing on the yields of the products. The same uncertainty in the magnitude of s in formula I was also encountered in the evaluation of the results summarized in Table 2. The average value obtained for the k.I.E. in the DDQ-oxidation of 1,2-dihydro(1-^3H)naphthalene to (1-^3H)naphthalene was 2·44 ± 0·11 (Table 3). As the compounds DHN, naphthalene and tetralin are recovered quantitatively from the reaction mixture, some material must have been converted into other compounds during the reaction. However, an increase of the yields of naphthalene in experiment 13 and 16 to 69% and 85% respectively (in order to create an equal recovery of 90% in all experiments of Table 3) has only a negligible influence on the average value of the k.I.E. (2·51 + 0·09), as the separate values for Exp. 13 and 16 only increase to 2·42 and 2·61, respectively. The average value of the k.I.E. is in reasonable agreement with the value calculated by use of formula II. In experiment 13 starting material with a specific activity of 7·32 μC/mM was isolated after the reaction. From this value we calculate k.I.E. = 2·63, if the degree of conversion equals 0·69. The s.I.E. of the reaction can be calculated with formula III if we combine the value of the k.I.E. with the value of the i.I.E. of step II calculated from Scheme II. We obtained in this way s.I.E. = 0·79 ± 0·04. A check on the values of s.I.E. and i.I.E. could be obtained by extrapolation of the ratio's of the specific activity of DHN and naphthalene to 0 and 100% yield. However, because of the limited range of yields which could be investigated (Table 3), a large error is introduced into extrapolated values. The best estimation of the ratio at 100% yield lead to an i.I.E. of about 10. By using relation III this value leads to s.I.E. = 0·75 in combination with k.I.E. = 2·44. The results obtained are summarized below:

	i.I.E.	k.I.E.	s.I.E.
step I :	10·3 ± 3·1	2·05 ± 0·05	0·89 ± 0·02
step II:	23·0 ± 7·2	2·44 ± 0·11	0·79 ± 0·04

The presence of isotope effects indicates that hydrogen abstraction from the α-position of tetralin and DHN is at least partly rate determining, thus supporting the proposed mechanism of hydride transfer.[2] From the theoretical maximum value of the i.I.E.[6] and the fact that at 100% conversion of (1-^3H)tetralin to (1-^3H)naphthalene the retention of tritium amounts to 94·3 ± 1·6% (see page 3213), it can be concluded that the rate determining hydrogen abstraction proceeds at least for 92% from the α-position. The fact that in DHN hydrogen is present in a vinyl-position does not change the location of the rate-determining hydrogen abstraction, but seems to decrease the magnitude of the s.I.E.

EXPERIMENTAL

(1-^{3}H)*Tetralin* was prepared by catalytic H-T-exchange between tetralin and molecular tritium with a specific activity of 17·2 μC/mM.[1] After purification by GLC the (1-^3H)tetralin was diluted from a specific activity of 24·0 μC/mM to 2·34 μC/mM.

(6-^3H)*Tetralin* was prepared by catalytic dehalogenation of 6-chlorotetralin with molecular tritium with a specific activity of 17·2 μC/mM.[7] After purification by GLC the (6-^3H)tetralin was diluted from a specific activity of 4·22 μC/mM to 1·19 μC/mM.

1,2-*Dihydronaphthalene* was prepared from 1-tetralol analogous to the procedure described by Hussey *et al.*[8] To a known amount of 1-tetralol a large excess of conc phosphoric acid (85%) was added. The mixture was heated for 1 hr at 110–120° and 1,2-dihydronaphthalene was isolated by extraction with diethyl ether and purified by distillation *in vacuo* (yield 63%). The NMR spectra of the synthesized compound and of the isolated intermediate in the DDQ-oxidation of tetralin were identical and showed clearly the identity of 1,2-dihydronaphthalene. The retention times of both compounds in temp programmed GLC on Carbowax-20M (5% w/w + 5% w/w KOH on Chromosorb-W) were also identical.

1,2-*Dihydro*-(1-^{3}H)*naphthalene* was prepared from 1-tetralol-(4-^3H) as described for the non-labeled compound from 1-tetralol. The 1-tetralol-(4-^3H) was prepared from 1-tetralone-(4-^3H), which was obtained by ring-closure of 4-phenyl-(3-^3H)butyric acid. The 4-phenylbutyric acid was labeled by catalytic H-T-exchange between 4-phenylbutyric acid and molecular tritium, using EtOH as solvent and Pd/$CaCO_3$ as catalyst.[1]

DDQ-oxidation of (1-^{3}H)*tetralin*. Diluted tetralin (0·5 mM with a specific activity of 2·34 μC/mM) was dissolved in 10 ml dried benzene. The reaction vessel was flushed with dry N_2. 5 equivs of DDQ were added and the mixture was refluxed under N_2. After the addition of 10 ml water the mixture was refluxed again for 30 min. Then, after cooling to room temp. sufficient THF was added to dissolve remaining solid material. The resulting soln was made alkaline by the addition of 20% Na_2CO_3aq (50 ml) and the (1-^3H)-naphthalene produced was extracted with light petroleum b.p. 28–40° and purified by GLC (yield 80%). The specific activity of the (1-^3H)naphthalene was 2·08 μC/mM.

DDQ-oxidation of (6-^{3}H)*tetralin*. Diluted (6-^3H)tetralin (specific activity 1·19 μC/mM) was oxidized to (2-^3H)naphthalene (specific activity 1·21 μC/mM) as described. Bromination of the (2-^3H)naphthalene obtained as described by den Hollander.[7] gave 1-bromo-(2-^3H)naphthalene with a specific activity of 1·20 μC/mM.

Purification and activity measurements. All compounds were purified by preparative, temp programmed GLC on Carbowax-20M (5% w/w + 5% w/w KOH on Chromosorb-W). Specific activities of solns in benzene were determined by gas chromatographic concentration determination and liquid scintillation counting on a Nuclear Chicago Unilux I, model 6850.

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