

REDUCTION OF N-ACYL,N'-TOSYLHYDRAZINES WITH DIBORANE

A SIMPLE, CONVENIENT PROCEDURE FOR THE CONVERSION OF THE CARBOXYLIC TO THE METHYL GROUP

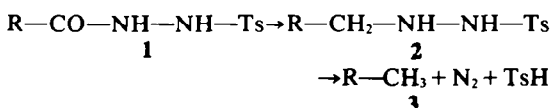
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Abstract—Aliphatic tosylhydrazides upon treatment with diborane followed by alkaline hydrolysis yield aliphatic hydrocarbons. Aromatic hydrocarbons are produced when aromatic tosylhydrazides undergo heating in presence of diborane and are subsequently oxidated by KIO₄. A discussion on the structures of intermediate products is reported.

The conversion of the carboxylic group to a methyl was earlier studied in our laboratory.¹ The most common reducing agent, LAH, was used in this reaction after conversion of the carboxylic group into the corresponding tosylhydrazide.^{2,4} This reduction constitutes a novel and effective method for converting carboxylic acids into hydrocarbons. It must be noted however that while N-acyl,N'-tosylhydrazines are reduced with good yields to hydrocarbons, N-aroil,N'-tosylhydrazines give very low yields.

The reaction in the case of tosylhydrazides previously described proceeds according to the scheme:



The tosylhydrazide (1) is first reduced to tosylhydrazine (2) which cannot be isolated and decomposes either by heating or through the action of bases to give nitrogen, hydrocarbon and *p*-toluenesulphinic acid or its derivatives. For satisfactory yields it is necessary that the carboxylic group be reduced to -CH₂- without change in the other groups present in the substrate.

The work reported here was aimed at extending the method described above to aromatic derivatives and rendering the reduction more selective, by examining the reactivity of diborane towards aliphatic and aromatic tosylhydrazides.

RESULTS AND DISCUSSION

In the reaction of N-acyl,N'-tosylhydrazines with diborane at room temperature proceeding accord-

ing to the above scheme, the N-alkyl,N'-tosylhydrazines (2) intermediate can be isolated without difficulty and in high yield. The reaction has been performed with tosylhydrazides of stearic, palmitic, miristic and 3-phenyl-propionic acids (1a-d). The corresponding N-alkyl, N'-tosylhydrazines (2a-d) were obtained pure with yields of 75-80%. The conversion to hydrocarbons (3a-d) was effected by heating 2 a-d in methanolic KOH solution with yields of 65-70%. The results obtained in the complete conversion into hydrocarbon, without isolating the intermediate, (method B, Experimental) are reported in Table 1.

The carboxylic group of a N-aroil,N'-tosylhydrazines are, in contrast, not reduced by diborane at room temperature. When this reduction is carried out at 65° a small amount of hydrocarbon is formed along a large amount of *p,p'*-ditolyl-disulphide and two principal nitrogenous products.

We have examined in detail the hot reaction of diborane with N-(1-naphthoyl), N'-tosylhydrazine (4e). As reported above, besides the theoretical quantity of *p,p'*-ditolyl-disulphide and a small amount of 1-methyl-naphthalene (7e), two major compounds containing both nitrogen and boron, were isolated.

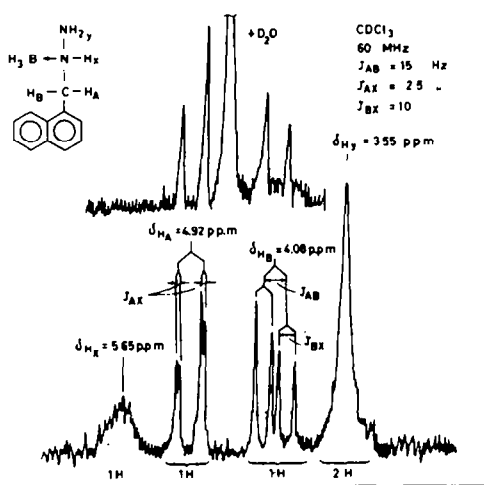
The first has the minimum formula C₁₁H₁₅N₂B, calculated from analytical data, and a molecular weight of 183, determined osmometrically, whence a monomeric structure is deduced. The IR spectrum contains a double band at 3310 and 3240 cm⁻¹ (NH stretching), a group of bands between 2350 and 2250 cm⁻¹ (BH stretching)^{5,6} while bands ascribable to the carbonyl or SO₂-group are absent. The UV spectrum is that typical of a monosubstituted naphthalenic system. The ¹H-NMR spectrum is shown in Fig 1.

In this spectrum may be noted the presence of seven aromatic protons assigned to the mono-

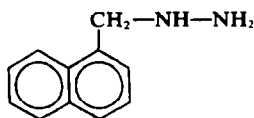
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Table 1

| R—CO—NH—NH—Ts (1) | R—CH ₃ (3) (yield %) |
|--|------------------------------------|
| a: R = n-C ₁₇ H ₃₅ | 64 |
| b: R = n-C ₁₅ H ₃₁ | 62 |
| c: R = n-C ₁₃ H ₂₇ | 64 |
| d: R = Ph-CH ₂ -CH ₃ - | 59 |

Fig. 1. ¹H-NMR spectrum of the compound 5e.

substituted naphthalene ring, and a system of the ABXY₂ type which on addition of D₂O collapses into an AB system centred at 4.44 δ with $|J_{AB}| = 15$ Hz, while simultaneously the disappearance of the other signals is observed. The presence of the above mentioned "spin system" is confirmed by double NMR measurements (not shown in Fig 1). The 15 Hz coupling constant between H_A and H_B is too large to be attributed to vic-protons while it is of the right order for gem-protons (-10: -18 Hz); furthermore the chemical shift (4.44 δ) is very close to that calculated for a -CH₂- bound to an aromatic ring and a N atom. The other three protons, which exchange with D₂O may be assigned to NH and NH₂ groups. The connection of these groups most consistent with the chemical shifts and with the spin multiplicities shown in Fig 1 is the following:

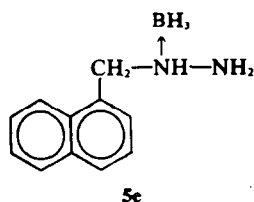


In the ¹H-NMR spectrum no significant signals ascribable to boron-linked protons can be detected. The whole proton integration, in contrast, shows

three more protons, in agreement with the presence of a BH₃-group. In fact, the BH₃-group generally gives four broad signals of relative intensities 1:1:1:1, having a high coupling constant. The presence of the BH₃-group is confirmed by the ¹¹B-NMR spectrum (Fig 2).

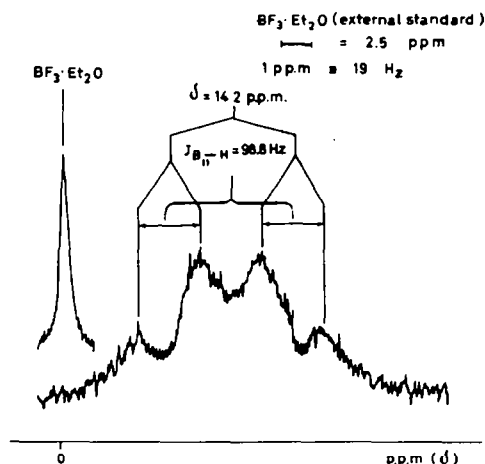
The chemical shift,^{8,9} the multiplicity (quartet of relative intensities 1:3:3:1) and the high coupling constant of the signal^{8,9} are consistent with the presence of a -NH → BH₃ group. Given that in the

¹H-NMR spectrum reported above, the methylenic protons are found to be nonequivalent, they must be adjacent to a heterosteric centre,⁷ probably due to the formation of a complex between BH₃ and the N atom of the NH-group of compound (5e). Thus the most probable structure seems to be the following:



The analytical and spectroscopic data of compound 6e (Experimental), the other one containing both nitrogen and boron, are very similar to those observed for compound 5e. Some differences are evident in the corresponding ¹H-NMR and ¹¹B-NMR spectra. In the ¹H-NMR spectrum of compound 6e, the signal singlet at 4.49 δ (2 protons) shows the equivalence of the methylenic protons (Ar-CH₂-N-), however in the ¹¹B-NMR

spectrum, the "chemical shift" of the signal of boron-11 moves to 20.8 δ *ca*. This value is very close to that reported in the literature for

Fig. 2. ¹¹B-NMR spectrum (THF) of the compound 5e.

$R-NH_2 \rightarrow BH_3$.^{8,9} The data led us to hypothesize that the compounds **5e** and **6e** are structural isomers, the latter having BH_3 bounded with the NH_2 -group.

Thus the reaction in the case of aromatic derivatives proceeds quite differently from that with aliphatic derivatives in that the reduction of the carbonyl group is accompanied or preceded by attack on the sulphonamide linkage. In the other words the reaction of tosylhydrazides of aromatic acids with diborane is marked by two principal pathways, one altogether similar to that encountered with the corresponding aliphatic compounds, leading to the formation of hydrocarbon presumably through the formation of a $N-CH_2Ar, N'$ -tosylhydrazine intermediate. This pathway explains the formation of hydrocarbon in low yields.

In the second pathway, on the other hand, there is a preceding or simultaneous attack on the sulphonamide linkage. It seems clear that the aromatic hydrazido-group has greater resistance to reduction than that of the aliphatic carbonyl group and the reaction conditions it is necessary to adopt on this account are such that the sulphonamide link is also reduced with consequent formation of a hydrazine-borane complex of type **5e** (or of a labile precursor of **5e**).

From the preparative point of view the fact that aroyl tosylhydrazines are reduced to $N-CH_2Ar, N'$ -hydrazine derivatives, has allowed the development of a method for the transformation of $-COOH$ into $-CH_3$ by oxidizing the intermediate hydrazine with inorganic oxidizing agents such as $AgNO_3$ or KIO_4 .¹⁰ This oxidation can be performed directly on the reaction mixture of tosylhydrazide with diborane as described under Experimental. Reduction with B_2H_6 in boiling THF, followed by oxidation with $AgNO_3$ or KIO_4 , has given good yields of hydrocarbons from tosylhydrazides of aromatic acids. In Table 2 are reported the results of the complete transformation of 1-naphthoic acid (**4e**), 2-naphthoic acid (**4f**) and *p*-methoxy-benzoic acid (**4g**), tosylhydrazides (method B, Experimental) to the corresponding hydrocarbons.

In conclusion the reduction of tosylhydrazides to hydrocarbons can be achieved by two methods: the first consisting in treatment at room temperature of aliphatic tosylhydrazides with diborane in THF, followed by hydrolysis of the excess B_2H_6 with methanolic KOH and subsequent heating to convert the alkyl tosylhydrazine intermediate into

hydrocarbon; the second in treating aromatic tosylhydrazide with B_2H_6 in boiling THF and "in situ" oxidation of the reaction intermediate into the corresponding hydrocarbon.

EXPERIMENTAL

Apparatus. All diborane reductions were performed in a 3-neck flask equipped with a magnetic stirrer, thermometer, reflux condenser and gas dispersion tube to inlet diborane. Hydrogen evolution was measured by attaching a series of burets through a dry-ice trap to the outlet of the condenser.

Equipment. IR spectra were recorded as film or KBr pellets with a Perkin-Elmer Model 337 and Model 621 grating spectrophotometers. NMR spectra were obtained with a Jeolco 60-HL spectrometer. TMS was used as an internal standard in the 1H -NMR spectra while $BF_3 \cdot Et_2O$ was used in the ^{11}B -NMR spectra as an external standard. All mps reported are uncorrected. The molecular weights were determined by a Hewlett-Packard 302 B Osmometer. Analytical data (% C, H and N) of **2a-d** are in agreement with the proposed structures. Gas-chromatographic analyses were performed on a Varian Aerographs Model 1440, using 3% SE-30 on C.W. 80-100 mesh (column A, 1 = 2 m) and Al_2O_3 Woelm 80-100 mesh (column B, 1 = 1 m) (GSC).

Reagents. Diborane was generated as described by Brown¹¹ and solutions of diborane in THF were prepared and standardized. THF was purified by the method of Feuer and Savides.¹² Dimethyl ether of diethylene glycol was purified by treatment with CaH_2 for 24 h, followed by decantation and vacuum distillation from LAH.

The starting tosylhydrazides (**1a-d**; **4e-g**) were obtained by reaction between tosylhydrazine and the corresponding acid chloride and then purified by recrystallization.

N-Alkyl, N'-tosylhydrazines from N-acyl, N'-tosylhydrazines

N-Octadecyl, N'-tosylhydrazine (2a). The following experiment is typical of the procedure employed for preparing N-alkyl, N'-tosylhydrazines. To a soln of **1a** (1.0 g, 2.2 mmol) in anhyd THF (5 ml), in Argon atmosphere, was added at room temp by syringe, a soln 3N of borane in THF (7 ml, 21.0 mmol of hydride). The mixture was left stirring for 24 h and then MeOH (30 ml) was added. After 30' the soln was evaporated under reduced press and hexane added to the residue. On cooling, crystals of (**2a**) were obtained (75-80% yield). An analytical sample, recrystallized from CH_2Cl_2 -hexane, shows m.p. 88-89° (dec); IR (nujol): 3310-3180 (multiplet, ν_{NH}); 1320, 1160 (ν_{SO_2}); 1600, 815 ($p-C_6H_4$); cm^{-1} . 1H -NMR: ($CDCl_3$) δ , 7.63 (q, 4 H, AA'BB', $J_{AB} = 8$ Hz, $p-C_6H_4$); 3.70 (bs, 1 H, D_2O exchange, $Ts-NH-NH-R$); 2.73 (t, 2 H, $-CH_2-N-N-$); 2.50 (s, 3 H, CH_3-Ar); 1.25 (m, 32 H, $-(CH_2)_{16}-$) and 0.90 (t, 3 H, $CH_3-(CH_2)_n-$), ppm; ($^2H_2-DMSO$) δ , 8.40 (bs, 1 H, D_2O exchange, $Ts-NH-N-$), ppm.

N-Hexadecyl, N'-tosylhydrazine (2b), was prepared as above described for **2a**, starting from **1b**, yield 70%, mp 77-79° (dec) (CH_2Cl_2 -hexane); IR (nujol): 3310-3180 (multiplet, ν_{NH}); 1320, 1150 (ν_{SO_2}); 1600, 815 ($p-C_6H_4$), cm^{-1} . 1H -NMR: ($CDCl_3$) δ , 7.50 (q, 4 H, AA'BB', $J_{AB} = 8$ Hz,

Table 2.

| $Ar-CO-NH-NH-Ts$ (4) | $Ar-CH_3$ (7) |
|-------------------------------|------------------------|
| (yield %) | |
| e: Ar = 1-naphthyl | 44 |
| f: Ar = 2-naphthyl | 30 |
| g: Ar = $p-CH_3O-C_6H_4-$ | 40 |

p -C₆H₄); 3.30 (bs, 1 H, D₂O exchange, Ts—NH—NH—R); 2.62 (t, 2 H, $J = 6$ Hz, —CH₂—N—N—); 2.40 (s, 3 H, CH₃—Ar); 1.26 (m, 28 H, —(CH₂)₄—); 0.88 (t, 3 H, CH₃—(CH₂)_n—), ppm; (²H_c—DMSO) δ , 8.40 (bs, 1 H D₂O exchange, Ts—NH—N—).

N-Tetradecyl, *N'*-tosylhydrazine (2c), was prepared as above from 1c, yield 80%, mp 65–66°(dec) (CH₂Cl₂-hexane). IR (nujol): 3310–3180 (multiplet, ν_{NH}); 1320, 1160 (ν_{SO_2}); 1600, 815 (p -C₆H₄), cm⁻¹. ¹H-NMR: (CDCl₃) δ , 7.50 (q, 4 H, AA'BB', $J_{AB} = 8$ Hz, p -C₆H₄); 3.70 (bs, 1 H, D₂O exchange, Ts—NH—NH—R); 2.65 (t, 2 H, $J = 6$ Hz, —CH₂—N—); 2.42 (s, 3 H, CH₃—Ar); 1.28 (m, 24 H, —(CH₂)₁₂—); 0.89 (t, 3 H, CH₃—(CH₂)_n—), ppm; (²H_c—DMSO) δ , 8.40 (bs, 1 H, D₂O exchange, Ts—NH—N—).

N-(3-Phenyl-propyl), *N'*-tosylhydrazine (2d), from 1d, yield 65%, mp 80–82°(dec) (CH₂Cl₂-hexane). IR (KBr): 3300–3215 (multiplet, ν_{NH}); 1320, 1160 (ν_{SO_2}); 1600, 815 (p -C₆H₄), cm⁻¹. ¹H-NMR: (CDCl₃) δ , 7.40 (m, 9 H, p -C₆H₄, C₆H₅); 2.65 (t, 2 H, $J = 7.5$ Hz, —CH₂—CH₂—N—); 2.50 (t, 2 H, $J = 7.5$ Hz, —CH₂—CH₂—C₆H₅); 2.36 (s, 3 H, CH₃—Ar); 1.68 (m, 2 H, Ph-CH₂—CH₂—CH₂—N—), ppm; (²H_c—DMSO) δ , 8.47 (bs, 1 H, D₂O exchange, Ts—NH—N—), ppm.

Aliphatic Hydrocarbons (3a-d)

(A) *From N-alkyl, N'-tosylhydrazines.* In a typical experiment, 2a (4.0 g) was refluxed for 1 h with a 1 N methanolic soln of NaOH (100 ml). The mixture was extracted with hexane. The collected extracts were dried (Na₂SO₄) and evaporated under reduced pressure to give crude 3a in a 63% yield. (The total yield was determined by gas chromatography, column A, using *n*-tetradecane as internal standard). The crude product was purified by filtration on a small column of silica gel, eluting with hexane. The remaining hydrocarbons (3b, c, d) were obtained in a similar way. The structures were determined by direct comparison with authentic samples (IR, NMR, GSC by column B, mass-spectra and TLC/AgNO₃).

(B) *From N-acyl, N'-tosylhydrazines.* The following experiment is typical of the procedure employed for preparing hydrocarbons directly from *N*-acyl, *N'*-tosylhydrazines. The reaction was carried out similarly to that reported for 2a. In the present case, the mixture was left for 24 h and then added of MeOH (20 ml) and finally maintained under magnetic stirring for 30'. To the mixture was added a 20% methanolic soln of KOH till pH 8.9 and then refluxed for 1 h. The resulting soln was extracted with hexane. The collected extracts were dried and finally evaporated under reduced pressure. The yields are reported in Table 1.

Treatment of *N*-(1-naphthoyl), *N'*-tosylhydrazine (4e) with diborane

Compound (4e) (2.0 g, 6.0 mmol) was treated with a 3 N soln of borane in THF (44 ml, 132 mmol of hydride), in Argon atmosphere. The mixture was refluxed for ca 13 h adding the soln of borane (5 ml) every 4 h in order to maintain an excess of borane. The soln was cooled then MeOH added and maintained under magnetic stirring for

30'. The residue obtained after evaporation of the solvents was chromatographed on a silica gel column (0.05–0.2 mm), using CHCl₃ as eluant.

1-Methyl-naphthalene (7e), in very small amount was first eluted and compared with an authentic sample.

p,p'-Ditolyl-disulphide, was then eluted and purified by recrystallization to give white needles with mp 48° (CH₂Cl₂-hexane). IR, NMR spectra and elemental analyses are in good agreement with the data obtained with an authentic sample.

Compound (5e), practically pure, was then eluted and recrystallized to give white crystals, mp 124–125° (CH₂Cl₂-hexane). IR (KBr): 3310, 3240 (ν_{NH}); 2350, 2280 (sh), 2250 (ν_{BH}); 1570 (arom), cm⁻¹. ¹H-NMR (CDCl₃), ¹³B-NMR (THF) reported in Figs 1 and 2 respectively. (Found: C, 71.24; H, 7.87; N, 15.05. C₁₁H₁₂N₂B, M.W. 185.8, requires: C, 71.06; H, 8.07; N, 15.06%.) Molecular weight: 183 (vapor pressure osmometer, 1,2-dichloroethane).

A mixture containing 5e as major component together with (6e) was then eluted from the column.

Compound 6e, practically pure, was finally eluted and purified by recrystallization to give white crystals, mp 118–119° (CH₂Cl₂-hexane). IR (KBr): 3250, 3200 (ν_{NH}); 2380, 2340 (sh), 2280 (ν_{BH}); 1575 (arom), cm⁻¹. ¹H-NMR (CDCl₃); δ , 8.20–7.30 (m, 7 H, naphthyl); 5.00 (m, 2 H, D₂O exchange, —NH₂); 4.49 (s, 2 H, Ar—CH₂—N—), ppm;

¹³B-NMR(THF): δ , +20.8(q, 1 B, ratio 1:3:3:1, $J_{BH} = 94$ Hz), ppm; (Found: C, 71.31; H, 7.84; N, 15.04. C₁₁H₁₂N₂B requires: C, 71.06; H, 8.07; N, 15.06%.)

Aromatic Hydrocarbons (7e-g)

(A) *From compounds (5e) or 6e.* Compounds 5e or 6e were hydrolysed with dil HCl by refluxing for 30', then alkalized and oxidized with an excess of KIO₄ under reflux for 3 h. The mixture was extracted with hexane. The collected extracts were dried, then evaporated under reduced pressure. The residue from the extraction was purified by filtration on a small column of silica gel eluting with hexane and was identified as 7e by comparison with an authentic sample, yield ca 50% (calculated by GLC, column A). In alternative procedure, AgNO₃ in acetonitrile soln was employed as oxidizing agent, yield ca 42%.

(B) *From N-aryl, N'-tosylhydrazines (4e-g).* In order to obtain aromatic hydrocarbons directly without isolation of intermediates it is necessary to follow the procedure described above in the case of the treatment of 4a with diborane. In the present case, the mixture was treated with MeOH and stirred for ca 30'. After acidification with dil HCl, the soln was refluxed for 30' then cooled, alkalized with 20% NaOH aq and finally oxidized by refluxing for 3 h with an excess of KIO₄. The resulting mixture was extracted with CH₂Cl₂ several times. The collected extracts after drying, were evaporated under reduced pressure. The residue obtained was chromatographed on a silica gel column (0.05–0.2 mm) using hexane as eluant. 1-Methyl-naphthalene was eluted in the early fractions. The remaining hydrocarbons (7f, g) were obtained in a similar way. The structures were determined by direct comparison with authentic samples (IR, NMR, GLC by column A and mass-spectra). The relative yields are reported in Table 2.

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