Aminopyrazoles. V [1]. Structure Assignment of 1*H*-Pyrazol-3- and 5-amines by Means of the ^{1}H NMR δ(4-H)-Values of Their *exo*-*N*-Toluenesulfonyl Derivatives

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From the extent of the low field chemical shift of 4-H caused by *exo*-*N*-tosylation of 1-substituted 1*H*-pyrazolamines it is possible to distinguish between the 3- and 5-amino-isomers. The pyrazole substituent increment system of Tensmeyer and Ainsworth has been extended to 3- and 5-amino, 3- and 5-tosylamino, 1-benzyl and 1-tosyl substituents. By comparison of δ(4-H) values, calculated with the aid of these increments, with measured δ(4-H) values, a differentiation between 3- and 5-tosylaminopyrazoles but not between 3- and 5-aminopyrazoles can be made.

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Many reactions of monosubstituted hydrazines lead to 1-substituted pyrazol-3- or 5-amines the structure of which cannot be predicted unequivocally [1-3]. Therefore an independent structure assignment is necessary. Proton resonance spectroscopy can be successfully applied in the following cases: i) Presence of vicinal pyrazole-hydrogens by means of the coupling constant measurement [4,5]; ii) 5- or 3-unsubstituted pyrazol-3- or 5-amines by determination of the chemical shift difference of either 5-H or 3-H in two solvents (method of Jacquier and Elguero [6,7]).

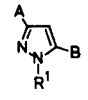
No structure determination for pyrazol-3- or 5-amines unsubstituted only in the 4-position was hitherto known by means of ^{1}H nmr. In this communication we present two ^{1}H nmr methods for structure determinations of C-4 unsubstituted pyrazolamines using their *exo*-*N*-toluenesulfonyl derivatives.

Method A: Influence of *exo*-*N*-Monotosylation on the Chemical Shift of 4-H in Pyrazol-3- and 5-amines **1a-i, 2a-g, 2j-k**.

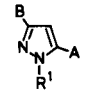
Δδ(NHTos − NH_2) (4-H)-values defined as the difference δ(NHTos) − δ (NH_2) are located in two different ranges (0.11-0.24 and 0.57-0.72) which are significantly separated (see Table 1). With the exception of **2b** and **2e** (R^1 = C_6H_5) δ-values in the range of 0.57-0.72 with mean of 0.67 correspond to the pyrazol-3-amine-structure **1** and those with Δδ-values in the range of 0.11-0.24 with mean of 0.17 to the pyrazol-5-amine-structure **2**. (The exceptional behavior of compounds **2b** and **2e** will be discussed later.) The fact that the influence of the tosyl group on the chemical shift of the neighbouring hydrogen 4-H is greater in the 3-aminopyrazoles in comparison with 5-aminopyrazoles is due to less compensation of the electron-withdrawing inductive effect of the tosyl group by the mesomeric donor effect of the *exo*-nitrogen.

Method B: Comparison of the 4-H ^{1}H-Chemical Shift of Aminotosylated Pyrazol-3- and 5-amines **1 Tos** and **2 Tos** with Calculated Values Based on an Increment System.

In 1966 Tensmeyer evaluated an increment system for the calculation of the 4-proton chemical shift δ(4-H) in 1*H*-pyrazoles [4]. With the exception of the phenyl-group in 3- or 5-position the values of the substituents at C-3 and C-5 do not differ enough in order to give a significant discrimination necessary for a structural assignment of the two possible isomers **3-A, 5-B** or **5-A, 3-B**.



3-A,5-B



5-A,3-B

Increments have not been evaluated for amino- or tosylamino-substituents. In this section we present the extension of the Tensmeyer increment system [4] to other substituents as for instance NH_2 and NH-Tos in 3 and 5 position, $C_6H_5CH_2$ and Tos in 1 position (Tos = 4-toluenesulfonyl).

Increment-values for these substituents are tabulated in Table 2 together with some others of the Tensmeyer table. Whereas the values for the amino group in 3 or 5 position nearly coincide, those of the tosylamino group are notably different. This difference proved to be sufficient for structure assignment by comparison of the calculated with the experimental δ(4-H)-values.

The increments have been obtained from a series of 38 pyrazoles of unequivocal structure by multilinear regression analysis. In Table 3 experimental and calculated δ(4-H)-values are listed for comparison. Whereas the calcula-

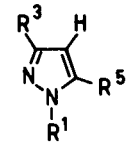
List 1

Combinations of Vicinal Substituents with Steric and Electronic Interaction

R^1	R^5
1-Tos	5-NH_2
1-C_6H_5	5-NH_2
1-C_6H_5	5-NHTos

Table 1

Chemical Shift Difference $\Delta\delta$ of 4-H Between *exo-N*-Tosylated Pyrazolamine and the Corresponding Pyrazolamine in Deuteriochloroform



	R^3		R^5
1	NH_2	2	NH_2
1 Tos	NHTos	2 Tos	NHTos

Pair of Compounds	R^1	R^5 in **1** R^3 in **2**	$\Delta\delta$ (NHTos − NH_2) exp.	(4-H) calcd.
1a, 1aTos	CH_3	H	0.72	0.67
1b, 1bTos	C_6H_5	H	0.62	0.67
1c, 1cTos	CH_2-C_6H_5	H	0.70	0.67
1d, 1dTos	CH_3	CH_3	0.62	0.67
1e, 1eTos	C_6H_5	CH_3	0.57	0.67
1f, 1fTos	CH_3	C_6H_5	0.67	0.67
1g, 1gTos	C_6H_5	C_6H_5	0.67	0.67
1h, 1hTos	Tos	H	0.70	0.67
1i, 1iTos	Tos	CH_3	0.64	0.67
2a, 2aTos	CH_3	H	0.17	0.18
2b, 2bTos	C_6H_5	H	0.59 [a]	0.18
2c, 2cTos	CH_2-C_6H_5	H	0.11	0.18
2d, 2dTos	CH_3	CH_3	0.17	0.18
2e, 2eTos	C_6H_5	CH_3	0.55 [a]	0.18
2f, 2fTos	CH_3	C_6H_5	0.14	0.18
2g, 2gTos	C_6H_5	C_6H_5	0.31	0.18
2j, 2jTos	CH_2-C_6H_5	CH_3	0.24	0.18
2k, 2kTos	CH_2-C_6H_5	C_6H_5	0.22	0.18

[a] Deviation because of steric or electronic reasons.

ted δ(4-H)-values of nearly all examples fit the experimental values, there are some exceptions, marked with [a] in Table 3, in the case of the following vicinal substituents R^1, R^5 (see List 1).

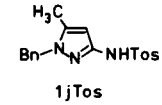
In these combinations additivity of incremental contributions is disturbed for sterical or electronic reasons of the vicinal substituents and therefore these compounds have not been used in the regression analysis.

With the increments α of NH_2 and NHTos the difference $\Delta\delta$(NHTos, NH_2) (4-H) = δ(NHTos) − δ(NH_2) for 4-H is calculable too and amounts to 0.67 for the pyrazol-3-amine structure **1** and 0.18 for the pyrazol-5-amine structure **2** (see Table 1). Thus $\Delta\delta$-values near 0.67 are demonstrating to a pyrazol-5-amine structure **1** and those near 0.18 to a pyrazol-3-amine structure **2**. Deviations from these characteristic values (0.67 and 0.18) are found in cases with the combinations of List 1.

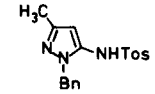
Application of the Extended Increment System for Structural Assignment to One of the Isomeric Pyrazol-3- or 5-Amines (Method B).

Example **2j** in Table 1.

In the reaction of benzylhydrazine with 2,3-dichlorobutanenitrile we isolated 1-benzyl-3-methylpyrazol-5-amine (**2j**) by column chromatography [1]. On distillation of the crude reaction product instead of column chromatography, we obtained a semicrystalline mass, an aliquot of which was used for tosylation, in order to get a crystalline product. The working up after a reaction time of 3 hours yielded a crystalline monotosyl-product with one of the following structures **1jTos** or **2jTos**.



1jTos



2jTos

Bn = CH_2-C_6H_5 Tos = SO_2-C_6H_4-CH_3

δ(4-H)$_{calcd}$ = 6.06
δ(4-H)$_{exp}$ = 6.12

δ(4-H)$_{calcd}$ = 5.53
δ(4-H)$_{exp}$ = 5.60

The experimental value for δ(4-H)$_{exp}$ is 6.12, which is in better agreement with the calculated δ(4-H)$_{calcd}$-value for **1jTos** compared to **2jTos**. Consequently the above crude

Table 2

δ(4-H) Chemical Shift Increments α_i for Substituents in Position i of the 1*H*-Pyrazole System

$$\delta(4\text{-H}) = 5.79\ [a] + \alpha_1 + \alpha_3 + \alpha_5$$

Substituent	α_1	a_3	α_5
CH_3 [b,c]	0.	0.	0.
C_2H_5 [c]	−0.02	0.02	0.02
H [c]	0.03	0.21	0.23
C_6H_5 [c]	0.22	0.51	0.30
CH_2-C_6H_5	0.03	—	—
NHTos	—	0.24	−0.29
NH_2	—	−0.43	−0.47
Tos	0.17	—	—

[a] Reference value for deuteriochloroform as solvent. [b] $\alpha_i = 0.$ by definition. [c] Increments α_i from lit [4].

distillate contained also 1-benzyl-5-methylpyrazol-3-amine as a by-product. On tosylation of pure 1-benzyl-3-methylpyrazol-5-amine **2j** the monotosylated **2jTos** is obtained whose experimental δ(4-H)-value with 5.60 is in good agreement with the calculated one of 5.53. For compound **2jTos** the Δδ(NHTos − NH_2) (4-H)-value amounts to 0.24 (Table 1) in good agreement with the calculated characteristic value of 0.18 for the pyrazol-5-amine structure **2** (see Table 1).

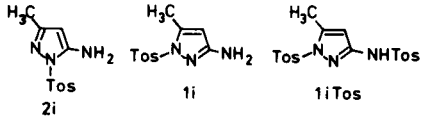
Example **1i** of Table 1.

On tosylation of 3(5)-methylpyrazol-5(3)-amine a mixture of alkaline insoluble monotosylated products (**1i** + **2i**) (40%) and of alkaline soluble material **1iTos** (10%) is obtained. Further separation of the alkaline insoluble fraction by column chromatography yielded two isomeric monotosylated products **X** and **Y** for which structure assignment **1i** respectively **2i** could be made by application of Method B:

δ_{calc}(4-H, **1i**) = 5.53
δ_{calc}(4-H, **2i**) = 5.49†
δ_{exp}(4-H, substance **X**) = 5.56
δ_{exp}(4-H, substance **Y**) = 5.17

†According to Table 3 this value is calculated too high for the combination 1-Tos, 5-NH_2 on an average of 0.35.

The assignment **X** = **1i**, **Y** = **2i** is in better agreement with the experimental values than the reversed combination.



This structure assignment is also supported by an independent synthesis of **2i** from 3-aminobut-2-enenitrile with tosylhydrazine. Likewise the structure of the ditosyl compound **1iTos** could be gained by comparison of the experimental δ(4-H) = 6.20 with the calculated value of 6.20 for **1iTos**. For the alternate structure 3-methyl-1-tosyl-5-tosylaminopyrazole a δ(4-H) of 5.67 was calculated. Further indication for this to be the correct assignment are the $^4J_{H,H}$ coupling constants $^4J_{(4\text{-}H,5\text{-}CH_3)}$ = 0.88 Hz for the compounds **1i** and **1iTos** whereas no analogous coupling exists in **2i**. It should be noted that the introduction of the electron withdrawing tosyl group at the exo amino position does not alter the size of the ^4J − coupling constant.

Comparison of Methods A and B.

Method A can only be applied if the δ(4-H) values of both the free aminopyrazole and its tosyl derivative have been determined. Method B, however, requires only $\delta(4\text{-H})_{exp}$ of the exo-tosyl derivative provided that the increment values of all substituents are known.

EXPERIMENTAL

Melting points were determined on a BOCK-Monoscope and are uncorrected. They are given together with yields, ^{1}H nmr and elemental analysis in Table 4. The ^{1}H nmr spectra were recorded on Varian EM 360 and 390 spectrometers at 60 MHz or 90 MHz, respectively.

General Procedure for the Preparation of the Tosylaminopyrazoles **1a-gTos, 2b-gTos, 2j-kTos.**

The corresponding pyrazolamine (2 mmoles) and 4-toluenesulfonylchloride (2 mmoles) have been dissolved separately in 3 ml of pyridine distilled from barium oxide for drying. The solutions were combined and allowed to stand overnight at room temperature. The solution was then poured on a mixture of 30 ml of 2*N* hydrochloric acid and the same volume of crushed ice. The precipitate was filtered by suction and thoroughly washed with water. After drying in a vacuum desiccator over phosphorus(V) oxide the crude product was recrystallized. The yields, the melting points, the solvents for recrystallization, the ^{1}H nmr and the elemental analysis are listed in Table 4.

1,5-Diphenylpyrazol-3-amine (**1g**).

A mixture of ethyl 3-amino-1,5-diphenylpyrazole-4-carboxylate [18] (8 g, 26 mmoles), 4*N* aqueous sodium hydroxide (200 ml) and ethanol (100 ml) were refluxed for 2.5 hours and allowed to stand overnight. After acidification with concentrated hydrochloric acid the free carboxylic acid precipitated (6.1 g, 76%), a sample of which was recrystallized from ethanol, mp 211° dec.

Anal. Calcd. for $C_{16}H_{15}N_3O_2 \cdot 3/5C_2H_5OH$: C, 67.31; H, 5.45; N, 13.69. Found: C, 67.10; H, 5.43; N, 13.53.

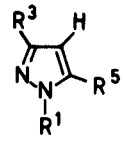
The dry crude product (5.5 g, 18 mmoles) was decarboxylated by heating above the melting point. After cooling, the solid was recrystallized from benzene to yield 3.6 g (85%) of compound **1g**, mp 139°, (lit [19] 136-137°).

Tosylation of 3(5)-Methylpyrazol-5(3)-amine.

A mixture of 3(5)-methylpyrazol-5(3)-amine (1.8 g, 18.5 mmoles), 4-toluenesulfonyl chloride (3.52 g, 18.5 mmoles) and dry pyridine (14 ml) was allowed to stand at room temperature for 20 hours. The solution was then poured on a mixture of 2*N* hydrochloric acid (200 ml) and crushed ice (200 ml) producing a precipitate which was filtered by suction, thoroughly washed with water and air dried. This crude product was slurrished in cold 2*N* aqueous sodium hydroxide, the suspension was filtered by suction through a glass filter funnel yielding 2.15 g (46%) of alkaline insoluble material of which 1 g was chromatographed on silica gel (150 g) with dichloromethane/methanol 20/1 v/v as eluent. The fraction with R_f = 0.74 contained 3-methyl-1-tosylpyrazol-5-amine (**2i**) (0.57 g, 26%) and

Table 3

Chemical Shifts δ for 4-H of 1-Substituted Pyrazoles in Deuteriochloroform



Compound	R^1	R^3	R^5	δ(4-H) exp.	δ(4-H) calcd.	Difference (calcd. − exp.)	Lit
1a	CH_3	NH_2	H	5.53	5.59	0.06	[3]
1aTos	CH_3	NHTos	H	6.25	6.26	0.01	
1b	C_6H_5	NH_2	H	5.82	5.81	−0.01	[2]
1bTos	C_6H_5	NHTos	H	6.44	6.48	0.04	
1c	$CH_2C_6H_5$	NH_2	H	5.57	5.58	0.01	[3]
1cTos	$CH_2C_6H_5$	NHTos	H	6.27	6.29	0.02	
1d	CH_3	NH_2	CH_3	5.38	5.36	−0.02	[1]
1dTos	CH_3	NHTos	CH_3	6.00	6.03	0.03	
1e	C_6H_5	NH_3	CH_3	5.63	5.58	−0.05	[1]
1eTos	C_6H_5	NHTos	CH_3	6.20	6.25	0.05	
1f	CH_3	NH_2	C_6H_5	5.66	5.66	0.	[1]
1fTos	CH_3	NHTos	C_6H_5	6.33	6.33	0.	
1g	C_6H_5	NH_2	C_6H_5	5.87	5.88	0.01	
1gTos	C_6H_5	NHTos	C_6H_5	6.54	6.55	0.01	
1h	Tos	NH_2	H	5.80	5.76	−0.04	[8]
1hTos	Tos	NHTos	H	6.50	6.43	−0.07	[9]
1i	Tos	NH_2	CH_3	5.56	5.53	−0.03	
1iTos	Tos	NHTos	CH_3	6.20	6.20	0.	
1jTos	$CH_2C_6H_5$	NHTos	CH_3	6.12	6.06	−0.06	
2a	CH_3	H	NH_2	5.50	5.53	0.03	[1]
2aTos	CH_3	H	NHTos	5.67	5.71	0.04	[10]
2b	C_6H_5	H	NH_2	5.56	5.75	(0.19) [a]	[2]
2bTos	C_6H_5	H	NHTos	6.15	5.93	(−0.22) [a]	
2c	$CH_2C_6H_5$	H	NH_2	5.56	5.50	−0.06	[1]
2cTos	$CH_2C_6H_5$	H	NHTos	5.67	5.74	0.07	
2d	CH_3	CH_3	NH_2	5.33	5.32	−0.01	[11]
2dTos	CH_3	CH_3	NHTos	5.50	5.50	0.	
2e	C_6H_5	CH_3	NH_2	5.43	5.54	(0.11) [a]	[12]
2eTos	C_6H_5	CH_3	NHTos	5.98	5.72	(−0.26) [a]	
2f	CH_3	C_6H_5	NH_2	5.83	5.83	0.	[13]
2fTos	CH_3	C_6H_5	NHTos	5.97	6.01	0.04	
2g	C_6H_5	C_6H_5	NH_2	5.92	6.05	(0.13) [a]	[14]
2gTos	C_6H_5	C_6H_5	NHTos	6.52	6.23	(−0.29) [a]	
2h	Tos	H	NH_2	5.33	5.70	(0.37) [a]	[8]
2i	Tos	CH_3	NH_2	5.17	5.49	(0.32) [a]	
2j	$CH_2C_6H_5$	CH_3	NH_2	5.36	5.35	−0.01	[1]
2jTos	$CH_2C_6H_5$	CH_3	NHTos	5.60	5.53	−0.07	
2k	$CH_2C_6H_5$	C_6H_5	NH_2	5.88	5.86	−0.02	[15]
2kTos	$CH_2C_6H_5$	C_6H_5	NHTos	6.10	6.04	−0.06	
2l	Tos	C_6H_5	NH_2	5.65	6.00	(0.35) [a]	
3a	$CH_2C_6H_5$	CH_3	CH_3	5.80	5.82	0.02	[16]
3b	$CH_2C_6H_5$	H	H	6.17	6.26	0.09	[4]
3c	$CH_2C_6H_5$	C_6H_5	C_6H_5	6.68	6.63	−0.05	
4a	Tos	CH_3	CH_3	5.88	5.96	0.08	[17]
4b	Tos	H	H	6.35	6.40	0.05	[17]
4c	Tos	C_2H_5	C_2H_5	5.96	6.00	0.04	[17]
4d	Tos	CH_3	H	6.20	6.19	−0.01	[17]

[a] Deviation, not used for the calculation of increments α_i.

Table 4

Physical Data of the Pyrazoles of the Experimental

Compound	Yield (%)	Mp (°C) (recrystallized)	^{1}H NMR (deuteriochloroform)	Molecular Formula (molecular weight)	Analysis % Calcd./Found C	H	N	S
1aTos	52	137-138.5 (1-propanol)	7.08-7.73 (m, 5H, C_6H_4, 5-H), 6.25 (d, 1H, 4-H, J = 2.5 Hz), 3.83 (s, 3H, N-CH_3), 2.38 (s, 3H, CH_3)	$C_{11}H_{13}N_3O_2S$ (251.31)	52.57 52.75	5.21 5.17	16.72 17.02	12.76 12.79
1bTos	96	125-126 (1-propanol)	7.0-7.8 (m, 11H, 1H exchangeable, NH, 5-H, C_6H_5, -C_6H_4-), 6.44 (d, 1H, J = 2.7 Hz, 4-H), 2.34 (s, 3H, -CH_3)	$C_{16}H_{15}N_3O_2S$ (313.38)	61.32 61.23	4.82 5.11	13.41 13.15	10.23 10.21
1cTos	88	165-168 (1-propanol)	9.7 (s, 1H, NH, exchangeable), 6.87-7.58 (m, 10H, C_6H_5, 5-H, -C_6H_4-), 6.27 (d, 1H, J = 2.6 Hz, 4-H), 5.25 (s, 2H, -CH_2-), 2.35 (s, 3H, -CH_3)	$C_{17}H_{17}N_3O_2S$ (327.41)	62.37 62.18	5.23 5.42	12.83 13.05	9.79 9.75
1dTos	75	208-209 (ethanol)	10.3 (s, 1H, NH), 7.58 (d, 2H, J = 8.7 Hz, *ortho*-protons), 7.14 (d, 2H, J = 8.7 Hz, *meta*-protons), 6.00 (s, 1H, 4-H), 3.69 (s, 3H, N-CH_3), 2.36 (s, 3H, CH_3), 2.18 (s, 3H, 5-CH_3)	$C_{12}H_{15}N_3O_2S$ (265.34)	54.32 54.41	5.70 5.80	15.84 15.38	12.08 11.98
1eTos	76	110 (PE/ether 5/1)	8.6 (s, broad, 1H, NH), 7.67 (d, 2H, J = 8.4 Hz, *ortho*-protons), 7.42 (s, 5H, C_6H_5), 7.26 (d, 2H, J = 8.4 Hz, *meta*-protons), 6.20 (s, 1H, 4-H), 2.40 (s, 3H, CH_3), 2.26 (s, 3H, 5-CH_3)	$C_{17}H_{17}N_3O_2S$ (327.41)	62.37 62.15	5.23 5.51	12.83 12.72	9.79 9.82
1fTos	52	183-184 (1-propanol)	9.93 (s, broad, 1H, NH, exchangeable), 7.68 (d, 2H, J = 8.4 Hz, *ortho*-protons), 7.42 (s, 5H, 5-C_6H_5), 7.20 (d, 2H, J = 8.4 Hz, *meta*-protons), 6.33 (s, 1H, 4-H), 3.83 (s, 3H, N-CH_3), 2.39 (s, 3H, CH_3)	$C_{17}H_{17}N_3O_2S$ (327.41)	62.37 62.47	5.23 5.51	12.83 12.56	9.79 9.70
1gTos	98	227 (1-propanol)	7.77 (d, 2H, J = 8.6 Hz, *ortho*-protons), 7.11-7.38 (m, 12H, 5-C_6H_5, N-C_6H_5, *meta*-protons), 6.53 (s, 1H, 4-H), 2.40 (s, 3H, CH_3), 1.9 (s, broad, NH)	$C_{22}H_{19}N_3O_2S$ (389.48)	67.85 68.12	4.92 5.20	10.97 10.97	8.23 8.47
1h	90	181 (ethanol)	7.80 (d, J = 2.93 Hz, 5-H) together with 7.79 (d, J = 8 Hz, *ortho*-protons, 3H), 7.63 (d, 2H, J = 8 Hz, *meta*-protons), 5.80 (d, 1H, J = 2.93 Hz, 4-H), 3.94 (s, 2H, NH_2), 2.40 (s, 3H, -CH_3) DMSO-d_6: 7.99 (d, 1H, J = 3 Hz, 5-H), 7.72 (d, 2H, J = 8 Hz, *ortho*-protons), 7.41 (d, 2H, J = 8 Hz, *meta*-protons), 5.86 (d, 1H, J = 3 Hz, 4-H), 2.38 (s, 3H, -CH_3)	$C_{10}H_{11}N_3O_2S$ (237.28)	50.62 50.57	4.67 4.94	17.71 17.46	13.51 13.71
1i	4	187-193 (1-propanol)	7.78 (d, 2H, J = 8.6 Hz, *ortho*-protons), 7.28 (d, 2H, J = 8.4 Hz, *meta*-protons), 5.56 (q, 1H, J = 0.88 Hz, 4-H), 3.60 (s, broad, 2H, NH_2), 2.45 (d, 3H, J = 0.88 Hz, 5-CH_3), 2.41 (s, 3H, CH_3)	$C_{11}H_{13}N_3O_2S$ (251.31)	52.57 52.74	5.21 5.47	16.72 16.91	12.76 12.56

Table 4 continued

Compound	Yield (%)	Mp (°C) (recrystallized)	^{1}H NMR (deuteriochloroform)	Molecular Formula (molecular weight)	Analysis % Calcd./Found C	H	N	S
1iTos	10	180-182 (1-propanol)	7.5-7.8 (m, 4H, *ortho*-protons), 7.44 (s, broad, 1H, NH), 7.1-7.4 (m, 4H, *meta*-protons), 6.20 (q, 1H, J = 0.88 Hz, 4-H), 2.46 (d, 3H, J = 0.88 Hz, 5-CH_3), 2.43 (s, 6H, 2 × C H $_3$)	$C_{18}H_{19}N_3O_4S_2$ (405.50)	53.32 53.14	4.72 4.84	10.36 10.28	15.81 15.60
1jTos	12	208 (1-propanol)	9.47 (s, 1H, NH), 6.8-7.7 (m, 9H, C_6H_5, -C_6H_4-), 6.12 (s, 1H, 4-H), 5.28 (s, 2H, -CH_2-), 2.38 (s, 3H, CH_3), 2.12 (s, 3H, 5-CH_3)	$C_{18}H_{19}N_3O_2S$ (341.44)	63.32 63.33	5.61 5.71	12.31 12.11	9.39 9.47
2bTos	25.5	166 (1-propanol)	6.9-7.9 (m, 11H, 3-H, -C_6H_5, -C_6H_4-, NH, 1H exchangeable), 6.15 (d, 1H, J = 1.8 Hz, 4-H), 2.42 (s, 3H, CH_3)	$C_{16}H_{15}N_3O_2S$ (313.38)	61.32 61.47	4.82 5.07	13.41 13.25	10.23 10.09
2cTos	76	145-147 (1-propanol)	7.56 (d, 2H, J = 8.2 Hz, *ortho*-protons), 7.30 (d, J = 2 Hz, 3-H), together with 6.93-7.25 (m, *meta*-protons, C_6H_5, NH, 1H exchangeable), 9H, 5.67 (d, 1H, J = 2 Hz, 4-H), 5.15 (s, 2H, -CH_2-), 2.40 (s, 3H, -CH_3)	$C_{17}H_{17}N_3O_2S$ (327.41)	62.36 62.10	5.23 5.32	12.83 13.03	9.79 9.89
2dTos	75	208-209 (ethanol)	10.3 (s, 1H, NH), 7.58 (d, 2H, J = 8.7 Hz, *ortho*-protons), 7.14 (d, 2H, J = 8.7 Hz, *meta*-protons), 6.00 (s, 1H, 4-H), 3.69 (s, 3H, N-CH_3), 2.36 (s, 3H, CH_3), 2.18 (s, 3H, 5-CH_3)	$C_{12}H_{15}N_3O_2S$ (265.34)	54.32 54.41	5.70 5.80	15.84 15.38	12.08 11.98
2eTos	15	216-220 (1-propanol)	6.9-7.7 (m, overlayed by 7.24 s, C_6H_4, C_6H_5, together 9H), 6.77 (s, broad, 1H, NH), 5.98 (s, 4-H), 2.38 (s, 3H, -CH_3), 2.21 (s, 3H, 3-CH_3)	$C_{17}H_{17}N_3O_2S$ (327.41)	62.37 62.37	5.23 5.38	12.83 12.58	9.78 9.84
2fTos	73	207 (1-propanol)	7.53-7.80 (m, 4H, *ortho*-protons), 7.15-7.45 (m, 5H, *meta*-protons), 6.4 (s, broad, NH, exchangeable), 5.97 (s, 1H, 4-H), 3.78 (s, 3H, N-CH_3), 2.44 (s, 3H, CH_3)	$C_{17}H_{17}N_3O_2S$ (327.41)	62.37 62.49	5.23 5.46	12.83 12.65	9.79 9.90
2gTos	9	188 (ethanol)	7.00-7.93 (m, 14H, 1-C_6H_5, 3-C_6H_5, -C_6H_4-), 6.8 (s, broad, 1H, NH, exchangeable), 6.52 (s, 1H, 4-H), 2.38 (s, 3H, CH_3)	$C_{22}H_{19}N_3O_2S$ (389.48)	67.85 67.38	4.92 5.27	10.79 10.60	8.23 8.63
2i	20	171 (1-propanol)	7.85 (d, 2H, J = 8.5 Hz, *ortho*-protons), 7.20 (d, 2H, J = 8.5 Hz, *meta*-protons), 5.17 (s, 1H, 4-H), 4.95 (s, broad, 2H, NH_2), 2.42 (s, 3H, CH_3), 2.07 (s, 3H, 3-CH_3)	$C_{11}H_{13}N_3O_2S$ (251.31)	52.57 52.30	5.21 4.88	16.72 16.44	12.76 12.73
2jTos	47	182 (1-propanol)	6.9-7.8 (m, 10H, 1H, exchangeable, C_6H_5, -C_6H_4-, NH), 5.60 (s, 1H, 4-H), 5.10 (s, 2H, -CH_2-), 2.43 (s, 3H, CH_3), 2.13 (s, 3H, 3-CH_3)	$C_{18}H_{19}N_3O_2S$ (314.43)	63.32 63.10	5.61 5.87	12.31 12.31	9.39 9.24
2kTos	94	189-192 (1-propanol)	7.0-7.8 (m, 14H, 2 × C_6H_5, -C_6H_4-), 6.35 (s, broad, 1H, exchangeable, NH), 6.10 (s, 1H, 4-H), 5.22 (s, 2H, -CH_2-), 2.42 (s, 3H, CH_3)	$C_{23}H_{21}N_3O_2S$ (403.51)	68.46 68.45	5.25 5.47	10.41 10.13	7.98 8.08

Table 4 continued

Compound	Yield (%)	Mp (°C) (recrystallized)	^{1}H NMR (deuteriochloroform)	Molecular Formula (molecular weight)	Analysis % Calcd./Found C	H	N	S
2l	71	127-128 (ethanol)	7.7 (m, 4H, *ortho*-protons), 7.3-7.6 (m, 5H, *meta*- and *para*-protons), 6.40 (s, broad, 2H, exchangeable, NH_2)	$C_{16}H_{15}N_3O_2S$ (313.38)	61.32 61.13	4.82 4.86	13.41 13.57	10.23 10.22
3c	46	120 (nitromethane)	7.77-8.13 (m, 2H, *ortho*-protons of 3-C_6H_5), 7.0-7.6 (m, 13H, 5-C_6H_5, -C_6H_5, *meta*- and *para*-protons of 3-C_6H_5), 6.68 (s, 1H, 4-H), 5.37 (s, 2H, -CH_2-)	$C_{22}H_{18}N_2$ (310.40)	85.13 85.14	5.85 6.04	9.02 8.81	

that with R_f = 0.54 contained 5-methyl-1-tosylpyrazol-3-amine (**1i**) (80 mg, 4%). Acidification of the alkaline filtrate with 2*N* hydrochloric acid precipitated 5-methyl-1-tosyl-3-tosylaminopyrazol (**1iTos**) (0.38 g, 10%).

3-Methyl-1-tosylpyrazol-5-amine (**2i**).

A mixture of 3-aminocrotononitrile (1.6 g, 20 mmoles), 4-toluenesulfonylhydrazine (3.72 g, 20 mmoles) in 150 ml of ethanol was allowed to stand for 50 hours at room temperature. After evaporation of the solvent and addition of ether the residue crystallized and was filtered by suction to yield compound **2i** (2.7 g, 54%).

1-Benzyl-5-methyl-3-tosylaminopyrazole (**1jTos**).

On preparation of 1-benzyl-3-methylpyrazol-5-amine [1] the crude oily product was purified by distillation *in vacuo* instead of column chromatography, yielding a yellowish oil (9.5 g,25%) with bp 144-153°/0.2 mm which solidified to a semicrystalline mass. Of this mass an aliquot (0.7 g, 3.7 mmoles) was dissolved in pyridine (2.5 ml) and combined with a solution of 4-toluenesulfonyl chloride (1.8 g, 9.4 mmoles) in pyridine (2.5 ml). After 3 hours the mixture was poured on 2*N* hydrochloric acid (50 ml). The usual workup yielded 1-benzyl-5-methyl-3-tosylaminopyrazol (**1jTos**) (150 mg, 12%), soluble in 2*N* sodium hydroxide.

3-Phenyl-1-(4-toluenesulfonyl)pyrazol-5-amine (**2l**).

A mixture of benzoylacetonitrile [20] (2.9 g, 20 mmoles) and 4-toluenesulfonylhydrazine (3.72 g, 20 mmoles) in ethanol (100 ml) was allowed to stand for 70 hours. The solvent was partially evaporated and the precipitate recrystallized from ethanol to give colorless crystals of **2l** (4.5 g, 71%).

1-Benzyl-3,5-diphenylpyrazole (**3c**).

A mixture of dibenzoylmethane (4.48 g, 20 mmoles), benzylhydrazine (2.44 g, 20 mmoles), concentrated hydrochloric acid (1 ml) in ethanol (50 ml) was refluxed for 4 hours. After evaporation of the solvent the residue was recrystallized from nitromethane to yield **3c** (2.88 g, 46%) with mp 120°, reported [21] mp 91-92° (from ethanol).

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