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cis-trans Pair of a *N*-Benzoylaziridine: Dependence of Carbonyl Reactivity on Nitrogen Pyramid

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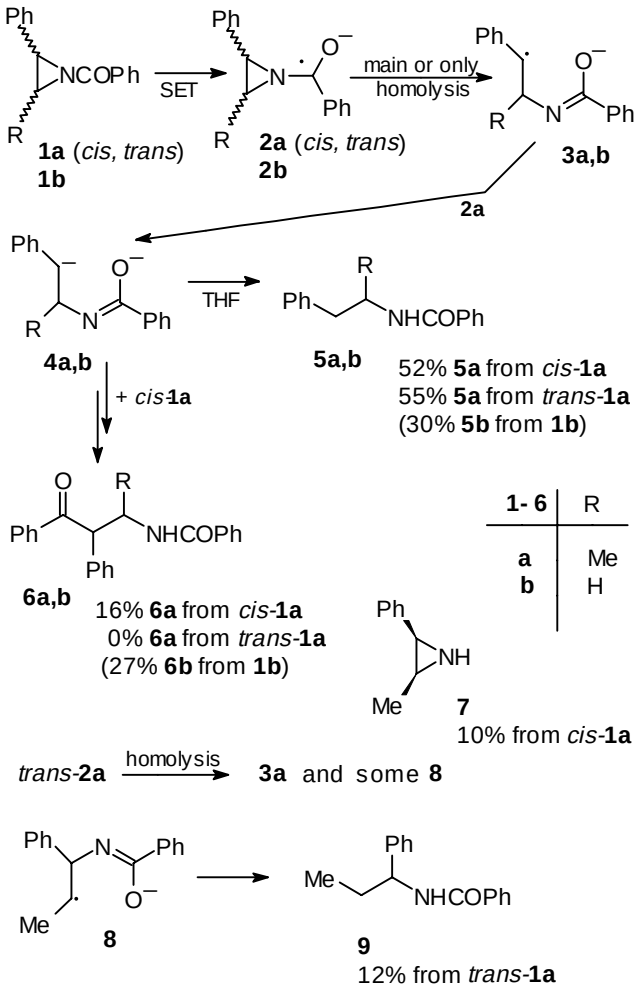
Abstract. In a multistep process, anthracenide and both 1-benzoyl-2-methyl-3-phenylaziridines **1a** form carbanion **4a** that abstracts a proton from the solvent THF. The steep N pyramid of *cis*-**1a** makes attack of **4a** on C=O of *cis*-**1a** fast enough to compete with proton abstraction while C=O of *trans*-**1a** with its flat and rapidly inverting pyramid did not react with **4a.** The initially generated ketyls of **1a** show another *cis-trans* effect of steric repulsion: their homolytic ring opening forms benzylic radical **3a**, the precursor of carbanion **4a**, but this opening is regiospecific for the *cis* ketyl only. The *trans* ketyl forms some isomeric radical too.

N-Acylaziridines are capable of various reactions which have close analogues in other fields of organic chemistry. However, their reactivities can in a unique manner depend on the nitrogen pyramid and its inversion which can be subject to steric respulsions of the N substituent by substituents of the aziridine carbons [1b]. This was already demonstrated by reactions of xanthyl anion $\mathbf{X}^-$ with *cis-trans* pairs of 2,3-substituted *N*-benzoylaziridines, *e.g.* of **1a** [2]. The *trans* isomers possess a flat and rapidly inverting nitrogen and hence an amide-like conformation resulting in an optimal leaving group for nucleophilic ring opening (NRO) [1b]. The *cis* isomers are characterized by a steep and slowly inverting pyramid that accentuates the ketonic character of the benzoyl group thereby drastically retarding NRO but increasing the ability to abstract an electron from $\mathbf{X}^-$.

A more general and more typical reaction of ketones is addition of a nucleophile while carbonyl additions are more difficult to realize with amides. The comparatively easy carbonyl attack [2] places *N*-acylaziridines into a borderline region between ketones and amides and should make them sensitive to even moderate changes in the N pyramid. Carbonyl attack by a carbanion, as well as by other nucleophiles, was often described [1b] particularly when the nucleophile may be classified as hard and when lithium was the counter ion of a carbanion. An influence of the N pyramid was so far never detected and a search for a *cis-trans* reactivity difference with the carbanions used was not possible for various reasons: the primary adduct was known or expected to arise either reversibly or not at all or from both isomers. Such a difference was now found in a regioselectivity study on homolytic ring opening of aziridino ketyls (Scheme 1).

Reactions of anthracenidyl (anthracenide) $\mathbf{A}^{\cdot-}$ with other *N*-acylaziridines (*cf*. [1a, 3]) have clarified the mechanistic steps to final products in such reactions. Hence, electron transfer from $\mathbf{A}^-$ to aziridines **1a** generates the aziridino ketyls **2a** that homolyze to amidatoalkyl radical **3a** which is reduced by **2a** to carbanion **4a**. The latter abstracts a proton from THF (main reaction) or adds to C=O of *cis*-**1a** providing finally



Scheme 1 Reactions of Aziridines **1a** with Anthracenidyl: Reaction Sequences with Intermediates, Products and Yields

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the *cis*-**1a** derived products **5a** (72%), **6a** (16% based on the formation from two equivalents of **1a**; inseparable 1.6:1 mixture of two diastereomers) and **7** (5% or 10%, respectively when based on the formation from two equivalents of **1a**). **7** is liberated from the carbonyl adduct when the reaction is quenched with methanol; however, part of **7** was obviously lost perhaps due to a certain volatility of **7** but more likely due to reactions during chromatography. In contrast and despite of identical conditions, *trans*-**1a** provided no **6a**; it yielded **5a** (55%) together with its isomer **9** (12%, arising from **8**). The finding that homolytic ring opening of *trans*-**2a** gives some radical **8** besides the main isomer **3a** is in accord with the behaviour of *trans*-**1a** towards Bu_3SNH/AIBN [4]. The stereoelectronic arrangement necessary for homolysis to the more stable **3a** suffers from steric repulsion (*cf.* [4]).

Structural assignment for **6a** comes from a precise molecular mass and in particular from fragments 196 (PhCH=COHPh) and 148 (M – PhCHCOPh) in the mass spectrum. ^{1}H-NMR indicates two diastereomers in the ratio 1.6:1 and supports the structure. The formation of **6a** from *cis*-**1a** only shows the different amount of ketonic character in the *cis*-*trans* pair of **1a** as expected from steric considerations of the nitrogen inversions. Attack of **4a** on the carbonyl group of *trans*-**1a** cannot compete with proton transfer. The ketonic character of *cis*-**1a** seems to be rather pronounced as follows from the observed addition of **4a** in spite of the counter ion sodium.

No product derived from coupling of radical **3a** with $\mathbf{A}^{\cdot-}$ was detected in contrast to the respective product in the published [4] reaction of $\mathbf{A}^{\cdot-}$ with **1b** that had provided **5b** (30%), **6b** (27%) and the coupling product (13%). The N pyramid of **1b** should resemble that one of *cis*-**1a** [2].

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Experimental

Compounds *cis*-**1a,** *trans*-**1a**, **5a** and **9** are known [4] as well as **7** [5]. For details of the experimental technique and instruments used *cf.* [3].

The two experiments were performed in dry THF under dry nitrogen with continuous stirring. 6 mmol of anthracene and 5 mmol of Na were stirred in 50 ml of THF for 1 d. A solution of 2.1 mmol of *cis*-**1a** or 2.0 mmol of *trans*-**1a** in 14 ml of THF was added within 5 – 10 s. 1 ml of MeOH was added after 1 min. The residue obtained by evaporation was taken up in CH_2Cl_2 and washed with water. Evaporation of the organic layer yielded a residue which was subjected to chromatography (silica gel Merck, 0.062 – 0.2 mm, column dimensions 80 × 2 cm). Elution with CH_2Cl_2 removed hydrocarbons. Further proceeding is given below.

Reaction of *cis*-1a

Subsequent elution with ethyl acetate provided 434 mg of a mixture consisting (^{1}H-NMR) of 362 mg (72%) of **5a**, 58 mg (16%, 1.6:1 mixture of diastereomers A and B) of **6a** and 14 mg (10%) of **7**. Several attempts to separate the products from one another were unsuccessful but PLC (silica gel Merck 5545, 2 mm thick, 4 times chromatographed with ethyl acetate/CH_2Cl_2 1:50) of 30 mg provided a sample of pure **6a** (mixture of diastereomers A and B, only one of them characterized by mp obtained from a tiny crystal picked out by hand).

N-(2,3-Diphenyl-1-methyl-3-oxopropyl)benzamide (**6a**)

Mixture (1.6:1) of diastereomers A and B. *m.p.* (A or B) 48 – 50 °C. – IR: ν/cm^{-1} = 3 310 (br), 1 685, 1 640, 1 540, 1 535 (sh). – ^{1}H-NMR: δ/ppm = 1.39 (d, J = 6.9, Me of A), 1.40 (d, J = 6.7, Me of B), 4.69 – 4.77 (m, NCH of A and B), 5.03 (d, J = 4.3, COCH of A), 5.10 (d, J = 7.3, COCH of B), 7.18 – 7.59 (m, 11 ArH each of A and B), 7.70 – 7.76 (m, *o*-H of NCOPh for A and B). 7.88 – 7.98 (m, *o*-H of CCOPh each of A and B). – MS (160 °C): *m/z* = 343 (0.6, M$^+$), 238 (0.6, M – COPh), 196 (58%, PhCH=COHPh), 148 (17, M – PhCH–COPh), 105 (100, PhCO). – HRMS (EI): *m/z* (M$^+$) = 343.1573, calcd. for $C_{23}H_{21}NO_2$ 343.1572.

Reaction of *trans*-1a

Subsequent elution with ethyl acetate provided 320 mg of a mixture consisting (^{1}H-NMR) of 263 mg (55%) of **5a** and of 57 mg (12%) of **9**.

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