Reactions with Aziridines, 53[1]. – Arene Hydrides, 9[2]

Intermediate Substitution in the Formation of a Benzylic Anion by an Aromatic Radical Anion as Observed with 1-Benzoyl-2-phenylaziridine

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The reaction of the title compound **1** with anthracene hydride AH^- or anthracenide $A^{-\bullet}$ leads to the formation of the benzylic anion **9** by fragmentation of the first generated substitution intermediate **7** or **8**. In the reactions with AH^- the carbanion **9** is completely trapped by protonation with dihydroanthracene AH_2 yielding the reduction product **3** (*N*-benzoylphenethylamine). In reactions with $A^{-\bullet}$ as well as with naphthalenide $N^{-\bullet}$ the carbanion **9** either abstracts a proton from the solvent THF (yielding **3**) or adds to the benzoyl group of unreacted **1** which finally results in β-benzamido-α-phenylpropiophenone (**6**).

Dissociative single electron transfer from aromatic radical anions to alkyl halides is well known[5]. The generated alkyl radical $R^\bullet$ can undergo various reactions, which may be divided into alkylating and non-alkylating (products R–R and RH) ones. While the alkylations with common alkyl halides play a substantial role [ca. 50%[5] from the radical anion $N^{-\bullet}$ of naphthalene (N), ca. 90%[6] from the radical anion $A^{-\bullet}$ of anthracene (A)], the analogous benzylation with benzylic halides is a minor reaction because the overall yield of the other products is ca. 90%[7]. We now demonstrate by a related example that benzylated dihydroarenes or rather their anions may be intermediates in the formation of the carbanion R^- and hence of both R–R and RH.

Our experiments with $A^{-\bullet}$ were prompted by a similar difficulty to obtain benzylation products in reactions of *N*-benzoylaziridines with anthracene hydride AH^- (carbanion of 9,10-dihydroanthracene AH_2)[8]. Thus, reactions with AH^- will be considered first. Reaction of **1** with AH^-Li^+ (Table 1, run 1) provided benzoyldihydroanthracene **2** and the open-chain amide **3** (corresponding to RH) but no ami-

Table 1. Reactions of **1** in THF at room temperature[a] (A = anthracene, N = naphthalene)

Run	mmol of 1	mmol of reagent		Time of addn.	Time of subseq. reactn.	% Products[b] 2	3	4	6	1 or artifacts thereof
1[c]	5	6	AH^-Li^+	?[c]	20 min	52	14	0	0	16 **1**
2	5	4	AH^-Li^+	≤10 s[d,e]	2 h[e]	(15)	(10)	(10)		(39) Oxa[f]
3	2	0.4	AH^-Na^+	1 min	1 h			(16)[g]		(36) Oxa[f], (8) **5a**, (6) **5b**
4	2	4	AH^-Na^+	1 min	1 min		95			
5	2	4	AH^-Na^+	2 min	14 d		99			
6	2.1[h]	6	AH^-Li^+	≤10 s[d]	5 min		(21)	(59)		
7	1.9	4.7	$A^{-\bullet}Na^+$	≤10 s[d]	5 s		(8)	(25)	(30)	
8	1.9	4.8	$A^{-\bullet}Na^+$	≤10 s[d]	1 min		(30)	(13)	(27)	
9	0.9	5.2	$A^{-\bullet}Na^+$	≤10 s[d]	1 d		(29)	0	(49)	
10	0.8	4.8	$A^{-\bullet}Na^+$	1 2 min	–		(51)	0	(14)	
11	2	4.1	$N^{-\bullet}Na^+$	≤10 s[d]	1 min		(13)		(67)	
12	10	13.1	$N^{-\bullet}Na^+$	1 min	1 min		(19)		(63)	
13	2	2.3	$N^{-\bullet}Na^+$	≤10 s[d]	1 min		(23)		(52)	
14	2	2.3	$N^{-\bullet}Na^+$	1 h	–		(44)		(12)	

[a] The solution of **1** in 15 ml of THF was added to a stirred solution of the reagent in 50–70 ml of THF. An excess of AH_2 was used in runs 1–6. All reactions were quenched with methanol or with acetic acid. – [b] Yields in parentheses are based on ^{1}H-NMR analysis. – [c] Taken from ref.[8] Time of addition is not precisely known but may have been about 10–30 min. – [d] Fastest possible flux from a dropping funnel. – [e] Addition of **1** at –65°C followed by warming (1 h) to room temperature. – [f] Oxa = 2,5-diphenyloxazoline. – [g] Yield based on **1**. When based on AH^-, the yield was 80%. – [h] 2.1 mmol of **5c**.

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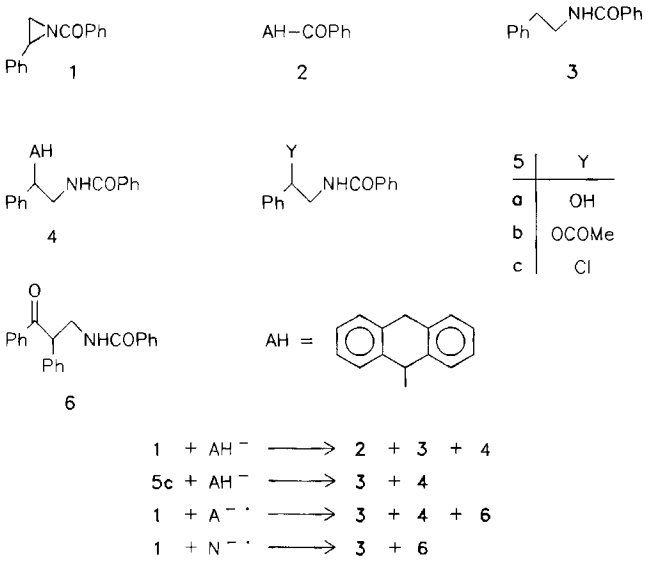
Scheme 1

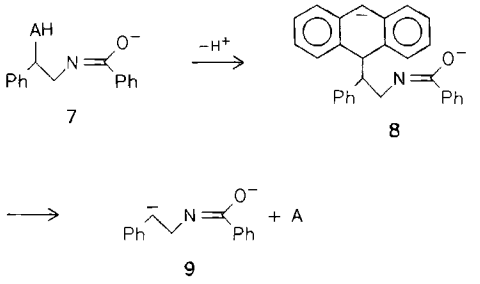


doethylated dihydroanthracene (**4**). The latter finding is in contrast to the behaviour of benzoylaziridines lacking a phenyl group on an aziridine carbon. However, it has recently been reported[4] that 9-benzyldihydroanthracenes can easily be cleaved to benzylic anions by an excess of AH^-. We therefore have repeated run 1 under conditions which should be unfavorable for this fragmentation. Thus, in run 2 we have slowed down the rate of the reaction by using a low temperature and have avoided the presence of an excess of AH^- by rapid addition of **1** to a small deficit of AH^-Li^+. Then, indeed, the elusive **4** could be detected together with an equal amount of **3** and with the expected ketone **2** resulting from an attack on the carbonyl group of **1**. The formation of ring-opened products should proceed faster[9] when Li^+ is replaced by Na^+. With this gegenion effect and with a huge excess of **1** it was possible to make **4** the only identifiable reaction product (run 3). The conversion of **4**, or rather its amide anion, into **3** by an excess of AH^- is demonstrated by runs 4 and 5 and by comparing them with run 3. Run 5 indicates the stability of the immediate anionic precursor of **3** under the reaction conditions. Thus, **3** is the only final product obtained with an excess of AH^- and in the presence of the free acid AH_2. The substitution product **4** in the form of its amide anion **7** is an intermediate on the reaction path to **3** or at least to a part of **3**. Carbanion **9**, a precursor of **3**, arises by a base-induced fragmentation of **7** in analogy to reported fragmentations[4].

Since pure **4** could not be obtained from **1** and AH^-, it has been prepared from the open-chain chloride **5c** and AH^- (run 6). Even then, **3** is obtained as a by-product. A separate experiment proved that **4** is quantitatively converted into **3** by an excess of AH^-.

We wondered if **4** or rather its dianion **8** might also be a detectable intermediate in the reaction of **1** with $A^{-\cdot}$, i.e. when an S_N2 process is very unlikely and when the solvent THF is the only acid present. This question found an affirmative answer under conditions of rapid mixing of the two reagents and of a short reaction time (runs 7 and 8). The amount of **4** decreased with time and was zero in runs 9 and 10. This decrease in **4** was in favour of increased yields of **3** and of the new β-amidoethyl ketone **6**. The change from the main product **6** in run 9 to the main product **3** in run 10 can be attributed to the slow addition of **1** to the solution of $A^{-\cdot}$ in run 10. The first step in these reactions will be SET from $A^{-\cdot}$ to **1**. This step can be expected[10] to be the fastest one in the reaction sequence leading to **4**. In run 10 each single drop of dissolved **1** is rapidly distributed in an excess of $A^{-\cdot}$. Under these conditions there cannot be sufficient **1** available for the formation of a carbonyl adduct which must be a precursor of **6**.

Scheme 2



If it obvious that the intermediacy of a benzylated dihydroanthracene species as **8** in reactions with $A^{-\cdot}$ may be relevant for previous results with benzyl halides[7]. In addition, the fragmentation of the detectable (by isolation of **4**) intermediate **8** in the absence of **7** shows that the AH^--induced fragmentation of **7** or **4** (separate experiment and runs 2–5) as well as of other benzylated dihydroanthracenes[11–13] is most probably not a concerted process.

The same two final products **3** and **6** and the same influence of mixing on their relative amounts has been observed in the reactions of **1** with $N^{-\cdot}$ (runs 11–14). We made no attempts to find an amidoethylated naphthalene or dihydronaphthalene corresponding to **4** since we have had no authentic samples of the possible products available and since we have expected the conversion of an intermediate benzylation product into **3** and **6** to be even faster in reactions with $N^{-\cdot}$ than with $A^{-\cdot}$. The reactions of **1** with $N^{-\cdot}$ probably resemble those with $A^{-\cdot}$ in mechanism although a participation of a benzylation process is uncertain. However, it may well be that a respective fragmentation of an intermediate 1-benzyldihydronaphthalene anion (a Birch intermediate) is responsible for the reported cleavage of 1-benzylnaphthalene by Na/K alloy in a mixture of glyme and triglyme[14]. This possibility has not been discussed so far.

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Experimental

^1H NMR: $CDCl_3$, Bruker W 250 (250 MHz) spectrometer. – IR: KBr unless otherwise stated, Perkin-Elmer 283 spectrometer.

All reactions were performed in dry THF with continuous stirring under dry nitrogen (see ref.[8]). The reactions were quenched with acetic acid or methanol. Subsequent evaporation provided a residue which was taken up in dichloromethane. The solution was washed with water. Evaporation of the organic layer yielded a residue whose treatment (column chromatography or NMR analysis) is described below. Column chromatography was performed with 0.063–0.2 mm silica gel (Merck); column dimensions (thickness × length, cm) are given for the specific workup.

N-(2-Chloro-2-phenylethyl)benzamide (**5c**): A solution of 690 mg (3.1 mmol) of **1** in 50 ml of diethyl ether was mixed with a mixture (1:1) of diethyl ether and concd. aqueous hydrochloric acid. After 15 min 100 ml of water was added. The resulting precipitate was taken up in dichloromethane and the solution washed three times with water. Evaporation of the dried organic layer provided 563 mg (70%) of **5c**: mp 123–124°C. – IR: $\tilde{\nu}$ = 3320 cm^{-1} (NH), 1640 (amide I), 1535 (amide II). – ^1H NMR: δ = 3.77 (m_c, 1 H of NCH_2), 4.12 (ddd, *J* = 13.1/7.0/5.0 Hz, 1 H of NCH_2), 5.16 (dd, *J* = 8.0/5.0 Hz, ClCH), 6.58 (s br, NH), 7.31–7.55 (m, 8 aromatic H), 7.70–7.81 (m, 2 *o*-H of benzoyl).

$C_{15}H_{14}ClNO$ (259.7) Calcd. C 69.37 H 5.43 N 5.39
Found C 69.06 H 5.55 N 5.42

Authentic *N-(2-hydroxy-2-phenylethyl)benzamide* (**5a**)[15] was prepared from 2-amino-1-phenylethanol and benzoyl chloride: mp 146–147°C (ref.[15] 145°C). – IR: $\tilde{\nu}$ = 3370 cm^{-1} (OH), 3300 (NH), 1620 (amide I), 1545 (amide II). – ^1H NMR: δ = 3.32 (d, *J* = 3.3 Hz, OH), 3.52 (ddd, *J* = 14.1/7.9/4.9 Hz, 1 H of NCH_2), 3.93 (ddd, *J* = 14.1/6.9/3.3 Hz, 1 H of NCH_2), 4.97 (m_c, NCCH), 6.60 (s br, NH), 7.28–7.56 (m, 8 aromatic H), 7.72–7.79 (m, 2 *o*-H of benzoyl).

Authentic *2-benzamido-1-phenylethyl acetate* (**5b**)[16] was prepared as described in ref.[16]: mp 113°C (ref.[16] 112–113°C). – IR: $\tilde{\nu}$ = 3320 cm^{-1} (NH), 1740 (ester), 1650 (amide I), 1545 (amide II). – ^1H NMR: δ = 2.12 (s, CH_3), 3.82–3.89 (m, NCH_2), 5.99 (dd, *J* = 7.5/4.8 Hz, NCCH), 6.43 (s br, NH), 7.26–7.51 (m, 8 aromatic H), 7.70–7.74 (m, 2 *o*-H of benzoyl).

Authentic *3,4-dihydro-2,5-diphenyloxazole* (Oxa)[17] was prepared from **1** and $AlCl_3$ in benzene analogously to the method described by Heine and Proctor[18]: oil. – ^1H NMR (better resolution than in ref.[17]): δ = 4.01 (dd, *J* = 14.5/9.8 Hz, 1 H of NCH_2), 4.50 (dd, *J* = 14.5/7.8 Hz, 1 H of NCH_2), 5.69 (dd, *J* = 9.8/7.8 Hz, OCH), 7.29–7.54 (m, 8 aromatic H), 8.00–8.07 (m, 2 *o*-H of 2-Ph).

Reaction of **1** *with 9,10-Dihydro-9-lithioanthracene* (Table 1, run 2): The generation of AH^-Li^+ from 900 mg (5.0 mmol) of AH_2 in 60 ml of THF and 4 mmol of *n*-butyllithium (hexane solution, ca. 1.5 M) followed by the addition of 5 mmol of **1** dissolved in 10 ml of THF was performed as described in ref.[8] and in Table 1. The reaction was quenched with 2 ml of methanol. Chromatography (3.5 × 60) with toluene provided a hydrocarbon fraction and then 214 mg (15%) of **2**[8]. Subsequent elution with ethyl acetate gave 749 mg of a mixture consisting (^1H NMR) of 113 mg (10%) of **3**[8], 201 mg (10%) of **4**, and 434 mg (39%) of Oxa.

Reactions of **1** *with 9,10-Dihydro-9-sodioanthracene* (Table 1, runs 3–5): 5.3 mmol (5.0 mmol in run 5) of AH_2 and 4 mmol (0.4 mmol in run 3) of $NaNH_2$ were refluxed in 70 ml of THF for 2 h. After cooling to room temp., a solution of 446 mg (2.0 mmol) of **1** in 15 ml of THF was added dropwise (1 min in runs 3 and 4, 2 min in run 5). The reactions were quenched with 0.5 g of glacial acetic acid. Chromatography (3 × 22) with toluene removed the hydrocarbons. Subsequent elution with ethyl acetate yielded the products: 427 mg (95%) of **3** in run 4; 444 mg (99%) of **3** in run 5; 364 mg of a mixture consisting (^1H NMR) of 162 mg (16%) of **4**, 129 mg (36%) of Oxa, 39 mg (8%) of **5a**, and 34 mg (6%) of **5b** in run 3.

Reaction of **5c** *with* AH^-Li^+ (Table 1, run 6): A solution of AH^-Li^+ was prepared from 7.0 mmol of AH_2, 100 ml of THF, and 6.0 mmol of *n*-butyllithium as described above. A solution of 545 mg (2.1 mmol) of **5c** in 20 ml of THF was added as fast as possible (≤ 10 s) from a dropping funnel. The reaction was quenched with 0.3 g of glacial acetic acid. By chromatography (3 × 42) with dichloromethane hydrocarbons were removed. Subsequent elution with ethyl acetate yielded 598 mg of products. Recrystallization of the latter from methanol yielded 228 mg (27%) of pure **4**. ^1H NMR analysis of the evaporated mother liquor indicated 271 mg (32%) of **4** and 99 mg (21%) of **3**.

9-(2-Benzamido-1-phenylethyl)-9,10-dihydroanthracene (**4**): Mp 88–89°C. – IR: $\tilde{\nu}$ = 3320 cm^{-1} (NH), 1635 (amide I), 1550 (amide II). – ^1H NMR: δ = 3.15 (d, *J* = 18.6 Hz, 10-H pseudo ax), 3.18–3.27 (m, NCCH), 3.55 (d, *J* = 18.6 Hz, 10-H pseudo eq), 3.73 (m_c, 1 H of NCH_2), 4.04 (m_c, 1 H of NCH_2), 4.26 (d, *J* = 6.6 Hz, 9-H pseudo eq), 5.75 (s br, NH), 6.63–6.67 (m, 2 *o*-H of Ph), 6.92–6.95 (m, 1 aromatic H, probably 1-H), 7.03–7.30 (m, 11 aromatic H), 7.34–7.42 (m, 4 aromatic H including 2 *o*-H of benzoyl).

$C_{29}H_{25}NO$ (403.4) Calcd. C 86.31 H 6.24 N 3.47
Found C 86.52 H 6.50 N 3.46

Separate Transformation of **4** *to* **3**: A solution of AH^-Li^+ was prepared from 2.0 mmol of AH_2, 40 ml of THF, and 1.5 mmol of *n*-butyllithium as described above. At room temp. a solution of 101 mg (0.25 mmol) of **4** in 15 ml of THF was rapidly added within ≤ 10 s. After 24 h the reaction was quenched with 0.3 g of glacial acetic acid. By chromatography (2 × 20) with dichloromethane the hydrocarbons were removed. Subsequent elution with ethyl acetate provided 55 mg (99%) of **3**.

Reactions of **1** *with* $A^{-\bullet}$ (Table 1, runs 7–10) *or* $N^{-\bullet}$ (runs 11–14): A solution of 6.0 mmol of A (6.0 mmol of N in run 11; 14 mmol of N in run 12; 3 mmol of N in runs 13 and 14) in 15 ml of THF was stirred with sodium (amount given in Table 1) for 1 d. A solution of the respective amount of **1** (Table 1) in 15 ml of THF was added as stated in Table 1. The reactions were quenched with 1 ml of methanol (0.3 g of glacial acetic acid in run 10). By chromatography (3 × 22 for runs 7–10; 2 × 80 for runs 11–14) with dichloromethane the hydrocarbons were removed. Subsequent elution with ethyl acetate provided the mixtures of products derived from **1**. These mixtures were analyzed by weight and ^1H NMR. In run 10 only part (2.09 g) of the total residue (4.01 g) was chromatographed yielding 763 mg of a mixture consisting (^1H NMR) of 223 mg (corresponding to 19%) of **3** and 540 mg (corresponding to 63%) of **6**. Subjection of 703 mg of this mixture to a second chromatography (2 × 45, dichloromethane/ethyl acetate 10:1) provided 198 mg of **6** and then 492 mg of a mixture of **3** and **6**.

N-(2-Benzoyl-2-phenylethyl)benzamide (**6**): Mp 138–140°C. – IR: $\tilde{\nu}$ = 3340 cm^{-1} (NH), 1685 (ketone), 1645 (amide I), 1540 (amide II). – ^1H NMR: δ = 3.86–4.08 (m, NCH_2), 5.05 (dd, *J* = 8.8/5.3 Hz, NCCH), 6.67 (s br, NH), 7.20–7.51 (m, 11 aromatic H), 7.66–7.72 (m, 2 *o*-H of PhCON), 7.91–7.97 (m 2 *o*-H of PhCOC).

$C_{22}H_{19}NO_2$ (329.4) Calcd. C 80.22 H 5.82 N 4.25
Found C 79.98 H 5.71 N 4.12

CAS Registry Numbers

1: 93638-44-9 / **2**: 50688-77-2 / **3**: 3278-14-6 / **4**: 128600-81-7 / **5a**: 34119-82-9 / **5b**: 109393-37-5 / **5c**: 68342-69-8 / **6**: 128600-82-8 / 3,4-dihydro-2,5-diphenyloxazole: 72088-10-9 / 9,10-dihydro-

anthracene: 613-31-0 / 9,10-dihydro-9-lithioanthracene: 17228-13-6 / 9,10-dihydro-9-sodioanthracene: 3970-43-2 / sodium anthracenide: 12261-48-2 / sodium naphthalenide: 3481-12-7

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[12] Two authors (Stamm, Werry) of ref.[11] propose that the reduction of a radical to a carbanion in reactions with AH^- is better formulated with AH^- as reductant than with the small amount of $A^{-\cdot}$ generated by a fragmentation process. This proposal removes the discrepancy existing between ref.[11] and ref.[6] in the reaction of $A^{-\cdot}$ with a radical.

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[137/90]

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