(weighed amounts, concentration of the *N*-nitropyrazole *ca.* 1%, *n*-pentadecane added as internal standard) in anisole, or, in the case of the rearrangement of **1**, in nitrobenzene, was inserted in a thermostated oil bath (166° for 1, 140° for **3** and **4**). A small stream of nitrogen was passed over. Aliquots were removed at 15- or 20-min intervals and analyzed by glc (column 1.5 m × 0.125 in., 4% OV-17 on 80–100 mesh Gas-Chrom Q), column temperature 160° (rearrangement of **1**), or ballistic programmed from 130° to 200° (rearrangement of **3** and **4**). The amounts of the *N*-nitropyrazoles and of the rearrangement products, relative to *n*-pentadecane, were calculated, using graphs obtained by injection (under the same glc conditions) of standard solutions of the various nitropyrazoles and *n*-pentadecane in anisole or in nitrobenzene. Reactions were followed to 90–95% conversion. During each run the sum of *N*-nitropyrazoles and *C*-nitropyrazoles was constant within experimental error. Plots of log C_0/C_t *vs.* time always gave straight lines (see Figure 1); k values for the isomerization of **1** and **3**, and $k_1 + k_2$ for the isomerization of **4**, were calculated from these graphs. To determine k_1/k_2 for the isomerization of **4**, the reaction mixture was analyzed after 3 hr of isomerization (completeness). It contained 93% of **9** and 7% of **7**. To control the proposed scheme for the isomerization of **4**, the amounts of **3** theoretically present during the reaction, calculated with the expression

$$x = \frac{C_0 k_2}{k_1 + k_2 - k_3} [e^{-k_3 t} - e^{-(k_1 + k_2)t}] \text{ (see Scheme I)}$$

were compared with the amounts found. The results are summarized in Table II.

TABLE II

COMPARISONS OF THE AMOUNTS OF **3**, PRESENT DURING A KINETIC RUN OF **4**, CALCULATED AND FOUND

Reaction time, min	Calcd, %[a]	Found, %[a,b]
5	0.8	0.5
25	2.4	2.5
45	2.8	3
65	2.5	2.5
85	2.0	2
105	1.6	1.5
125	1.2	1

[a] Per cents from C_0. [b] Approximations.

Registry No.—**1**, 7119-95-1; **2**, 31163-83-4; **3**, 31163-84-5; **4**, 31163-85-6; **5**, 26621-44-3; **6**, 31163-87-8; **7**, 31163-88-9.

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Nitration of Indazoles in the 3 Position

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Nitration of indazole with nitric acid and acetic anhydride gives the 3-nitro and 3,5-dinitro derivatives. With this reagent, the four Bz-mononitro indazoles undergo nitration at N-2. The N-2 nitro group in these compounds rearranges to C-3 on heating. The mechanism of the reagent-dependent nitration of indazoles is discussed.

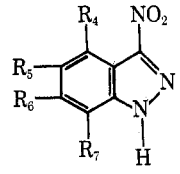
Although numerous indazoles containing nitro groups are known,[1] to our knowledge no 3-nitroindazoles have been described in the literature. The majority of the reported nitroindazoles were obtained directly by ring closure reactions. Nitration of indazole with nitric acid yields the 5-nitro derivative[2] which according to Davies[3] gives a *m*-dinitroindazole on further nitration with mixed acid.[4] Nmr analysis (see Experimental Section) clearly indicated this compound to be 5,7-dinitroindazole. The formation of 5,6-dinitroindazole on nitration of 6-nitroindazole, first reported by Fries,[5] was confirmed by Davies.[3]

We have discovered a facile nitration of indazole in the 3 position. Treatment of an acetic acid solution of indazole in the cold, with nitric acid and acetic anhydride successively, afforded a mixture of two products, 3-nitroindazole (**1**, 55%) and 3,5-dinitroindazole (**2**, 20%), which were easily separated by column chromatography. The nitration of 5-nitroindazole by the same procedure also gave **2** (42%) in addition to the *N*-nitro derivative 2,5-dinitroindazole (**3**, 51%). From the nitration of 6-nitroindazole only 3,6-dinitroindazole (**4**, 97%) was obtained. On the other hand, nitration of 4-nitro- and of 7-nitroindazole gave the *N*-nitro compounds 2,4-dinitroindazole (**5**, 95%) and 2,7-dinitroindazole (**6**, 85%). On heating[6] in anisole solution these *N*-nitro compounds **3**, **5**, and **6** could easily be converted to the 3-nitro derivatives **2**, 3,4-dinitroindazole (**7**), and 3,7-dinitroindazole (**8**). Moreover, **3** appeared to disproportionate in solution at room temperature as observed in tlc experiments. 2,6-Dinitroindazole (**9**, 75%) and 2,3-dinitroindazole (**10**, 30%) were obtained on nitration of 6-nitro- and 3-nitroindazole, respectively, at room temperature in acetic acid solution by treatment with acetylnitrate. On heating **9** rearranged into the 3-nitro compound **4**, but the 2,3-dinitroindazole (**10**) decomposed on heating. **1** was identified on comparison (ir and nmr spectra, tlc, and mixture melting points) with authentic samples of 4-, 5-, 6-, and 7-nitroindazole. The nmr spectrum consisted of two multiplets centered at δ 8.13 and 7.60, with relative intensities of 1:3 for the C–H protons and the ir spectrum showed a strong absorption at 748 cm^{-1} indicating four vicinal aromatic protons. The structure assignments of **2**, **4**, **7**, amd **8** were based on their nmr spectra and on comparison of these spectra with those of

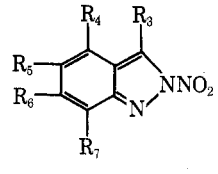
(1) L. C. Behr in "The Chemistry of Heterocyclic Compounds," A. Weissberger, Ed., Vol. 22, Interscience, New York, N. Y., 1967, p 289.
(2) K. von Auwers and H. Kleiner, *J. Prakt. Chem.*, **118**, 67 (1928).
(3) R. R. Davies, *J. Chem. Soc.*, 2412 (1955).
(4) This in contrast to what is described in ref 1.
(5) K. Fries, K. Fabel, and H. Eckhardt, *Justus Liebigs Ann. Chem.*, **550**, 31 (1942).
(6) Similar rearrangements have been observed in the case of *N*-nitropyrazoles where isomerization takes place thermally[7] as well as under acid conditions.[7,8]
(7) J. W. A. M. Janssen and C. L. Habraken, *J. Org. Chem.*, **36**, 3081 (1971).
(8) R. Hüttel and F. Büchele, *Chem. Ber.*, **88**, 1586 (1955).

the mononitroindazoles[9] and of 5,6- and 5,7-dinitroindazole. The absence in all spectra of a singlet due to a 3 proton as observed in the spectra of the latter compounds clearly indicated that in **2**, **4**, **7**, and **8** the 3 position is occupied by the second nitro group (Chart I).

CHART I



1, $R_4 = R_5 = R_6 = R_7 = H$
2, $R_4 = R_6 = R_7 = H$; $R_5 = NO_2$
4, $R_4 = R_5 = R_7 = H$; $R_6 = NO_2$
7, $R_4 = NO_2$; $R_5 = R_6 = R_7 = H$
8, $R_4 = R_5 = R_6 = H$; $R_7 = NO_2$



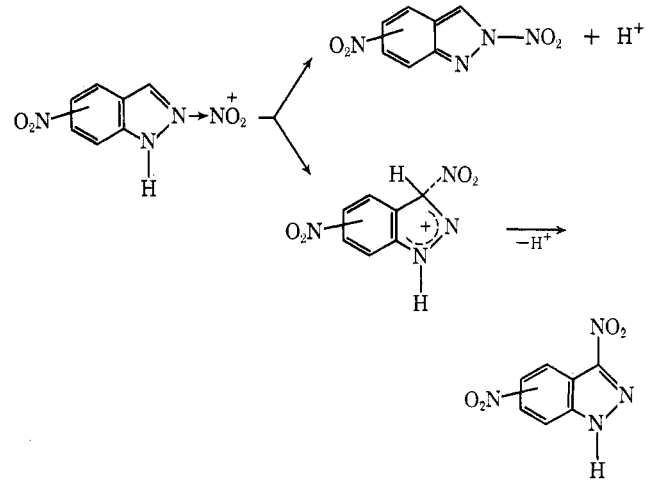
3, $R_3 = R_4 = R_6 = R_7 = H$; $R_5 = NO_2$
5, $R_3 = R_5 = R_6 = R_7 = H$; $R_4 = NO_2$
6, $R_3 = R_4 = R_5 = R_6 = H$; $R_7 = NO_2$
9, $R_3 = R_4 = R_5 = R_7 = H$; $R_6 = NO_2$
10, $R_3 = NO_2$; $R_4 = R_5 = R_6 = R_7 = H$

2 showed the expected nmr spectrum for a 1,2,4-trisubstituted benzene derivative (see Experimental Section), but in the spectrum of **4** only two weakly coupled signals were found for the C–H protons with relative intensities 1:2. Ir analysis of compounds **3**, **5**, **6**, **9**, and **10** showed the absence of a N–H band. In addition to the normal absorptions for a nitro group (ν_{asym} 1506–1530 and ν_{sym} 1320–1345 cm^{-1}), each compound showed a strong band at much higher frequency (1620–1650 cm^{-1}) and one at much lower frequency (1265–1285 cm^{-1}) indicating the presence of a second nitro group attached to a nitrogen atom.[10] The nmr spectrum of **3** as compared to that of 5-nitroindazole showed a large displacement to lower field for the 3-H (from δ 8.34 to 9.53); similar displacements appeared in the spectra of **5**, **6**, and **9**. On the other hand, no such displacements were found for the 7-H in the spectra of the *N*-nitroindazoles. From this we tentatively conclude that in the *N*-nitroindazoles the nitro group is attached to the N-2 atom.

Concerning the mechanism of this reagent-dependent nitration of indazole, we assume that in strong acid media electrophilic substitution occurs in the indazolium cation.[11] The Coulomb repulsion will direct the attack of the NO_2^+ to the benzenoid ring resulting in the formation of 5-nitroindazole and 5,7-dinitroindazole, respectively. It has been shown in the case of several other N heteroaromatics that nitration involves electrophilic substitution on the cation.[12,13] The results of modified MO calculations by Finar[14] and by Lynch,[15] taking into account the energy required to bring the electrophile to the site of attack in the opposing charge field of the cationic substrate, are also in excellent concordance with the orientation and reactivity on nitration in strong acid media.

In weak acid media, on the other hand, nitration will take place on the neutral molecule, and in the neutral molecule a N atom will be the position most susceptible for electrophilic attack. Consequently the formation of *N*-nitroindazoles concurrent with the nitration on the 3 position seems to be quite consistent (see Chart II). Investigations by Lynch[15] have shown that the predominantly ortho nitration of acetanilides can be explained by a nucleophilic attack of a free electron pair of the amide moiety on the nitrating species. In our case the occurrence of N-nitration of indazoles suggests an attack of the free electron pair of a N atom of the neutral molecule on the NO_2^+. Subsequent formation of a σ complex then may lead to the formation of a 3-nitroindazole and direct loss of a proton from the adjacent N atom would result in the formation of 2-nitroindazoles. Such a facile nitration on a nitrogen in azoles seems not to be restricted to pyrazoles[7,8] and indazoles as is indicated by the synthesis of 1-nitrobenztriazole (**11**) (73%, see Experimental Section) on nitration in acetic acid.

CHART II



Experimental Section

General.—4-, 5-, 6-, and 7-nitroindazole were purchased from Aldrich Chemical Co.; indazole and 5,6-dinitroindazole were prepared according to literature procedures.[16,17] For the separation of products the short column chromatography technique of Hunt and Rigby[18] was used on silica gel H according to Stahl (Merck) with $CHCl_3$–EtOAc 3:1 as eluent.

All melting points are uncorrected. Analyses were performed by Mr. W. J. Buis, TNO Laboratories of Organic Chemistry, Utrecht, The Netherlands. Ir (KBr disk) and mass spectra

(9) J. Elguero, A. Fruchier, and R. Jacquier, *Bull. Soc. Chim. Fr.*, 2075 (1966).
(10) A. D. Cross and R. Allan Jones, "An Introduction to Practical Infrared Spectroscopy," 3rd ed, Butterworth, London, 1969.
(11) We are grateful to Professor B. M. Lynch for comments and suggestions concerning the nitration mechanism.
(12) A. R. Katritzky and C. D. Johnson, *Angew. Chem.*, **79**, 629 (1967).
(13) J. H. Ridd, *Z. Chem.*, **8**, 201 (1968).
(14) I. L. Finar, *J. Chem. Soc. B*, 725 (1968).
(15) B. M. Lynch, Abstracts of Papers, Joint Conference, The Chemical Institute of Canada/American Chemical Society, Toronto, Canada, 1970; B. M. Lynch, C. M. Chen, and Y.-Y. Wigfield, *Can. J. Chem.*, **46**, 1141 (1968).
(16) P. Petitcolas and R. Sureau, *Bull. Soc. Chim. Fr.*, 466 (1950).
(17) R. Huisgen, *et al.*, *Org. Syn.*, **42**, 69 (1962); *Justus Liebigs Ann. Chem.*, **586**, 84 (1954).
(18) B. J. Hunt and W. Rigby, *Chem. Ind. (London)*, 1868 (1967).

were recorded on Perkin-Elmer IR-137 and AE MS-902 spectrometers, respectively. Nmr spectra were recorded on a JEOLCO Mimimar instrument.

Nitration Procedure A (Used in All Cases except for the Synthesis of 9 and 10).—The addition of 0.35 ml of nitric acid (*d* 1.5) to a stirred solution of indazole, 0.87 g (0.73 mol) in 6 ml of acetic acid, resulted in a rapid increase of the temperature to 45° and the separation of a voluminous precipitate which almost prevented further stirring. After 30 min 1 ml of acetic anhydride was added at once. This resulted in a slow increase of the temperature to approximately 40° and the dissolution of the precipitate. The reaction mixture was allowed to stand at room temperature for another 30 min and was then poured on ice. The nitration products were collected, thoroughly washed with water, air-dried, and separated by chromatography.[18] Similar results were obtained when the reaction temperature, by external cooling, was kept below 10° and also when the reaction was performed on a tenfold scale.

The nitrations of 5- and 6-nitroindazole were performed on suspensions in acetic acid.

Nitration Procedure B.—A solution of HNO_3 (*d* 1.52, 3 ml) in acetic anhydride (7.5 ml), prepared at 20–30° and cooled to −15°, was added to a solution of the indazole (2 g) in acetic acid (15 ml) at 15–25°. Immediately afterward the reaction mixture was poured on ice. The nitration products were filtered off, thoroughly washed with water, air-dried, and separated by column chromatography. Procedure B was used for the synthesis of **9** and **10**.

Thermal Rearrangement.—The thermal rearrangement of *N*-nitro compounds to the corresponding 3-nitroindazoles was affected in the crystalline phase by slowly raising the temperature of the thermostat to 140° in approximately 4 hr. Thereafter the crystals (0.5 g) were allowed to stay at 140° for another 5 hr. Raising the temperature more rapidly resulted in the decomposition of the *N*-nitroindazole.

Analytical samples of the 3-nitroindazoles as well as of the 2-nitro derivatives were difficult to obtain by crystallization; the analytical sample of **1** was obtained by sublimation.

3-Nitroindazole (**1**): mp 205°; ir 3260 (NH), 748 (4 adjacent arom protons), 1535 and 1385 cm^{-1} (NO_2); nmr δ 8.13 (m, 1) and 7.60 (m, 3).

Anal. Calcd for $C_7H_5N_3O_2$: C, 51.54; H, 3.00; N, 25.76; mol wt, 163.0382. Found: C, 51.57; H, 3.20; N, 25.72; mol wt, 163.0387.

3,5-Dinitroindazole (**2**): mp 273° dec; ir 3260 (NH), 1540 and 1345 cm^{-1} (NO_2); nmr δ 8.72 (d, 1, J = 3 Hz, 4-H), 8.26 (dd, 1, J = 3 and 10 Hz, 6-H), and 7.85 (d, 1, J = 10 Hz, 7-H).

Anal. Calcd for $C_7H_4N_4O_4$: C, 40.39; H, 1.94; N, 26.92; mol wt, 208.0233. Found: C, 40.87; H, 2.22; N, 26.48; mol wt, 208.0233.

3,6-Dinitroindazole (**4**): mp 233°; ir 3340 (NH), 1520 and 1364 cm^{-1} (NO_2); nmr δ 8.16 (2, 4- and 5-H, identical chemical shifts) and 8.51 (1, 7-H).

Anal. Calcd for $C_7H_4N_4O_4$: C, 40.39; H, 1.94; N, 26.92; mol wt, 208.0233. Found: C, 40.89; H, 2.06; N, 26.71; mol wt, 208.0232.

2,5-Dinitroindazole (**3**): ir 1506 and 1337 (NO_2), 1650 and 1266 cm^{-1} (NO_2 attached to a nitrogen atom[7,10]); nmr δ 9.53 (s, 1, 3-H), 8.73 (d, 1, J = 3 Hz, 4-H), 8.04 (dd, 1, J = 3 and 10 Hz, 6-H), and 7.78 (d, 1, J = 10 Hz, 7-H). Due to disproportionation in solution as observed in tlc experiments, no good analytical sample could be obtained.

Anal. Calcd for $C_7H_4N_4O_4$: C, 40.39; H, 1.94; N, 26.92. Found: C, 40.91; H, 2.26; N, 26.34.

When heated extremely slowly in a sealed melting point tube **3** melted at 258° with decomposition. Kept without melting at 184° for 1.5 hr only the presence of **2** could be detected on tlc.

2,4-Dinitroindazole (**5**): ir 1506 and 1340 (NO_2), 1640 and 1275 cm^{-1} (NO_2 attached to a nitrogen atom); nmr δ 9.20 (s, 1, 3-H), 7.46 (t, 1, J = 9 Hz, 6-H), 7.97–8.18 (m, 2, 5- and 7-H).

Anal. Calcd: C, 40.39; H, 1.94; N, 26.92. Found: C, 40.56; H, 1.90; N, 26.65.

2,7-Dinitroindazole (**6**): ir 1520 and 1340 (NO_2), 1650 and 1265 cm^{-1} (NO_2 attached to a nitrogen atom); nmr δ 9.70 (s, 1, 3-H), 8.50 (d, 1, J = 7 Hz, 6-H), 8.26 (d, 1, J = 9 Hz, 4-H), 7.38 (t, 1, 5-H).

Anal. Calcd: C, 40.39; H, 1.94; N, 26.92. Found: C, 40.58; H, 1.88; N, 26.75.

3,4-Dinitroindazole (**7**): mp 227°; ir 3360 (NH), 1525 and 1345 cm^{-1} (NO_2); nmr δ 7.76 (t, 1, J = 7 Hz, 6-H), 8.08–8.32 (m, 2, 5- and 7-H).

Anal. Calcd: C, 40.39; H, 1.94; N, 26.92. Found: C, 40.64; H, 2.09; N, 26.85.

3,7-Dinitroindazole (**8**): mp 220°; ir 3320 (NH), 1500 and 1530 (NO_2, asym), and 1335 cm^{-1} (NO_2, sym); nmr δ 7.69 (t, 1, J = 7 Hz, 5-H), 8.53 (dd, 1, J = 7 and 1 Hz, 4- or 6-H), 8.58 (dd, 1, J = 7 and 1 Hz, 6- or 4-H).

Anal. Calcd: C, 40.39; H, 1.94; N, 26.92. Found: C, 40.78; H, 2.22; N, 26.78.

2,6-Dinitroindazole (**9**): ir 1530 and 1345 (NO_2), 1650 and 1285 cm^{-1} (NO_2 attached to a nitrogen atom); nmr δ 9.54 (s, 1, 3-H), 8.71 (d, 1, 7-H), 7.74–8.14 (m, 2, 4- and 5-H).

Anal. Calcd: C, 40.39; H, 1.94; N, 26.92. Found: C, 40.42; H, 1.94; N, 26.80.

2,3-Dinitroindazole (**10**): mp 154° dec; ir 1525 and 1320 (NO_2), 1620 and 1265 cm^{-1} (NO_2 attached to a nitrogen atom); nmr δ 7.50–8.25 (m, 4, 4-, 5-, 6-, and 7-H).

Anal. Calcd: C, 40.39; H, 1.94; N, 26.92. Found: C, 40.79; H, 2.64; N, 26.59.

1-Nitrobenztriazole (**11**): mp 74°; ir 1630 and 1280 cm^{-1} (NO_2 attached to a nitrogen atom); nmr δ 7.25–8.00 (m, 4, adjacent phenyl protons).

Anal. Calcd for $C_6H_4N_4O_2$: C, 43.91; H, 2.46; N, 34.14. Found: C, 44.17; H, 2.46; N, 34.31.

5,7-Dinitroindazole.—This compound was synthesized from 5-nitroindazole by following the same procedure as for the nitration of 6-nitroindazole described by Petitcolas and Sureau:[16] mp 217° (lit.[2] mp 215, 222°); ir 3220 (NH), 1550, 1342, and 1320 cm^{-1} (NO_2); nmr δ 9.03 (d, 1, J = 2.2 Hz, 6-H), 8.73 (d, 1, J = 2.2 Hz, 4-H), and 8.50 (s, 1, 3-H).

Anal. Calcd: C, 40.39; H, 1.94; N, 26.92. Found: C, 40.84; H, 2.32; N, 26.86.

Registry No.—**1**, 31164-27-9; **2**, 31164-28-0; **3**, 31164-29-1; **4**, 31163-64-1; **5**, 31208-75-0; **6**, 31163-65-2; **7**, 31163-66-3; **8**, 31163-67-4; **9**, 31163-68-5; **10**, 31163-69-6; **11**, 31163-70-9; 5,7-dinitroindazole, 31208-76-1.

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