5*H*-DIBENZ[*b,f*]AZEPINES, PART 5. [1] COMPARATIVE STUDY OF 10,11-DIHYDRO-5*H*-DIBENZ[*b,f*]AZEPINE AND ITS ANALOGUES IN THE HYDROGEN TRANSFER DEHYDROGENATION REACTION

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Abstract---Improved hydrogen transfer reaction of 10,11-dihydro-5*H*-dibenz-[*b,f*]azepine (**1**) was elaborated and generalized to 1,2-diphenylethane (**10**) and 9,10-dihydroanthracene (**20**) analogues Kinetic constants and activation parameters were determined. Stereomutation of (*Z*)-stilbene (**11**) was achieved by supported palladium catalyst.

The 5*H*-dibenz[*b,f*]azepine (**2**) moiety is substantial in numerous pharmaceuticals, such as carbamazepine, dehydroimipramine, opipramol, etc.[2] Formation of double bond starting from 10,11-dihydro-5*H*-dibenz-[*b,f*]azepine (**1**) can be achieved by the following methods. i) oxidation by oxidising agents (e.g. sulphur, nickel peroxide),[3,4] ii.) bromination with **NBS** followed by dehydrobromination [5] iii) catalytic dehydrogenation in vapour phase [3,6] and iv.) hydrogen transfer reaction in liquid phase [7] This latter method (i e. catalytic dehydrogenation in the presence of dimethyl maleate as hydrogen acceptor and solvent) developed by R. Huisgen seems the most convenient one-step synthesis.

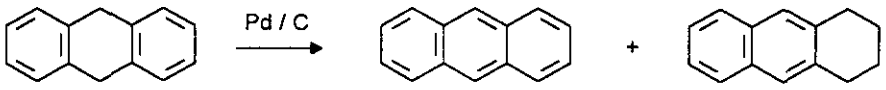
1,2-Diphenylethane (**10**) is an open-chain hydrocarbon analogue of 10,11-dihydro-5*H*-dibenz[*b,f*]azepine Dehydrogenation of compound (**10**) is characterised by moderate yields either in the oxidation reaction with **DDQ** [8] and in the photocatalytic oxidation reaction with O_2 in the presence of TiO_2 [9] or in the catalytic dehydrogenation reaction in liquid phase in the presence of palladium on charcoal. [10,11]

This article is dedicated to Professor Rolf Huisgen on the occasion of his 75th birthday

Oxidative dehydrogenation of compound 9,10-dihydroanthracene (**20**), the homoaromatic analogue of 10,11-dihydro-5*H*-dibenz[*b,f*]azepine is complete with Fe_2O_3 at 350 °C [12] and with O_2 at 70 °C catalysed by $H_5Mo_{10}V_2O_{40}$. [13] Catalytic dehydrogenation of compound (**20**) with supported palladium yields equal amounts of anthracene (**22**) and 1,2,3,4-tetrahydroanthracene (**21**) by disproportionation. [10,11]

Results and discussion

Catalytic dehydrogenation of 10,11-dihydro-5*H*-dibenz[*b,f*]azepine (**1**) and 1,2-diphenylethane (**10**) took place with Pd / C at 230 °C only in a small extent. 9,10-Dihydroanthracene (**20**) provided 41% anthracene (**22**) and 42% 1,2,3,4-tetrahydroanthracene (**21**) within 20 minutes (see Table 1) This latter reaction may be regarded as a 'hydrogen transfer' reaction, half of the starting material acts as substrate and the second half as a hydrogen acceptor The yield is 82% calculated on this assumption.



20 **22** **21**

Scheme 1

R. Huisgen performed reaction of 10,11-dihydro-5*H*-dibenz[*b,f*]azepine with dimethyl maleate and palladium black in 1 : 32 : 1.9 molar ratio and obtained 5*H*-dibenz[*b,f*]azepine between 48 and 60% [7] Our study showed that even using optimum molar ratio (1 1.5 · 0.01) at 230 °C the hydrogen transfer reactions of 10,11-dihydro-5*H*-dibenz[*b,f*]azepine and 1,2-diphenylethane with diethyl maleate and Pd / C were not complete. On the other hand, the greater reactivity of 9,10-dihydroanthracene manifested itself in a complete reaction to anthracene (**22**) within 10 minutes. (see Table 1)

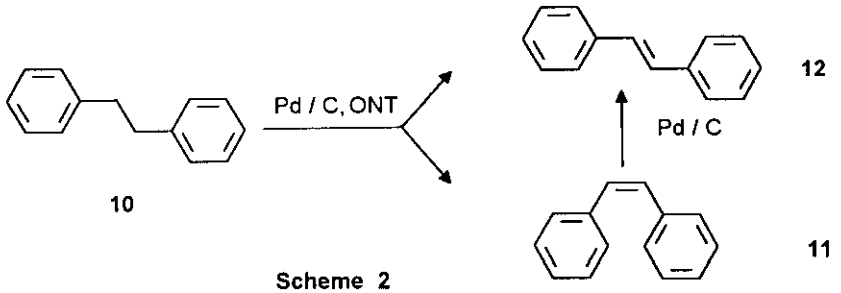
Nitroaromatic compounds, such as *o*-nitrotoluene (**ONT**) proved to be suitable hydrogen acceptors. The hydrogen transfer reactions of 10,11-dihydro-5*H*-dibenz[*b,f*]azepine (**1**) and 1,2-diphenylethane (**10**) were complete in one and a half hours using optimum molar ratio (1 0.8 0.01) at 230 °C Hydrogen transfer reaction of 9,10-dihydroanthracene (**20**) was very fast again High reactivity of 9,10-dihydroanthracene is supported by the reaction of compound (**20**) and **ONT** in the absence of catalyst Similar but less effective oxidative dehydrogenation is described in the literature with pyridine- and quinoline-*N*-oxides. [14]

Table 1 Rate of dehydrogenations of model compounds

Compound	Hydrogen acceptor	Rate $\times 10^3$ mol $l^{-1}min^{-1}$	Product [1] %	Time min
1	-	1.1	2.8	300
10	-	6.1	16 5	300
20	-	92	82 [2]	20
1	diethyl maleate	25 4	64.6	300
10	diethyl maleate	24.3	71 1	300
20	diethyl maleate	154	98 8	10
1	*o*-nitrotoluene	60.2	98.2	90
10	*o*-nitrotoluene	63.4	94 6	90
20	*o*-nitrotoluene	238	100	10
20 [3]	diethyl maleate	-	-	300
20 [3]	*o*-nitrotoluene	76 9	95.9	40

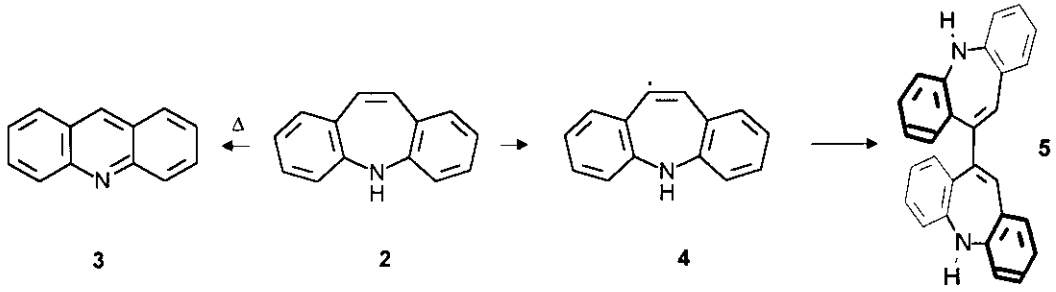
[1] Percentage was determined by glc of the reaction mixture [2] see Scheme 1 [3] in the absence of catalyst

In the hydrogen transfer dehydrogenation reaction of 1,2-diphenylethane (**10**) (*E*)-stilbene (**12**) was the sole product. Its formation can proceed *via* (*Z*)-stilbene (**11**) as well, since independent experiments showed that (*Z*)-stilbene was isomerised to (*E*)-stilbene in the presence of catalytic amount of Pd / C at 230 °C in one hour (see Scheme 2) Compound (**11**) dissolved in **ONT** remained unchanged at 230 °C High temperature and the hydrogen acceptor caused no isomerisation



Scheme 2

Side-products beside 5H-*dibenz*[b,f]*azepine* (**2**).Thermal decomposition of 5*H*-dibenz[*b,f*]azepine afforded about 1% acridine (**3**). [2] Moreover, recombination of radical (**4**) formed during partial, further dehydrogenation of 5*H*-dibenz[*b,f*]azepine (**2**) resulted 1-2% 10-(10-(5*H*-dibenz[*b,f*]azepinyl))-5*H*-dibenz-[*b,f*]azepine (**5**). (see Scheme 3) This new compound was isolated by column chromatography.[15]



3 **2** **4**

Scheme 3

Activation parameters. To get further insight into the dehydrogenation processes we have determined activation parameters of the hydrogen transfer dehydrogenation of 10,11-dihydro-5*H*-dibenz[*b,f*]azepine and 1,2-diphenylethane and of the oxidative dehydrogenation of 9,10-dihydroanthracene with *o*-nitrotoluene at the temperatures ranging from 170 to 230 °C The hydrogen transfer reactions of **1** and **10** were first order in the concentration of substrate at constant catalyst loading. The oxidative dehydrogenation of **20** was zero order Complexicity of hydrogen transfer reaction of **20** did not allow kinetic evaluation.

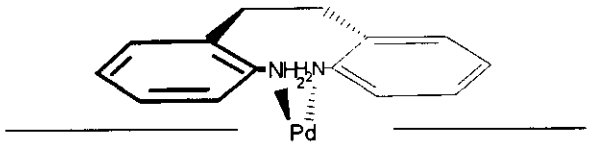
Activation enthalpies ($\Delta H^{\ddagger}$) and activation enthropies ($\Delta S^{\ddagger}$) were determined by statistical calculation of Eyring-equation. Reactivity of compounds (**1**) and (**10**) were found to be practically the same (see table 2)

Table 2 Kinetic and activation parameters

Compound	Dihydrodibenz[*b,f*] azepine	1,2-Diphenylethane	Dihydroanthracene[❶]
Rate constant $\times 10^5$ at	sec $^{-1}$	sec $^{-1}$	mol l $^{-1}$ sec $^{-1}$
170 °C	2.0	1 62	2.44
185 °C	15.5	3.67	8.13
200 °C	36.5	16 8	23.9
215 °C	49 5	25 9	37.2
230 °C	74 0	48 7	133.0
$\Delta H^{\ddagger}$ kcal mol $^{-1}$	24 3	25 0	27.5
$\Delta S^{\ddagger}$ cal degree $^{-1}$ mol $^{-1}$	-24.8	-24 6	-18.0

❶ in the absence of catalyst

In our earlier study we have examined the reactivity of substituted 10,11-dihydro-5*H*-dibenz[*b,f*]azepines.[1] Introduction of an electron donating group increased the reaction rate and the hydrogen transfer reaction completed within 20 minutes. Electron withdrawing groups caused reduction or loss of reactivity The generalisation of these results prompted us to study the reactivity of selected substituted diphenylethanes 1,2-Di-*o*-nitrophenylethane (**13**) and 1,2-di-*p*-nitrophenylethane (**14**) showed no reactivity under hydrogen transfer circumstances, similarly to 3-nitro-5acetyl-10,11-dihydro-5*H*-dibenz[*b,f*]azepine (**6**). The 1,2-di-aminophenylethanes were expected to possess higher reactivity. Indeed, 1,2-di-*p*-aminophenylethane (**15**) converted to *p,p'*-diaminostilbene (**16**) within 20 minutes. The rate of hydrogen transfer reaction was 74.2×10^{-3} mol l^{-1} min^{-1} and the conversion was 94 5% at 20 minutes.The corresponding values of 3-amino-10,11-dihydro-5*H*-dibenz[*b,f*]azepine (7) are practically the same, $74\ 2\times10^{-3}$ mol l^{-1} min^{-1} and 97.3% at 20 minutes, respectively. Surprisingly, 1,2-di-*o*-aminophenylethane (**17**) showed no reactivity, which may be explained with steric effects. Instead of planar coordination on the surface of catalyst, formation of a *cis*-amine type chelate is postulated



Cross reactions between model compounds. Enhanced reactivity of 9,10-dihydroanthracene (**20**) is a consequence of the aromatisation in the middle ring Further evidences for the greater driving force are the reactions of compound (**20**) with 5*H*-dibenz[*b,f*]azepine (**2**) and (*E*)-stilbene (**12**) as hydrogen acceptors Equimolar amounts of **20** and **2** or **12** in the presence of Pd / C at 230 °C gave 100% anthracene (**22**) and 83% 10,11-dihydro-5*H*-dibenz[*b,f*]azepine (**1**) or 87% 1,2-diphenylethane (**10**) within 20 minutes The rest of the eliminated hydrogen evolved as H_2. Similar observation is reported by american authors [16] Cross reaction between 10,11-dihydro-5*H*-dibenz[*b,f*]azepine (**1**) and(*E*)-stilbene (**12**) in the presence of Pd / C at 230 °C reached equilibrium in 40 minutes. Equlibrium molar ratio of **1** and **2** was 1:1 (Percentage of **1** and **2** were 50.4% and 49.6%, respectively Accuracy of glc determination was ● 0.5%.) Hence, equlibrium constant (*K*) is about 1 $K = [\ 2\ ]\ [\ 10\ ] / [\ 1\ ]\ [\ 12\ ] \approx 1$

In conclusion hydrogen transfer ability of 10,11-dihydro-5*H*-dibenz[*b,f*]azepine and 1,2-diphenylethane is identical in terms of kinetic and activation parameters and thermodinamic properties.

Hydrogen transfer reaction with appropriate hydrogen acceptor is the method of choice for dehydrogenation of model compounds.

General procedure . Substrate (30 mmol) was mixed with *o*-nitrotoluene (3.43 g, 25 mmol) and 10 % palladium on charcoal catalyst (0.36 g, 0.34 mmol Pd) was added. The mixture was heated to 230 °C and kept stirring for 5 h in nitrogen atmosphere. Samples were taken periodically. When the hydrogen transfer reaction stopped, the reaction mixture was diluted with acetone and catalyst was filtered. The filtrate was cooled and the solid obtained was isolated and recrystallised or filtrate was evaporated and worked-up by column chromatography.

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15. Physical and spectral data of compound (**5**) mp 247-249 °C (acetone), uv (MeOH) λ_{max}: 265 nm. ir (KBr) ν_{max} : 3361 5 ; 2961 7 ; 1608.9 , 1485.8 ; 1113.6 and 750.4 cm^{-1}, ^1H nmr (acetone-d_6, 200 MHz) δ 7.06-6.52 (m, 16H, Ar-H), 6 45-6.32 (brs, 1H, N-H), 6 06 (s, 2H, 11,11'-H), EI-ms m/z (%) 384 (M^+, 100), 192 (24), Anal Calcd for $C_{28}H_{20}N_2$: C, 87 47 , H, 5 24 , N, 7.29. Found . C, 87 3 , H, 5 3 , N, 7 6
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