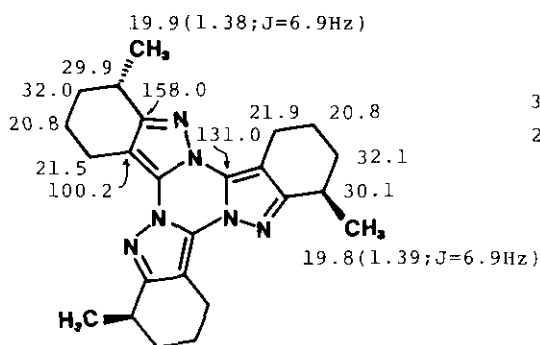
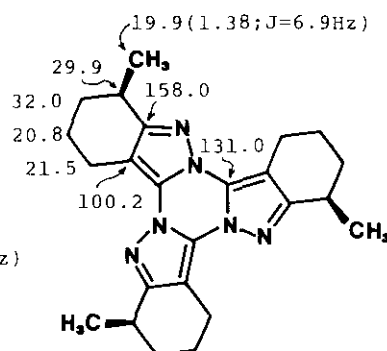


Owing to our interest in 1,1'-bipyrazole and related systems,⁶ we repeated the reaction of **1** with bromine, submitting the resulting reaction mixture to flash chromatography. Elution with dichloromethane afforded a solid with identical m.p. to von Auwers' "dimer" **2**. The substance showed no N-H absorption in its ir spectrum (KBr disk). However, microanalytical data and mass spectrometry (molecular peak at m/z 402) suggested that we were dealing with a cyclic trimer instead of a dimer (a linear trimer would require a mass weight of 404). Moreover, tlc analysis showed that the substance was actually a mixture of two components. Careful column chromatography allowed us to isolate a pure compound **7**, mp 290-291°C, and an isomer **8**, mixed with minor amounts of **7**. We were unable to further purify compound **8**. Both isomers showed identical mass spectra, and their ratio was calculated (from ^1H nmr) to be 75:25, respectively. On the basis of their nmr spectra, the following structures were assigned (^{13}C and ^1H nmr values, in CDCl_3 , are indicated on the figures, those in parenthesis corresponding to ^1H resonances).

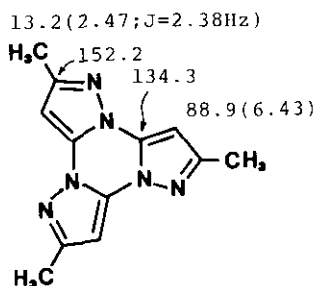


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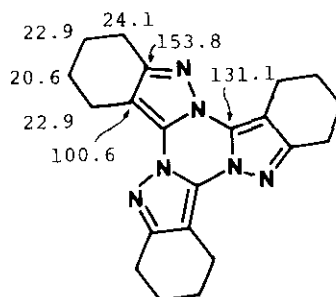


8

Trimers **6** ($\text{R}=\text{H}$)⁵ and **9** (prepared by the reaction of 4,5,6,7-tetrahydroindazole with bromine) were used as model compounds for the nmr study. The simple tetrahydroindazoles **10-14** were also prepared and their spectra registered for comparison (Table I).

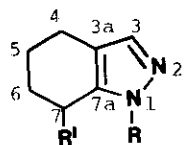


6 ($\text{R}=\text{H}$)

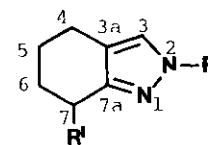


9

The carbocyclic counterparts of the ^{13}C spectra were assigned by comparison with cyclohexene derivatives.⁷ DEPT experiments were carried out to distinguish between all CH , CH_2 , and CH_3 signals. The spectra of isomers **7** and **8**, as well as those of their cyclic models **6** and **9** are fully consistent with the structures proposed. In



10a	R = H ; R' = H	10b
11a	R = H ; R' = CH ₃	11b
12a	R = CH ₃ ; R' = H	12b
13a	R = CH ₃ ; R' = CH ₃	13b
14a	R = C ₆ H ₅ ; R' = H	14b

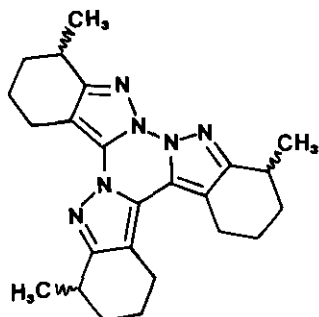
Table I. ¹H and ¹³C nmr chemical shifts of 4,5,6,7-tetrahydroindazoles (**10-14**).

Compound	¹ H Nmr chemical shifts ^a						¹³ C Nmr chemical shifts							
	CDCl ₃		(CD ₃) ₂ SO		C ₆ D ₆		CDCl ₃							Other signals
	Me ₇	H ₃	Me ₇	H ₃	Me ₇	H ₃	C ₃	C _{3a}	C ₄	C ₅	C ₆	C ₇	C _{7a}	
10a/10b	-	7.31	-	7.25	-	7.17	131.7	114.8	23.6	20.5	22.1	23.2	143.2	
11a/11b	1.31	7.30	1.19	7.21	1.28	7.22	132.3	114.5	22.3	20.7	32.4	28.2	147.5	Me ₇ , 20.2
12a	-	7.22	-	7.10	-	7.41	136.2	115.8	23.0	20.6	21.2	22.7	138.1	N-Me, 35.3
13a	1.22	7.22	1.16	7.09	0.86	7.35	135.7	114.8	20.5	18.7	30.8	25.5	141.8	Me ₇ , 20.0; N-Me, 35.5
14a	-	7.46	-	7.52	-	7.48	138.7	117.7	23.6	20.7	22.8	23.2	138.0	C ₆ H ₅ : C _i , 140.3; C _o , 123.0 C _m , 128.9; C _p , 126.4
12b	-	6.89	-	7.28	-	6.49	127.0	115.8	23.5	20.5	23.2 [*]	23.5 [*]	148.8	N-Me, 38.4
13b	1.30	7.02	1.18	7.26	1.47	6.49	126.4	114.9	21.9	20.4	32.3	28.8	153.1	Me ₇ , 19.2; N-Me, 38.0
14b	-	7.59	-	8.12	-	7.20	123.6	118.2	23.5	20.7	23.5	23.5	151.3	C ₆ H ₅ : C _i , 140.6; C _o , 118.6 C _m , 129.2; C _p , 125.5

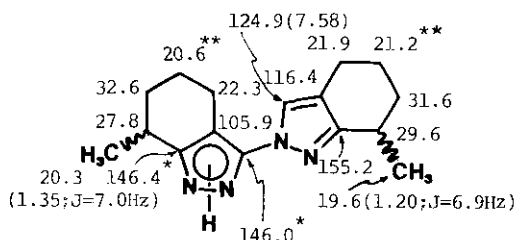
^aOther signals(CDCl₃): (**10a/10b**) 1.7-1.9m(H₅,H₆), 2.54m(H₄), 2.68m(H₇), 9.4broad(N-H); (**11a/11b**) 1.3-2.1m(H₅,H₆), 2.52m(H₄), 2.87m(H₇), 10.4broad(N-H), J_{H-Me}=7.0Hz; (**12a**) 1.5-1.7m(H₅,H₆), 2.51m(H₄), 2.66m(H₇), 3.81(N-Me); (**13a**) 1.6-1.9m(H₅,H₆), 2.49m(H₄), 2.89m(H₇), 3.77(N-Me), J_{H-Me}=6.9Hz; (**14a**) 1.7-1.8m(H₅,H₆), 2.49m(H₄), 2.89m(H₇), 7.2-7.5m(C₆H₅); (**12b**) 1.7-1.8m(H₅,H₆), 2.39m(H₄), 2.53m(H₇), 3.71(N-Me); (**13b**) 1.6-1.9m(H₅,H₆), 2.49m(H₄), 2.89m(H₇), 3.83(N-Me), J_{H-Me}=6.9Hz; (**14b**) 1.7-1.9m(H₅,H₆), 2.60m(H₄), 2.77m(H₇), 7.61m(H_o), 7.38m(H_m), 7.20m(H_p).

• These assignments can be reversed.

particular, their relative simplicity (only three quaternary carbon atoms, and one signal for the 's-triazine' framework) ruled out the alternative mode of cyclization to an unsymmetrical triazine central ring (*i.e.*, structure **15**, with one *N,N'*-, one *C,C'*-, and one *C,N'*-bond).



15



(*,** These assignments can be reversed)

16

Further elution of the column containing the crude reaction mixture with CH_2Cl_2 /ethyl acetate (80:20) afforded a second solid substance, mp 153-154°C, for which we propose the structure **16** on the basis of the following considerations:

- i) The compound shows molecular formula $\text{C}_{16}\text{H}_{22}\text{N}_4$ (microanalysis, mass spectrum: m/z 270), one aromatic pyrazolic C-H resonance (7.59 ppm in CDCl_3), and a broad N-H resonance at ca. 8.5 ppm, as expected for a *C,N'*-linked dimer of 7-methyl-4,5,6,7-tetrahydroindazole.
- ii) The chemical shift of the C_3 resonance (124.9 ppm in CDCl_3) clearly demonstrates the nature of the *C,N'* linkage (*i.e.*, C_3 to N_2). As shown in Table I, values for C_3 in tetrahydroindazoles are comprised between 123 and 126 ppm in N_2 -substituted models, whereas values for N_1 -substituted tetrahydroindazoles are always above 130 ppm.

Another way to deduce the position of the *C,N'*-bond could be the study of the solvent effects on the proton nmr spectra of **16**. It is well known⁸ that the H_5 proton resonance of 1-substituted pyrazoles is distinguished from the H_3 signal by the higher field shift that it suffers when changing solvent from CDCl_3 to C_6D_6 . In addition, the shift is to lower field in going to more polar solvents as $(\text{CD}_3)_2\text{SO}$. Values for models of Table I are in full agreement with this prediction. However, this solvent effect does not apply to **16**. The following chemical shifts for H_3 , were found: 7.58 (CDCl_3), 7.72 [$(\text{CD}_3)_2\text{SO}$], and 7.95 (C_6D_6). A comparison with 1,5'-bipyrazoles **17** and **18** (Table II) reveals that the solvent effect is present in the *N*-substituted compound, but not in the N-H model. The lack of solvent effect in the unsubstituted series has been attributed by Habraken *et al.*⁹ to intramolecular hydrogen bonding.

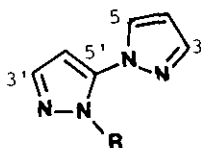
- iii) Only one compound was found either in CDCl_3 (^1H and ^{13}C nmr) or $(\text{CD}_3)_2\text{SO}$ (^1H nmr). In C_6D_6 , however, one of the methyl proton signals splitted into two well resolved doublets of almost equal intensities. This may be attributed to the presence of both possible diastereoisomers of **16**.

Although the origin of trimers **7** and **8** was not carefully investigated, it seems likely that they are generated from **16**. Considering that asymmetric induction is

not present, and that the salt **1** is a racemic, statistical distribution explains why **16** is a 50:50 mixture of *RR(SS)* and *RS(SR)* diastereoisomers, whereas trimers **7** (*RRS* and *SSR*) and **8** (*RRR* and *SSS*) are in a 75:25 ratio.

Finally, other dimers were not found in the remaining mixture of reaction compounds, since no molecular peaks at m/z 270 appeared in the mass spectra of aliquots taken at regular intervals from the chromatographic column. Only some peaks corresponding to bromine-containing compounds were detected, although we were unable to isolate 3-bromo-7-methyl-4,5,6,7-tetrahydroindazole (**3**), also reported by von Auwers.¹

Table II. ^1H nmr chemical shifts for H_5 in some 1,5'-bipyrazoles.



Compound	R	CDCl_3	$(\text{CD}_3)_2\text{SO}$	C_6D_6
17	H	8.07 ^a	8.22 ^a	8.07 ^b
18	CH_3	7.58 ^b	8.16 ^b	6.93 ^b

^aFrom ref. 9; ^bFrom ref. 10.

EXPERIMENTAL

Melting points are not corrected. Nmr spectra were registered on a Bruker WP 200 SY instrument. For the recording of ir and mass spectra, Unicam SP 1100 and Hewlett-Packard 5985 instruments were used, respectively. The following compounds were prepared according to known procedures: 2,6,10-trimethyl-tripyrzolo[1,5-a:1',5'-c:1'',5''-e]-s-triazine (**6**),⁵ 4,5,6,7-tetrahydroindazole (**10**),¹¹ 7-methyl-4,5,6,7-tetrahydroindazole (**11**),¹¹ 1-methyl-4,5,6,7-tetrahydroindazole (**12a**),¹² 2-methyl-4,5,6,7-tetrahydroindazole (**12b**),¹² 1,7-dimethyl-4,5,6,7-tetrahydroindazole (**13a**),¹³ 2,7-dimethyl-4,5,6,7-tetrahydroindazole (**13b**),¹³ 1-phenyl-4,5,6,7-tetrahydroindazole (**14a**),¹¹ 2-phenyl-4,5,6,7-tetrahydroindazole (**14b**),¹¹ 1,5'-bipyrazole (**17**),^{9,10} and 1-methyl-5-(1-pyrazolyl)pyrazole (**18**).¹⁰ The new compounds **7**, **9**, and **16**, gave elemental analyses corresponding to their molecular formulae for C, H, and N, within a $\pm 0.3\%$ error.

Tri-4,5,6,7-tetrahydroindazolo[2,3-a:2',3'-c:2'',3''-e]-s-triazine (**9**). To a solution of 4,5,6,7-tetrahydroindazole (**10**) (0.390 g, 3.10 mmol) in dry chloroform (4 cm^3), a solution of bromine (0.11 ml, 3.10 mmol) in chloroform (3 ml) was slowly added, under stirring. The reaction mixture was refluxed for 1 h and then kept overnight at room temperature. Water (20 ml) and solid NaHCO_3 were added, and the organic layer was separated, washed with water, and dried (Na_2SO_4). Evaporation of the solvent gave an oil which was purified by column chromatography (acidic silica gel¹⁴). Minor impurities were first eluted with toluene, and further elution with toluene/ethyl acetate (80:20) afforded 0.097 g (8.4%) of **9**, mp 274-275°C(dec.), ir(nujol): 1650, 1540, and 1500 cm^{-1} . Mass spectrum: m/z 360(M^+ , 48.8), 332(36.2), and 41(100).

Reaction of 7-methyl-4,5,6,7-tetrahydroindazole, silver salt (**1**) with bromine.

To a stirred and cooled (0°C) solution of **1** (2.68 g, 11.0 mmol) in dry ethyl ether (150 ml) was added bromine (0.53 ml, 15.0 mmol). The mixture was stirred for 2.5 h at 0°C, and silver bromide filtered and washed with ether. The combined ethereal solutions were washed sequentially with aqueous sodium bisulfite, water, and brine, dried (MgSO_4), and evaporated. The residue was purified by flash

chromatography.¹⁵ Elution with dichloromethane afforded 0.411 g (9.3%) of a solid of mp 272-273°C (mixture of diastereoisomers **7** and **8**). Further elution with dichloromethane/ethyl acetate (80:20) gave 2,3'-bi-7-methyl-4,5,6,7-tetrahydroindazole (**16**), mp 153-154°C (0.670 g, 22.5%), $\nu(\text{nujol})$: 3240, 1620, and 1555 cm^{-1} . Mass spectrum: m/z 270(M^+ , 100), 255(45.2), and 135(65.3).

The mixture of trimers **7** and **8** was again submitted to flash chromatography (dichloromethane), yielding 0.080 g of pure (2*R**,8*R**,14*S**)-2,8,14-trimethyl-tri-4,5,6,7-tetrahydroindazolo[2,3-*a*:2',3'-*c*:2'',3''-*e*]-s-triazine (**7**), mp 290-291°C, $\nu(\text{nujol})$: 1650 and 1500 cm^{-1} . Mass spectrum: m/z 402(M^+ , 100), 387(4.4), and 360(36.5). A mixture (0.320 g) of compounds **7** and **8** was also recovered.

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Received, 10th June, 1985