Non Conventional Syntheses of Heterocyclic Compounds. 3. Synthesis of Indazole Derivatives

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The thermal cyclization of a few 2,6-dimethylphenylazo compounds to indazole derivatives is described.

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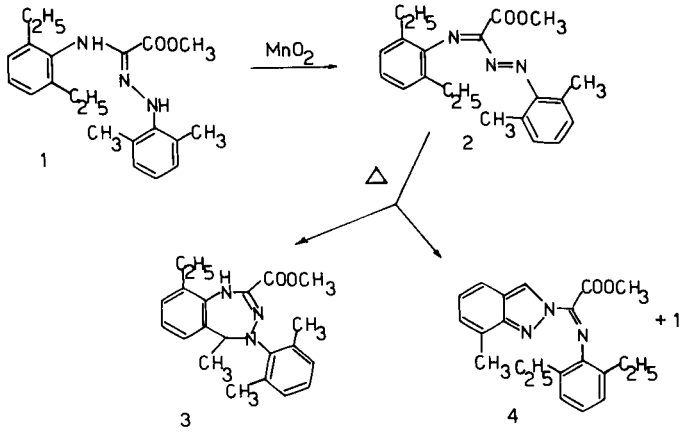
The present paper deals with a new indazole synthesis which we discovered whilst developing research on the synthesis of benzotriazepine derivatives recently reported in this journal [1].

By refluxing the arylazoimine **2** (synthesized by oxidation of **1**) in xylene solution in the presence of catalytic amounts of DABCO, compounds **1**, **3** and **4** were formed. We isolated them in a pure state by chromatography.

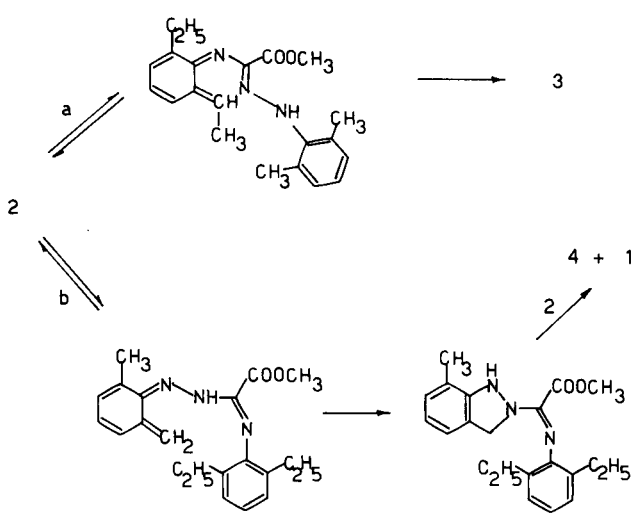


The benzotriazepine derivative **3** is the product expected from cyclization of **2** in accordance with the results previously obtained from similar substrates [1]; its structure was inferred from analytical and spectral data.

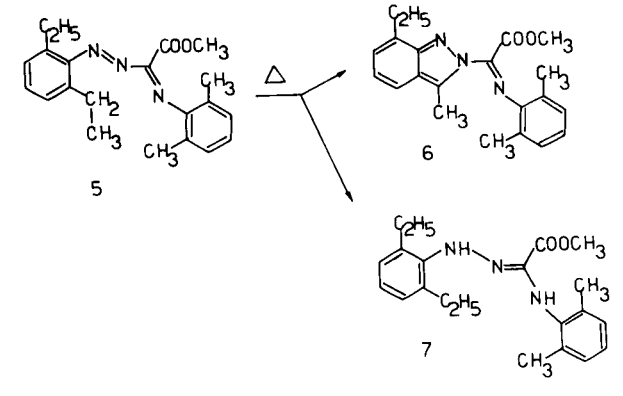
The hydrolysis of **4** in a refluxing hydrochloric acid solution, giving 7-methylindazole, 2,6-xylidine and oxalic acid, confirmed the assigned structure, which perfectly matches the analytical and spectral data [2]. In the preceding paper a mechanistic hypothesis was presented to explain the formation of the triazepine ring involving an intermediate tautomeric methylenecyclohexadienoneimine species (Scheme I, path a). The concurrent formation of the indazole derivative **4** reported above could occur through a different tautomeric intermediate of the starting arylazoketimine **2** (Scheme I, path b).

This second cyclization mode would give a dihydroindazole undergoing, in its turn, oxidation to indazole **4**. The

Scheme I

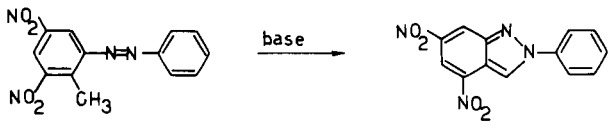


oxidizing reagent should be **2**; its reduced form **1** was really found amongst the reaction products. A second experiment was performed on substrate **5** in which the positions of methyl and ethyl groups are exchanged with respect to the arylazoketimine **2**; only the reaction path b of Scheme I was observed and **6** and **7** were recovered as reaction products in good yields [3].



To interpret this result, we needed to keep in mind that, even for the formation of the benzotriazepine ring, there was a remarkable increase in the reaction rate when the

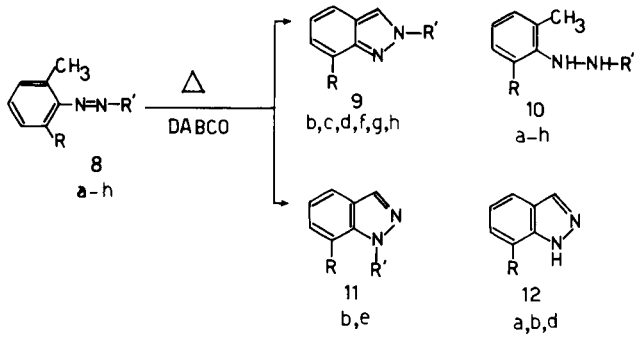
cyclization process involved an ethyl group, as compared with that involving a methyl group. It seems reasonable to admit that this parameter should play an analogous role even in the indazole ring formation. Between the two competing paths (a and b in Scheme I), the one affording the pentatomic heterocycle seems to be preferred, provided that the alkyl groups involved in the ring formation are equal. The formation of indazole derivatives is apparently similar to that observed by Chardonnes [4], who synthesized a few indazoles starting from 2-methyl substituted azobenzene compounds under basic conditions in refluxing alcoholic solution.



The same author observed that this reaction was quite satisfactory for substrates carrying strongly electron-withdrawing substituents (nitro or acyl groups) in positions *ortho* and *para* with respect to the methyl group; the cyclization was instead very difficult when such groups were absent or, if present, located in different positions of the aromatic ring. Though this mechanism was not fully clarified, it is evident that it cannot be the same which is effective in our indazole synthesis, as it requires the presence, unnecessary in our case, of groups able to render acidic the hydrogen atoms of the alkyl group involved in the cyclization process.

In order to evaluate the scope of this new synthesis and at the same time to clarify the structural parameters affecting it, several substrates having general formula **8** were prepared: according to our basic hypothesis R′ had always to be an electron-withdrawing substituent. The following scheme and the Table I report the different reaction products and the corresponding isolation yields.

Scheme II



a, R = CH_3 R′ = $CONH_2$
b, R = CH_3 R′ = $COOC_2H_5$
c, R = CH_3 R′ = $COC_6H_4NO_2$
d, R = H R′ = $COC_6H_4NO_2$
e, R = H R′ = COC_6H_5
f, R = CH_3 R′ = COC_6H_5
g, R = CH_3 R′ = 2,4-diNO_2-C_6H_3
h, R = CH_2 R′ = 1,3,5-triazinyl

Table I

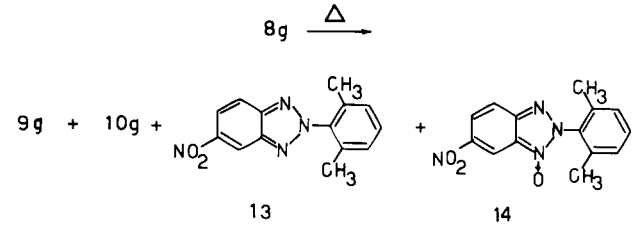
Substrate	Products (yields %) [a]	Reaction time (hours)
2	**4** (51) **1** (50) **3** (11)	0.5
5	**6** (55) **7**	0.5
8a	**10a** (70) **12a** (80) cyanuric-acid (41)	12 [b]
8b	**9b** (traces) **10b** (23) **12b** (27) **11b** (34)	1.5
8c	**9c** (48) **10c** (60)	0.1
8d	**9d** (29) **10d** (43) **12d** (16)	4
8e	**10e** (57) **11e** (54)	12
8f	**9f** (29) **10f** (25)	1
8g	**9g** (31) **10g** (19) **13** (28) **14** (16)	12
8h	**9h** (43) **10h**	1

[a] Isolation yields. [b] Solvent, chlorobenzene.

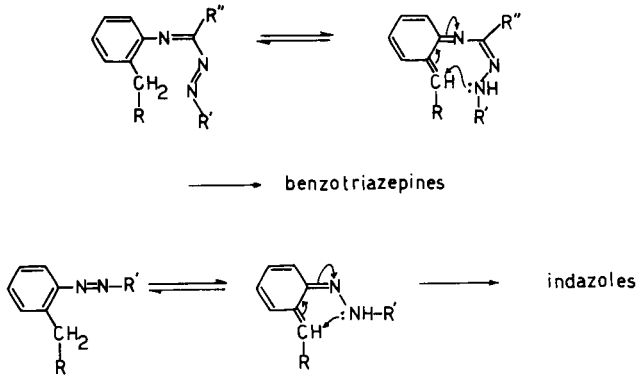
Products **10** resulting from the reduction process were always formed; the indazole derivatives **9** were nearly always isolated, as expected. The rearrangement of **9b,e** to **11b,e** is a well known thermal rearrangement of 2-acylindazoles [5].

In our opinion the formation of unsubstituted indazoles **12** is the result of an alternative reaction mechanism which involves the homolytic cleavage of the bond between R′ and the azo group [6]. This interpretation is in agreement with both the extensive formation of cyanuric acid, which arises from the trimerization of the cyanic acid produced from the thermolysis of **8a**, and with the results of other experiments performed in *m*-xylene or mesitylene solution. In these cases, a few products resulted from the attack on the solvent of aryl radicals deriving from the decomposition of the substrate.

The behaviour of **8g** merits a short comment: together with the expected **9g** and **10g**, even the benzotriazole derivatives **13** and **14** were isolated. As a consequence of a



known reaction scheme their formation must be associated with the interaction between the nitro group and the *ortho* hydrazine chain of **10g** [7]. The combination of the results reported in this and in our previous paper [1] makes evident the analogy between the reaction mechanisms controlling the cyclization of these arylazoic substrates into dihydrobenzotriazepines or dihydroindazole derivatives. In addition to the possible development of this research along more synthetic lines, it is interesting to point out that the mechanistic rationalization of both routes involves two new tautomeric equilibria (even occurring simultaneously in a few substrates) which produce the loss of the aromaticity of an electron rich ring. The driving force of these tautomerizations, both favourably influenced by a basic catalyst, can be due to the presence in the molecule of the substrate of two portions, one electron rich and the other electron poor; these tautomerizations can be described as internal oxo-reduction processes.



EXPERIMENTAL

Melting points are uncorrected. The ^{1}H nmr spectra were recorded on a A90 Varian spectrometer, using deuteriochloroform as solvent unless otherwise stated and tetramethylsilane as internal standard; chemical shifts are given in δ units and refer to the center of the signal (s, singlet, m, multiplet, d, doublet, dd, double doublet, t, triplet, q, quartet).

Methyl Chloro[(2,6-dimethylphenyl)hydrazono]acetate.

A solution of sodium nitrite (5.0 g) in water (20 ml) was dropped into a solution of 2,6-dimethylaniline (8.2 g) in a 10% hydrochloric acid solution (80 ml) under stirring and keeping the temperature below 5°. The resulting solution was stirred for 10 minutes after the end of the addition; the *p*H was adjusted to 6 by adding solid sodium bicarbonate, then a solution of methyl 2-chloroacetoacetate (10 g) in methanol (20 ml) and anhydrous sodium acetate (5.5 g) were added. The mixture was left under stirring at room temperature overnight; the dark red oil separated was extracted with ethyl ether. The organic layer was washed with water and dried over sodium sulfate; the solvent was removed under reduced pressure and the oily residue was chromatographed on a silica gel column (eluant, chloroform). The first fractions eluted gave a red viscous oil, which solidified on standing to give the title compound as a light brown solid with mp 53° (*n*-pentane), yield 53%; ^{1}H nmr: 2.40 (6H, s, 2 CH_3), 3.92 (3H, s, OCH_3), 7.05 (3H, s, aromatic); 8.07 (1H, broad s, NH).

Anal. Calcd. for $C_{11}ClN_2O_2$: C, 54.89; H, 5.44; N, 11.64. Found: C, 54.68; H, 5.37; N, 11.42.

Methyl [(2,6-Diethylphenyl)amino][(2,6-dimethylphenyl)hydrazono]acetate **1**.

A solution of methyl chloro[(2,6-dimethylphenyl)hydrazono]acetate (described above) (3.0 g), 2,6-diethylaniline (1.9 g) and triethylamine (1.0 g) in methanol (50 ml) was refluxed for 1 hour. The solvent was evaporated under reduced pressure and the residue treated with a 5% hydrochloric acid solution and ethylether; the organic layer was washed with water, dried over sodium sulfate and evaporated to dryness. The oily residue, impure of some diethylaniline, was purified by column chromatography (silica gel-chloroform) to give the title compound as a light yellow solid with mp 67° (*n*-hexane), yield 43%; ^{1}H nmr: 1.32 (6H, t, $2CH_2CH_3$), 2.05 (6H, s, $2CH_3$), 2.80 (4H, q, $2CH_2CH_3$), 3.95 (3H, s, $COOCH_3$), 6.47 and 6.55 (each 1H, 2 broad s exchanging with deuterium oxide, 2NH), 6.7-7.2 (6H, m, aromatic).

Anal. Calcd. for $C_{21}H_{27}N_3O_2$: C, 71.36; H, 7.70; N, 11.89. Found: C, 71.56; H, 7.75; N, 11.99.

Methyl [(2,6-Diethylphenyl)imino][(2,6-dimethylphenyl)azo]acetate **2**.

Active manganese dioxide (10 g) was added portionwise to a solution of **1** (5 g) in methylene chloride (50 ml) under stirring. The mixture was refluxed for 30 minutes then cooled, filtered on a cell cake and the solvent removed under reduced pressure to give **2** as a red oily residue.

Anal. Calcd. for $C_{21}H_{25}N_3O_2$: C, 71.77; H, 7.17; N, 11.90. Found: C, 71.69; H, 7.20; N, 11.69.

Thermolysis of **2**.

A solution of **2** (3.2 g) in xylene was refluxed for 30 minutes in the presence of a catalytic amount of DABCO. The solvent was removed under reduced pressure to give a residue which was chromatographed on a silica gel column (eluant: chloroform). The first product eluted was the methyl [(2,6-diethylphenyl)imino][2-(7-methyl)-2*H*-indazolyl]acetate **4** in a pure state, mp 79° (*n*-hexane) (0.82 g); ^{1}H nmr: 1.15 (6H, t, $2CH_2CH_3$), 2.54 (7H, superimposed q and s, CH_3 and 2 CH_2CH_3), 3.70 (3H, s, OCH_3), 6.9-7.5 (6H, m, aromatic), 8.80 (1H, s, aromatic in position 3 of the indazole ring); ms: 349.

Anal. Calcd. for $C_{21}H_{23}N_3O_2$: C, 72.18; H, 6.63; N, 12.03. Found: C, 72.01; H, 6.39; N, 12.00.

Short refluxing of **4** in 20% hydrochloric acid solution afforded the 7-methylindazole, purified by column chromatography (silica gel, eluant, benzene) and identified by comparison with an authentic sample [8], 2,6-diethylaniline, and oxalic acid. From the following fractions the 2-carbomethoxy-4,5-dihydro-4-(2,6-dimethylphenyl)-9-ethyl-5-methyl-1*H*-1,3,4-benzotriazepine (**3**) was obtained as a viscous oil (0.36 g); ^{1}H nmr: 1.28 (3H, t, CH_2CH_3), 1.58 (3H, d, CH-CH_3), 2.20 and 2.44 (each 3H, 2 broad s, 2 CH_3), 2.65 (2H, q, CH_2-CH_3), 3.82 (3H, s, OCH_3), 4.42 (1H, q, $CHCH_3$), 6.7-7.15 (6H, m, aromatic), 7.48 (1H, broad s, NH); ms: 351.

Anal. Calcd. for $C_{21}H_{25}N_3O_2$: C, 71.77; H, 7.17; N, 11.96. Found: C, 71.98; H, 6.73; N, 12.00.

The last product eluted was **1** (0.8 g), identified by comparison with an authentic sample.

Methyl Chloro[(2,6-diethylphenyl)hydrazono]acetate.

The procedure was identical to that described above for the synthesis of the methyl chloro[(2,6-dimethylphenyl)hydrazono]acetate, with the only difference that 2,6-diethylaniline was employed instead of 2,6-xylidine; in the present case the neutralized diazo solution was filtered. The title compound was purified by chromatagraphy on a silica gel column (eluant, carbon tetrachloride). It was a brown viscous oil; ^{1}H nmr: 1.28 (6H, t, 2 CH_2CH_3), 2.75 (4H, q, 2 CH_2CH_3), 3.92 (3H, s, OCH_3), 7.12 (3H, m, aromatic), 8.04 (1H, broad s, NH).

Anal. Calcd. for $C_{13}H_{17}ClN_2O_2$: C, 58.10; H, 6.33; N, 10.43. Found: C, 57.88; H, 6.22; N, 10.26.

Methyl [(2,6-Dimethylphenyl)amino][(2,6-diethylphenyl)hydrazono]acetate **7**.

This product was obtained by reaction of the halohydrazone described above and 2,6-xylidine following the method described for the synthesis

of **1**. It was obtained in a 67% yield as a yellow solid with mp 55° (*n*-hexane); ^{1}H nmr: 1.09 (6H, t, 2 CH_2CH_3), 2.45 (10H, m, 2 CH_2CH_3 and $2CH_3$), 3.95 (3H, s, OCH_3), 6.45 and 6.50 (each 1H, 2 broad s exchanging with deuterium oxide, 2NH), 6.95 and 7.10 (2 × 3H, 2s, aromatic).

Anal. Calcd. for $C_{21}H_{27}N_3O_2$: C, 71.36; H, 7.70; N, 11.89. Found: C, 71.06; H, 7.50; N, 11.80.

Methyl [(2,6-Dimethylphenyl)imino][(2,6-diethylphenyl)azo]acetate **5**.

This compound was obtained as a dark red viscous oil by oxidation of the aminohydrazone described above with manganese dioxide (twice in weight) in refluxing methylene chloride solution (2 hours). It was directly submitted to the thermolysis without any further purification.

Thermolysis of **5**.

A solution of crude **5** (2.2 g) in xylene (50 ml) was refluxed for 30 minutes in the presence of a trace of DABCO. Evaporation of the solvent *in vacuo* left a residue which was chromatographed on a silica gel column (eluant, chloroform). The fractions initially eluted gave the methyl [(2,6-dimethylphenyl)imino][2-(7-ethyl-3-methyl)-2*H*-indazolyl]acetate **6** in a pure state with mp 82° (*n*-hexane) (0.60 g); ^{1}H nmr: 1.35 (3H, t, CH_2CH_3), 2.20 (6H, s, $2CH_3$), 2.97 (5H, superimposed q and s, CH_2CH_3 and CH_3 in position 3 of the indazole ring), 6.8-7.5 (6H, m, aromatic).

Anal. Calcd. for $C_{21}H_{23}N_3O_2$: C, 72.18; H, 6.63; N, 12.03. Found: C, 72.21; H, 6.58; N, 12.03.

The following fractions gave the methyl [(2,6-dimethylphenyl)amino][(2,6-diethylphenyl)hydrazono]acetate **7**, identical under every respect with the product described above.

(2,6-Dimethylphenyl)semicarbazide **10a**.

This compound was prepared according to a general method [9], starting from (2,6-dimethylphenyl)hydrazine hydrochloride [10] and potassium cyanate in aqueous solution, mp 206°; ^{1}H nmr (DMSO/deuterium oxide): 2.31 (6H, s, $2CH_3$), 6.7-7.1 (3H, m, aromatic), 6.70 (1H, s, NH-CO).

Anal. Calcd. for $C_9H_{13}N_3O$: C, 60.31; H, 7.31; N, 23.45. Found: C, 60.42; H, 7.19; N, 23.61.

[(2,6-Dimethylphenyl)azo]carboxamide **8a**.

A solution of chromium trioxide (4.1 g) in water (40 ml) was dropped into a stirred solution of (2,6-dimethylphenyl)semicarbazide **10a** (10.4 g) in the minimum volume of acetic acid and keeping the temperature at 5-10°. The resulting solution was diluted with water and the precipitated red solid was filtered and dried, mp 124° (8.2 g); ^{1}H nmr: 2.48 (6H, s, $2CH_3$), 6.42 (2H, broad s exchanging with deuterium oxide, NH_2), 7.0-7.4 (3H, m, aromatic).

Anal. Calcd. for $C_9H_{11}N_3O$: C, 61.00; H, 6.26; N, 23.72. Found: C, 60.82; H, 6.08; N, 23.56.

Thermolysis of **8a**.

A solution of **8a** (2 g) in chlorobenzene (60 ml) was refluxed for 12 hours in the presence of catalytic amounts of DABCO. Cyanuric acid was formed on the surface of the condenser; it was dissolved in methanol and precipitated by dilution with diisopropyl ether (0.2 g). The chlorobenzene solution was exhaustively extracted with a 5% hydrochloric acid solution; the combined extracts were made alkaline and the separated product was extracted in turn with ethyl ether. The organic layer was dried over sodium sulfate and evaporated to dryness to give the 7-methylindazole **12a** (0.6 g), identical to an authentic sample prepared by independent synthesis [8]. The chlorobenzene solution was washed with a 5% sodium bicarbonate solution, dried over sodium sulfate and evaporated to dryness under reduced pressure. The colorless residue was the (2,6-dimethylphenyl)semicarbazide **10a** (0.7 g) whose physical and spectral data were identical to those obtained from an authentic sample.

N-(2,6-Dimethylphenyl)-*N'*-ethoxycarbonylhydrazine **10b**.

A solution of ethyl chloroformate (4.5 g) in ethyl ether (20 ml) was dropped into a solution of 2,6-dimethylphenylhydrazine [10] (5.6 g) and triethylamine (6.9 ml) in ethyl ether (50 ml) under stirring and keeping the temperature at 0-5°. The mixture was stirred for 30 minutes at room temperature then treated with water, the organic layer was dried and evaporated to dryness to give a solid residue which was crystallized from hexane, mp 62° (7.3 g); ^{1}H nmr: 1.20 (3H, t, OCH_2CH_3), 2.40 (6H, s, 2 CH_3), 4.10 (2H, q, OCH_2CH_3), 5.72 (1H, broad s exchanging with deuterium oxide, ArNH), 6.43 (1H, broad s, NHCO), 6.7-7.1 (3H, m, aromatic).

Anal. Calcd. for $C_{11}H_{16}N_2O_2$: C, 63.44; H, 7.74; N, 13.45. Found: C, 63.26; H, 7.47; N, 13.54.

Ethyl (2,6-Dimethylphenyl)azocarbonate **8b**.

A solution of chromium trioxide (2 g) in water (10 ml) was dropped into a solution of the *N*-(2,6-dimethylphenyl)-*N'*-ethoxycarbonylhydrazine **10b** described above (4.1 g) in 70% acetic acid (20 ml) under stirring and keeping the temperature below 5°. After 20 minutes the solution was diluted with water and the precipitated oil extracted with methylene chloride; the organic layer was washed with a 5% sodium bicarbonate solution, dried over sodium sulfate and evaporated to dryness to give **8b** as a dark oil (3.5 g); ^{1}H nmr: 1.48 (3H, t, OCH_2CH_3), 2.48 (6H, s, $2CH_3$), 4.53 (2H, q, OCH_2CH_3), 7.0-7.4 (3H, m, aromatic).

Anal. Calcd. for $C_{11}H_{14}N_2O_2$: C, 64.06; H, 6.84; N, 13.58. Found: C, 64.00; H, 6.50; N, 13.11.

Thermolysis of **8b**.

A solution of crude **8b** (3.5 g) in xylene was refluxed for 90 minutes in the presence of catalytic amounts of DABCO, then cooled and exhaustively extracted with a 5% hydrochloric acid solution. The aqueous layer was neutralized with a 5% sodium hydroxide solution and the separated oil extracted with ethyl ether; the organic layer was dried over sodium sulfate and evaporated to dryness to give the 7-methylindazole **12a** as a light yellow solid which was crystallized from *n*-hexane (0.3 g). The physical and spectral data were coincident with those shown by an authentic sample [8]. The xylene solution, after removal of the solvent, gave a residue (0.6 g) which was chromatographed on a silica gel column (eluant, benzene-ethyl acetate, 9:1). The first fractions eluted gave the 7-methyl-1-ethoxycarbonylindazole (**11**), which was further purified by distillation *in vacuo;* ^{1}H nmr: 1.53 (3H, t, OCH_2CH_3), 2.78 (3H, s, CH_3), 4.58 (2H, q, OCH_2CH_3), 6.9-7.7 (3H, m, aromatic in position 4,5 and 6), 8.20 (1H, s, aromatic in position 3).

Anal. Calcd. for $C_{11}H_{12}N_2O_2$: C, 64.71; H, 13.73; N, 5.88. Found: C, 64.45; H, 13.90; N, 5.82.

In a few fractions **11** was contaminated by the 7-methyl-2-ethoxycarbonylindazole **9b**, whose presence was clearly indicated in the ^{1}H nmr spectrum by a singlet at 8.66, typical of the aromatic proton in position 3 of the 2*H*-indazole ring. The last fractions eluted gave **10b** (0.4 g), whose physical and spectral data were coincident with those described above.

N-(2,6-Dimethylphenyl)-*N'*-(4-nitrobenzoyl)hydrazine **10c**.

A solution of 4-nitrobenzoylchloride (7.6 g) in dry THF (100 ml) was dropped into a stirred solution of (2,6-dimethylphenyl)hydrazine [10] (5.6 g) and triethylamine (6.9 ml) in ethyl ether (100 ml) keeping the temperature at 0°. At the end of the addition, the temperature was allowed to rise to 25°. Water was added and the organic solvent evaporated under reduced pressure. The product was extracted with ethyl acetate, and the organic layer was washed with water, dried over sodium sulfate and evaporated to dryness. The yellow residue (4.4 g) was crystallized from 2-propanol and showed, mp 209° (2.5 g); ^{1}H nmr: 2.25-2.72 (6H, m, 2 CH_3), 6.26 (1H, broad s exchanging with deuterium oxide, Ar-NH), 6.78-7.28 (3H, m, C_6H_3), 8.00-8.56 (4H, m, C_6H_4), 10.48 (1H, broad s, exchanging with deuterium oxide, NHCO).

Anal. Calcd. for $C_{15}H_{15}N_3O_3$: C, 63.15; H, 5.30; N, 14.73. Found: C, 63.50; H, 5.50; N, 14.80.

4-[(2,6-Dimethylphenyl)azocarbonyl]nitrobenzene **8c**.

A saturated solution of potassium permanganate in water (10 ml) was rapidly added to a solution of **10c** (1 g) in the minimum amount of acetic acid. The mixture was diluted with water and the red solid precipitate was filtered and submitted to the thermolysis without any further purifi-

cation, mp 98° (0.65 g); ^{1}H nmr: 2.55 (6H, s, 2 CH_3), 7.1-7.4 (3H, m, C_6H_4), 8.2-8.5 (4H, m, C_6H_3).

Anal. Calcd. for $C_{15}H_{13}N_3O_3$: C, 63.60; H, 4.59; N, 14.84. Found: C, 63.40; H, 4.39; N, 14.63.

Thermolysis of **8c**.

A solution of **8c** (0.5 g) in xylene (30 ml) was refluxed in the presence of traces of DABCO for a few minutes. The hydrazide **10c** precipitated on cooling the solution and was filtered and identified by comparison of its physical properties with those shown by an authentic sample (0.15 g). The solution was evaporated to dryness and the residue crystallized from 2-propanol to give the 7-methyl-2-(4-nitrobenzoyl)indazole **9b** (0.12 g) with mp 165°; ^{1}H nmr: 2.58 (3H, s, CH_3), 6.86-7.58 (3H, m, aromatic in position 4,5 and 6 of the indazole ring), 8.25-8.60 (4H, m, C_6H_4), 8.88 (1H, s, aromatic in position 3 of the indazole ring).

Anal. Calcd. for $C_{15}H_{11}N_3O_3$: C, 64.06; H, 3.91; N, 14.95. Found: C, 64.21; H, 4.09; N, 14.49.

N-(2-Methylphenyl)-*N'*-(4-nitrobenzoyl)hydrazine **10d**.

The reaction between (2-methylphenyl)hydrazine [10] (6.3 g) and 4-nitrobenzoyl chloride in the presence of triethylamine was carried out following the procedure described above for the synthesis of **10c**. Compound **10d** had mp 176° (2-propanol) (5.1 g); ^{1}H nmr: 2.34 (3H, s, CH_3); 6.68-7.24 (4H + 1H exchanging with deuterium oxide, m, C_6H_4-NH); 8.12-8.42 (4H, m, C_6H_4CO).

Anal. Calcd. for $C_{14}H_{13}N_3O_3$: C, 61.98; H, 4.83; N, 15.49. Found: C, 62.29; H, 5.00; N, 15.72.

4-[(2-Methylphenyl)azocarbonyl]nitrobenzene **8d**.

The oxidation of **10d** (5 g) to the title compound was performed following the procedure described above for the synthesis of **8c**. Compound **8d** had mp 130° (2-propanol), (4.3 g); ^{1}H nmr: 2.86 (3H, s, CH_3), 6.80-7.78 (4H, m, C_6H_4-N), 8.16-8.48 (4H, m, C_6H_4CO).

Anal. Calcd. for $C_{14}H_{11}N_3O_3$: C, 62.45; H, 4.12; N, 15.61. Found: C, 62.66; H, 4.24; N, 15.77.

Thermolysis of **8d**.

A solution of **8d** (3.5 g) in xylene was refluxed for 4 hours in the presence of a trace of DABCO. The hydrazide **10d** precipitated by cooling the solution and was filtered and identified by comparison of its physical properties with those shown by an authentic sample (0.75 g). The mother liquors were exhaustively extracted with a 5% hydrochloric acid solution; the combined aqueous extracts were made alkaline with a 33% sodium hydroxide solution. The separated product was extracted with ether to give, after the usual work up, the indazole **12d** (0.12 g), identical to a sample prepared according to the literature [11]. The xylene solution was evaporated to dryness at reduced pressure and the residue (2.64 g), which contained more **12d** and **9d** was chromatographed on a silica gel column (eluant, chloroform). From the first fractions eluted the 2-(4-nitrobenzoyl)indazole **9d** was obtained in a pure state with mp 162° (diisopropyl ether) (0.49 g); ^{1}H nmr: 7.26-7.88 (3H, m, aromatic in position 4, 5 and 6 of the indazole ring), 8.10-8.66 (6H, m, C_6H_4 and aromatic in position 6 and 3 of the indazole ring).

Anal. Calcd. for $C_{14}H_9N_3O_3$: C, 62.92; H, 3.39; N, 15.73. Found: C, 63.02; H, 3.42; N, 15.59.

The following fractions gave more **10d** (0.18 g).

(2-Methylphenyl)azocarbonylbenzene **8e**.

A saturated solution of potassium permanganate (20 ml) was rapidly added to a solution of *N*-benzoyl-*N'*-(2-methylphenyl)hydrazine **10e** [11] (3.5 g) in acetic acid (20 ml). The resulting solution was diluted with water and the precipitated manganese dioxide filtered by suction on a cell cake. The clear filtrate was exhaustively extracted with methylene chloride; the combined organic extracts were washed with water, dried over sodium sulfate, then evaporated to dryness. The title compound **8e** was obtained as a dark red oil (1.4 g), which was used in a crude state; ^{1}H nmr: 2.70 (3H, s, CH_3), 6.90-7.76 (9H, m, aromatic), 8.03 (2H, m, aromatic in position *ortho* to the CO group).

Thermolysis of **8e**.

A solution of **8e** (1.4 g) in xylene (25 ml) was refluxed in the presence of a trace of DABCO for 12 hours; the solvent was removed at reduced pressure and the residue chromatographed on a silica gel column (eluant, chloroform). Fractions first eluted gave the 2-benzoylindazole **11e** in a pure state (0.38 g); analytical and spectral data were identical to those shown by an authentic sample [12]. The following fractions gave the *N*-benzoyl-*N'*-(2-methylphenyl)hydrazine **10e**, identical to the starting product in the synthesis of **8e** (0.40 g).

N-Benzoyl-*N'*-(2,6-dimethylphenyl)hydrazine **10f**.

The reaction between (2,6-dimethylphenyl)hydrazine and benzoyl chloride was performed in ethyl ether solution in the presence of an equimolar amount of triethylamine at 5°. The precipitated product was filtered off, washed with water, then crystallized from 2-propanol to give **10f** with mp 134°, yield 55%; ^{1}H nmr: 2.51 (6H, s, 2CH_3), 6.31 (1H, d, exchanging with deuterium oxide, Ar-NH), 6.80-7.14 (3H, m, C_6H_3), 7.26-7.52 (3H, m, aromatic in position 3,4,5 of the benzoyl group), 7.66-7.84 (2H + 1H exchanging with deuterium oxide, m, aromatic in position 2,6 of benzoyl group and NH-CO).

Anal. Calcd. for $C_{15}H_{16}N_2O$: C, 74.97; H, 6.71; N, 11.66. Found: C, 74.70; H, 6.27; N, 11.52.

[(2,6-Dimethylphenyl)azocarbonyl]benzene **8f**.

The oxidation of the *N*-benzoyl-*N'*-(2,6-dimethylphenyl)hydrazine **10f** (3 g) was performed as described before for the synthesis of **10e**. The title product was obtained as a dark red oil (2.3 g), which was submitted to the thermolysis in a crude state; ^{1}H nmr: 2.53 (6H, s, 2CH_3), 7.20 (3H, m, C_6H_3), 7.55 (3H, m, aromatic), 8.10 (2H, m, aromatic in position *ortho* to the CO group).

Thermolysis of **8f**.

A solution of **8f** (3.2 g) in xylene (60 ml) was refluxed in the presence of a trace of DABCO for 1 hour. The solvent was removed under reduced pressure and the residue chromatographed on a silica gel column (eluant, chloroform). The first product eluted was the 2-benzoyl-7-methylindazole **9f** with mp 78° (*n*-hexane) (0.47 g); ^{1}H nmr: 2.61 (3H, s, CH_3), 7.06 (2H, s, aromatic), 7.58 (4H, m, aromatic), 8.33 (2H, m, aromatic in position *ortho* to the CO group), 8.84 (1H, s, aromatic in position 3 of the indazole ring); ms: 236.

Anal. Calcd. for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86. Found: C, 75.98; H, 5.08; N, 12.06.

The following fractions gave the hydrazide **10f** (0.40 g), whose physic and spectral data were identical to those given by an authentic sample.

N-(2,6-Dimethylphenyl)-*N'*-(2,4-dinitrophenyl)hydrazine **10g**.

A solution of 2,6-dimethylphenylhydrazine [10] (5.5 g) and 2,4-dinitrochlorobenzene (4.1 g) in benzene (100 ml) was left to stand in the dark at room temperature for one week. The precipitated solid was filtered off and the filtrate was washed with a 35% sodium hydroxide solution, then with water, dried over sodium sulfate and evaporated to dryness under reduced pressure. The residue was treated with diisopropyl ether to give **10g** in a pure state (3.7 g) with mp 162°; ^{1}H nmr: 2.30 (6H, s, 2 CH_3), 5.73 (1H, s, exchanging with deuterium oxide, NH carrying the xylyl group), 7.06 (3H, s, aromatic of the xylyl group), 8.00 (1H, d, aromatic in position 6 of the 2,4-dinitrophenyl group), 8.40 (1H, dd, aromatic in position 5 of the 2,4-dinitrophenyl group), 9.14 (1H, d, aromatic in position 3 of the 2,4-dinitrophenyl group), 9.35 (1H, broad s, NH).

Anal. Calcd. for $C_{14}H_{14}N_4O_4$: C, 55.62; H, 4.67; N, 18.54. Found: C, 55.39; H, 4.62; N, 18.59.

2,6-Dimethyl-2',4'-dinitroazobenzene **8g**.

The oxidation of **10g** to the title compound **8g** [13] was effected with manganese dioxide in methylene chloride solution at 20°; **8g** showed mp 163° (*n*-hexane); ^{1}H nmr: 220 (6H, s, 2CH_3), 7.20-7.60 (3H, m, aromatic of

the xylyl group), 7.90 (1H, d, aromatic in position 6 of the 2,4-dinitrophenyl group), 8.27 (1H, dd, aromatic in position 5 of the 2,4-dinitrophenyl group), 8.95 (1H, d, aromatic in position 3 of the 2,4-dinitrophenyl group).

Anal. Calcd. for $C_{14}H_{12}N_4O_4$: C, 56.00; H, 4.03; N, 18.66. Found: C, 56.10; H, 4.00; N, 18.33.

Thermolysis of **8g**.

A solution of **8g** (3.5 g) in xylene (40 ml) was refluxed in the presence of a trace of DABCO for 12 hours. The solvent was removed under reduced pressure and the residue was chromatographed on a silica gel column (eluant, chloroform). The first fractions eluted gave some unreacted starting product (0.11 g). The following fractions gave the 3-(2,6-dimethylphenyl)-5-nitrobenzo-1,2,3-triazole **13** (0.45 g) which was purified through a new chromatography (silica gel - benzene:petroleum ether -7:3) followed by distillation *in vacuo*. The product solidified on standing and showed mp 70° (*n*-hexane); ^{1}H nmr: 2.03 (6H, s, $2CH_3$), 7.40 (3H, m, aromatic of the xylene ring), 8.15 (1H, dd, aromatic in position 7 of the benzotriazole ring), 8.40 (1H, dd, aromatic in position 6 of the benzotriazole ring), 9.05 (1H, d, aromatic in position 4 of the benzotriazole ring); ms: 268.

The following fractions gave the hydrazine **10g** (0.3 g), identified by comparison of its physical data with those shown by an authentic sample. The combined following fractions (1.2 g) were constituted by a mixture of two products: the more abundant, which was eluted in a pure state in few fractions, was the 2-(2,6-dimethylphenyl)-6-nitro-benzotriazole-1-oxide **14** which showed mp 117°; ^{1}H nmr: 2.04 (6H, s, 2 CH_3), 7.3 (3H, m, aromatic of the xylene ring), 7.90 (1H, d, aromatic in position 7 of the benzotriazole ring), 8.24 (1H, dd, aromatic in position 6 of the benzotriazole ring), 8.87 (1H, d, aromatic in position 4 of the benzotriazole ring); ms: 286.

Anal. Calcd. for $C_{14}H_{12}N_4O_3$: C, 59.15; H, 4.26; N, 19.71. Found: C, 59.05; H, 4.16; N, 19.39.

The second product of the mixture **9g** [14] was obtained in a pure state by direct crystallization of the mixture from 2-propanol and showed mp 151°; ^{1}H nmr: 2.52 (3H, s, CH_3); 7.05 and 7.50 (2H, and 1H, 2m, aromatic in position 4,5 and 6 of the indazole ring), 7.90 (1H, d, aromatic in position 6 of the 2,4-dinitrophenyl group), 8.20 (1H, s, aromatic in position 3 of the indazole ring), 8.50 (1H, dd, aromatic in position 5 of the 2,4-dinitrophenyl group), 8.71 (1H, d, aromatic in position 3 of the 2,4-dinitrophenyl group) [14]; ms: 298.

Anal. Calcd. for $C_{14}H_{10}N_4O_4$: C, 56.38; H, 3.38; N, 18.79. Found: C, 56.20; H, 3.33; N, 18.72.

N-(2,6-Dimethylphenyl)-*N'*-[2-(4,6-dichloro-1,3,5-triazinyl]hydrazine **10h**.

A solution of 2,6-dimethylphenylhydrazine [10] (2.7 g) in benzene (20 ml) was dropped into a suspension of cyanuric chloride (1.8 g) in benzene (20 ml) under stirring at room temperature. The 2,6-dimethylphenylhydrazine hydrochloride immediately precipitated and, at the end of the addition, was filtered off. the clear filtrate was evaporated to dryness under reduced pressure and the residue crystallized from diluted ethanol to give **10h** (0.8 g) with mp 176°; ^{1}H nmr: 2.43 (6H, s, 2 CH_3), 6.08 (1H, broad s exchanging with deuterium oxide, Ar-NH), 6.95 (3H, s, C_6H_3), 7.58 (1H, broad s exchanging with deuterium oxide, NH-triazine group).

Anal. Calcd. for $C_{11}H_{11}Cl_2N_5$: C, 46.50; H, 3.90; N, 24.64. Found: C, 46.69; H, 4.04; N, 24.46.

4,6-Dichloro-2[(2,6-dimethylphenyl)azo]-1,3,5-triazine **8h**.

A mixture of the hydrazine **10h** (0.41 g), manganese dioxide (0.8 g) and methylene chloride (20 ml) was stirred at room temperature for 20 minutes, then filtered on a cell cake. The solution was evaporated to dryness to give a red solid which showed mp 157° dec and was submitted to thermolysis in a crude state.

Anal. Calcd. for $C_{11}H_5Cl_2N_5$: C, 46.83: H, 3.22; N, 26.82. Found: C, 46.85; H, 3.12; N, 24.75.

Thermolysis of **8h**.

A solution of **8h** (0.35 g) in xylene (20 ml) was refluxed in the presence of traces of DABCO for 1 hour. Solvent was removed under reduced pressure and the residue was chromatographed on a silica gel column (eluant, chloroform). The first fractions gave the 4,6-dichloro-2-[2-(7-methylindazolyl]-1,3,5-triazine **9h** in a pure state with mp 204° (*n*-hexane) (0.075 g); ^{1}H nmr: 2.70 (3H, s, CH_3), 6.9-7.5 (3H, m, aromatic), 9.08 (1H, s, aromatic in position 3 of the indazole ring).

Anal. Calcd. for $C_{11}H_7Cl_2N_5$: C, 47.16; H, 2.51; N, 25.00. Found: C, 46.88; H, 2.68; N, 25.39.

The following fractions gave the hydrazine **10h** (0.12 g), which was identified by comparison with an authentic sample.

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