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Syntheses of *gem*-Dinitro Heterocyclic Compounds, their Ring-Opening Reactions and Transformations into Indoles, Indazoles and Benzoxazinones

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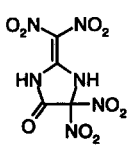
Dedicated to Professor Henk van der Plas on the occasion of his 70th birthday.

Abstract: The synthesis of some novel 3,3,5,7-tetranitrooxindoles and 4,4-dinitropyrazol-5-ones and their behaviour towards various nucleophiles and electrophiles are reported. Reactions with hydroxide ions or secondary amines produced salts of *e.g.* 2-amino-3,5-dinitrophenyldinitromethane, which subsequently could be further transformed into indazoles, indoles or benzoxazinones depending upon substrate and conditions used. Mechanisms are discussed.

Keywords: nitration, nitro compounds, indolines/indolinones, pyrazolones

Introduction. Several methods are available for the introduction of *gem*-dinitro functions in organic molecules, including the Ponzio reaction and nitration of active methylene compounds with HNO_3/H_2SO_4,[1-4] or, as recently reported, with cerium ammonium nitrate.[5] From some recent studies in our laboratory it is evident that the method of direct nitration has a much broader applicability provided that the reaction mixtures are worked up appropriately. Thus, nitration of 2-methyl-4-nitroimidazole with HNO_3/H_2SO_4 produced the tetranitro compound **1**, as a white solid in the medium, which did not survive aqueous work-up, because the ring is quickly ruptured giving 1,1-diamino-2,2-dinitroethylene.[6]

Similar nitration of oxindole produced 3,3,5,7-tetranitrooxindole **2a**, also as a white solid, which could be isolated by collection on a glass filter followed by several washings with trifluoroacetic acid, a technique also used for the isolation of **1**. However compound **2a** is considerably less sensitive towards ring cleavage and here aqueous work-up is possible (keeping the temperature below 5 °C).[7]



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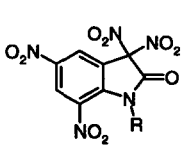

2a: R = H
2b: R = Me
2c: R = Et

In the present paper we discuss the chemistry of 3,3,5,7-tetranitrooxindoles and some related compounds featuring their ring-opening and recyclisation reactions.

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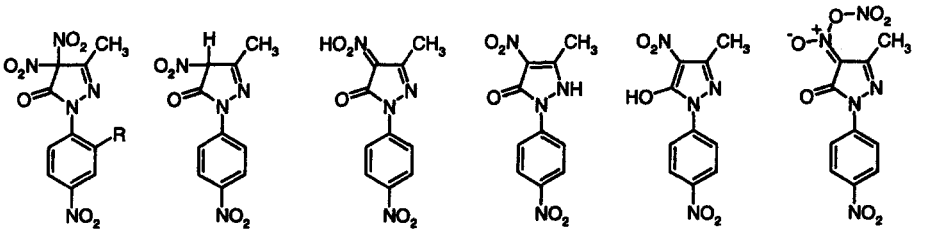
Results and discussion. Only a few active methylene compounds have been converted directly into *gem*-dinitro compounds. Thus diethyl malonate has been transformed to diethyl dinitromalonate[8] and 3-methyl-1-phenylpyrazol-5-one to the trinitrated derivative **3a**, which in turn was the precursor for the preparation of the analytical reagent picrolonic acid **4** (in the literature considered to occur in either of the two tautomeric forms **4a** and **4b**) although **3a** was at the time (1906) incorrectly formulated[9] as the isomer **5**.[10]

From our studies of the NMR spectra of picrolonic acid in various media we conclude that it does exist in different tautomeric forms, none of which however carry hydrogen on carbon as in **4a**, but in DMSO-d_6 it existed as a mixture of **4c** and **4d** in a 5:1 ratio. In $CDCl_3$ this ratio was 1:12. This agrees well with related studies of prototropic equilibria of pyrazolones.[11,12]

The nitration of 3-methyl-1-phenylpyrazol-5-one was studied in considerable detail by the Knorr school with **5** (*i.e.* **3a**) as the pivotal molecule.[9,13,14] In 1941 Iseki *et al.*,[15] without mentioning the previous extensive work, obtained evidence for **3a** as the structure of the trinitrated product from 3-methyl-1-phenylpyrazol-5-one, which is in harmony with the spectral data obtained now.

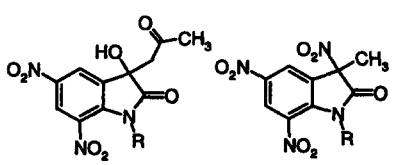


3a: R = H
3b: R = NO_2

4a **4b** **4c** **4d** **5**

With this background it would not be unreasonable to expect 3,3,5,7-tetranitrooxindole as the product of exhaustive nitration of oxindole, in spite of the fact that none of the previous workers, studying the nitration of oxindole, had reported any nitrated oxindoles beyond 5,7-dinitrooxindole.[16-20] Nevertheless, nitration of oxindole at 0-5 °C with an excess of nitric acid in sulfuric or mixtures of trifluoroacetic and sulfuric acids readily gives 3,3,5,7-tetranitrooxindole **2a** in good to excellent yields, which can be collected by filtration (preferably after dilution with trifluoroacetic acid to reduce the viscosity). In connection with this work the literature procedure[17] for the preparation of 5,7-dinitrooxindole was reproduced and co-formation of 3,3,5,7-tetranitrooxindole was invariably observed. However, the reported method of purification (recrystallization from acetone) eliminates 3,3,5,7-tetranitrooxindole due to formation of compound **6**.

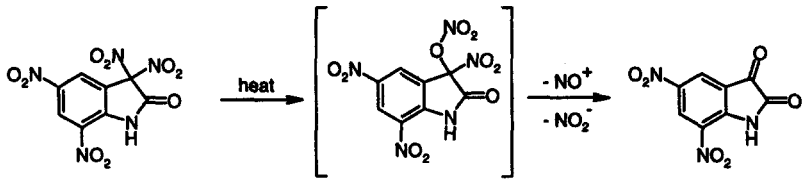
Nitration of alkyl derivatives of oxindoles gave similar products. Thus, nitration of *N*-methyloxindole and *N*-ethyloxindole gave the tetranitro derivatives **2b** and **2c** respectively, whereas 3-methyloxindole and *N*,3-dimethyloxindole gave **7a** and **7b** respectively. Nitration of picrolonic acid **4**, under these conditions, gave the tetranitro derivative **3b**, rather than the previously observed trinitro derivative **3a**. Interestingly, the tetranitro pyrazolone **3b** was somewhat more stable than the trinitro derivative **3a**. We ascribe this phenomenon to the steric interactions of the additional *ortho* nitro group, which forces the two rings somewhat out of planarity.



6

7a: R = H
7b: R = CH_3

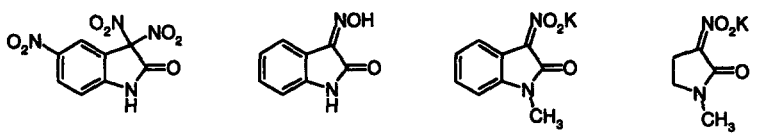
3,3,5,7-Tetranitrooxindole **2a** can, when dry and free from acids, be stored for long periods even at room temperature, which should be compared with the tetranitro derivative **1**, which has a half-life of less than 1 h at 20 °C. In the temperature region 35-40 °C **2a** starts to give off nitrogen oxides, and at 80 °C this decomposition can conveniently be followed in an NMR-tube. The formation of the known[21] compound 5,7-dinitroisatin **8** is complete within 15 minutes. No intermediates could be detected in this presumed nitro-nitrito rearrangement[22-24] (Scheme 1).



2a **9** **8**

Scheme 1. Nitro-nitrito rearrangement of 3,3,5,7-tetranitrooxindole

As no independent proof was available that **2a** was not in fact **9**, it was studied with ^{15}N NMR spectroscopy which gave 3 -NO_2 signals (δ -17, -19 and -23) in the ratio 1:1:2 thereby corroborating structure **2a**. The influence of the nitro groups of the molecule **2a** were obvious in *e.g.* the IR spectrum. Thus the vibration of the C=O group changed from 1697 cm^{-1} in oxindole to 1794 cm^{-1} in **2a**, whereas 5,7-dinitrooxindole absorbs at 1745 cm^{-1}.



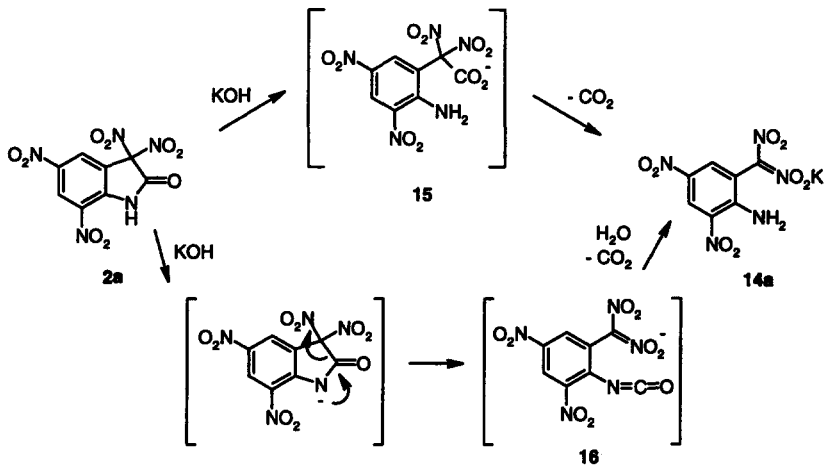
10 **11** **12** **13**

When heated without a solvent to ca 140 °C 3,3,5,7-tetranitrooxindole **2a** reveals its nature as a powerful explosive. The *N*-ethyl tetranitrooxindole **2c**, however, melted at 100 °C and with only slow decomposition. The much less sensitive trinitro derivative **10** could be prepared by treatment of isatin-3-oxime **11** with NO_2 in hot acetonitrile (*i.e.* a Ponzio reaction).[2] In this context it was also found that the potassium salt **12**, obtained in good yield from *N*-methyloxindole using conditions (*tert*-BuOK and butyl nitrate in THF) previously developed by Feuer for the synthesis of the related salt **13**,[25,26] gave *N*-methyl-3,3,5,7-tetranitrooxindole **2b** in fair yield when the salt **12** was subjected to HNO_3/H_2SO_4. This compound was however more conveniently prepared as described above, in excellent yields, by direct nitration of *N*-methyloxindole.

The amide bond in the tetranitrooxindoles **2a** and **2b** is readily attacked by nucleophiles and, when added to aqueous potassium hydroxide at 35-40 °C, quick dissolution occurred, followed within a few minutes by precipitation of the corresponding potassium salts **14a** and **14b**. The mechanism (exemplified by the reaction of **2a** in Scheme 2) is believed to proceed either via nucleophilic attack of hydroxide on the amide carbonyl with $ArNH_2$ as leaving group, followed by quick decarboxylation of the intermediate carboxylate **15**, which could not be isolated, or alternatively the hydroxide ion will first deprotonate the amide, and then the dinitro carbon will act as an intramolecular leaving group whereby an isocyanate **16** is formed, which quickly undergoes hydrolysis, yielding the observed product. A detailed discussion of hydrolysis of isocyanates has

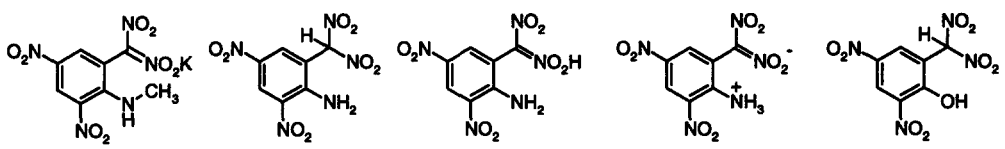
recently been published by Hegarty *et al.*[27] Decarboxylations of simple dinitroacetic acids have been reported previously in the literature.[4,28]

The potassium salts **14a** and **14b** are quite stable and can be recrystallized from water. The free acid **17**, obtained by addition of dilute sulfuric acid to a water solution of the salt **14a** at 25 °C, is relatively unstable and heating of impure material above 70 °C is likely to result in an explosion.



Scheme 2. Formation of the potassium salt **14a** from 3,3,5,7-tetranitrooxindole **2a**

Theoretically compound **17** can occur in several tautomeric forms (**17a-c**). Solutions of the 2-OH analogue of **18** were reported to exhibit a double set of signals in the NMR spectra, something which was accounted for by the existence of two possible modes of hydrogen bonding, either between the hydroxy group and the 6-NO_2 or with the $CH(NO_2)_2$ group.[2] In contrast, compound **17**, when dissolved in dry chloroform, gave a nice simple spectrum featuring a $CH(NO_2)_2$ singlet at δ 7.31 and a broad singlet of the NH_2 group at δ 7.53. The presence of the nitro-nitronic acid isomer **17b** or the zwitterion **17c** could not be detected in this medium.

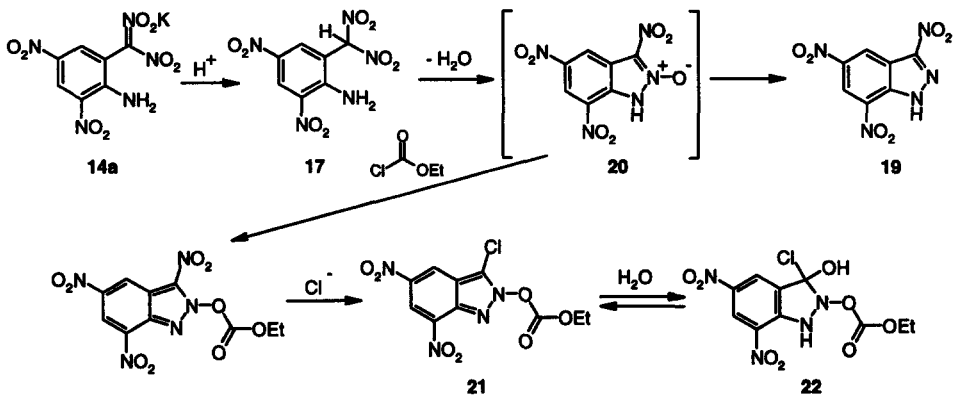


14b **17a** **17b** **17c** **18**

When dissolved in dimethyl sulfoxide, however, compound **17** gave a ^{13}C NMR spectrum identical with that of the potassium salt **14a**, indicating that **17** is acidic enough to protonate dimethyl sulfoxide (pK_a -1.5).[29] The high acidity of this group had previously been recognized by Koletsetskaya *et al.* who have prepared a range of aryldinitromethane salts (*e.g.* 4-amino-3,5-dinitrophenyldinitromethane) by the Ponzio reaction.[30]

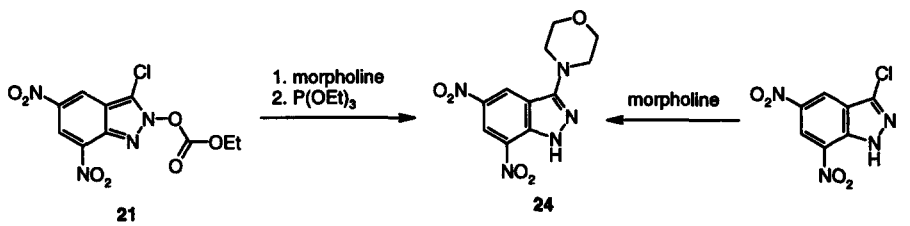
When a solution of **17** in chloroform was refluxed, cyclisation occurred yielding the known[31] compound 3,5,7-trinitroindazole **19** (Scheme 3), which could more conveniently be prepared by adding a small amount of water at 30 °C to 3,3,5,7-tetranitrooxindole **2a** when still in the reaction mixture (*i.e.* sulfuric acid plus some nitric acid).

The cyclisation **17** to **19** is presumed to involve the intermediate indazole 2-oxide **20**, which should readily undergo deoxygenation. Furthermore, if the salt **14a** is heated (80 °C) in the presence of ethyl chloroformate and some acid (*e.g.* HCl), the indazole 2-oxide could be trapped and the product **21** isolated as the corresponding covalent hydrate[32] **22**, probably formed *via* a final exchange of the 3-nitro group by chlorine (Scheme 3). The potential product **23**, or its tautomers, which would have been formed had the initial electrophilic attack taken place at the amino group, was not observed here. It should also be noted that the salt **14a** is stable up to 100 °C in the presence of ethyl chloroformate, but when heated to 105 °C in DMF, **22** can be isolated after aqueous work-up.



Scheme 3.

The structure of the indazole **21** was ascertained with the relations outlined in Scheme 4 and in the final correlation, involving nucleophilic displacement with morpholine to obtain compound **24** this particular secondary amine was chosen because Wrzeciono had previously studied the displacement of chloride from 3-chloro-5-nitroindazole with this amine.[33,34]



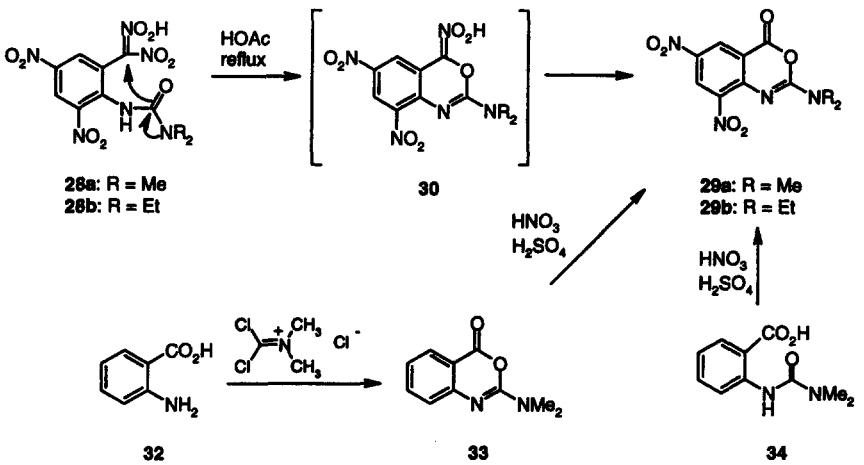
Scheme 4.

It might be added that indazole 2-oxides as a class is known, but only a few members have been studied in any detail.[35,36] Relatively more knowledge is available from the pyrazole series due to Begtrup and Vedsö and both oxygenations/deoxygenations[37] as well as acylations of pyrazole oxides have been studied.[38]

It should also be noted that presence of HNO_2, as previously believed,[7] is not necessary to effect the cyclisation **17** to **19**. In the literature there are several examples of indazole formation by intramolecular reactions of NH_2 groups with NO_2 groups. Thus **25** can, under slightly basic or acidic conditions, be transformed to the indazole 1-oxide **26**.[39] All previous examples however, have involved aromatic nitro compounds.[40]

The NH in **2a** is, as described above, quite acidic and is easily abstracted by weak bases *e.g.* dimethylamine, yielding the corresponding anion (deeply coloured), which ruptures, forming the unisolable isocyanate **16** (*cf.* Scheme 2), which in this case will be trapped by the amine, the product being the salt **27**, that could be transformed into the corresponding acid **28a**. Performing the same reaction sequence with diethylamine or morpholine gave the corresponding derivatives **28b-c**.

The compound **28a**, when dissolved in $CDCl_3$ predominantly exists as the *gem*-dinitro tautomer rather than the nitro-nitronate tautomer, which was particularly evident in the ^{13}C NMR spectrum where the dinitromethyl carbon resonates at 107 ppm.



Scheme 5.

Dissolution of **28a** in DMSO-d_6 gave different spectra because of the high acidity of the proton in the nitronate group. This molecule was (in analogy with compound **17**) converted into the corresponding anion in the medium and gave two sets of signals in the ratio 6:1, which might be explained in terms of different modes of hydrogen bonding of the amide hydrogen as previously discussed for the (2-hydroxy-3,5-dinitrophenyl)dinitromethane **18**.

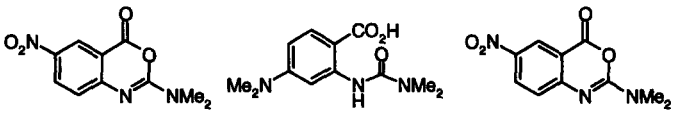
Heating in acetic acid (reflux 2 min) of the acid **28a** resulted in decomposition with evolution of NO_x. Cooling the reaction mixture produced a solid whose structure was identified as 2-dimethylamino-6,8-dinitro-3,1-benzoxazin-4-one (**29a**) by the relations outlined in Scheme 5. The corresponding diethylamino compound **28b** reacted in the same way, yielding **29b**.

These transformations are certainly complex. As a rationalisation we suggest initial nucleophilic attack by the carbonyl oxygen on the nitronate function, leading to **30**, which subsequently will undergo hydrolysis in a Meyer type reaction,[41] to form the observed product, *e.g.* **29a** (IR absorbtion for C=O group at 1791 and 1771 cm^{-1}).

The basicity of the dimethylamino group of **29a** is low due to the strong interaction with the two nitro groups and in the bond to the ring has partial double bond character as evidenced by the NMR spectra, which showed two well separated methyl signals in the ^1H NMR spectrum at room temperature (coalescing at approximately 50 °C). The mononitro derivative **31**, prepared from 5-nitroanthranilic acid by treatment with

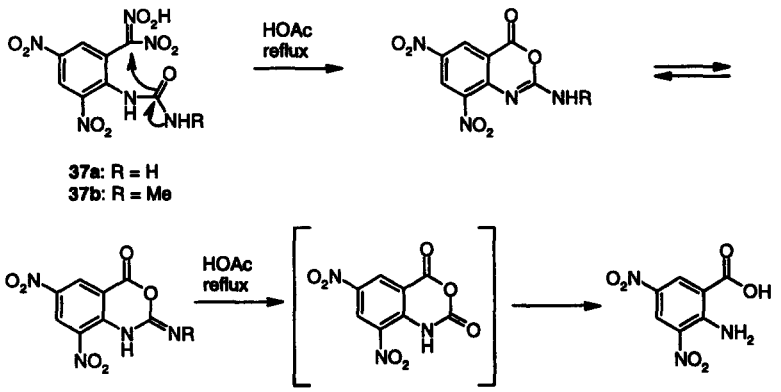
N,N-dimethyl dichloromethyleneiminium chloride (Viehe's reagent) in methylene chloride,[42] and the diethylaminobenzoxazi-none **29b** showed similar behaviour.

Compound **29a** was likewise conveniently and independently prepared by reacting anthranilic acid **32** with Viehe's reagent followed by nitration (HNO_3/H_2SO_4/70 °C) of the thus formed benzoxazinone **33** (C=O absorption at 1772 and 1758 cm^{-1}).



31 **35** **36**

In connection with the development of an independent synthesis of benzoxazinone **29a**, it was found that nitration (HNO_3/H_2SO_4/70 °C) of 2-(*N,N*-dimethylureido)benzoic acid **34**, a compound described by Bitter,[42] also gave the benzoxazinone **29a**, presumably via a cyclisation induced by sulfuric acid (Scheme 5). Similar cyclisations have previously been reported by Krantz *et al.*[43] Thus treatment of the ureido derivative **35** with sulfuric acid gave the benzoxazinone **36**.



37a: R = H
37b: R = Me

38

Scheme 6.

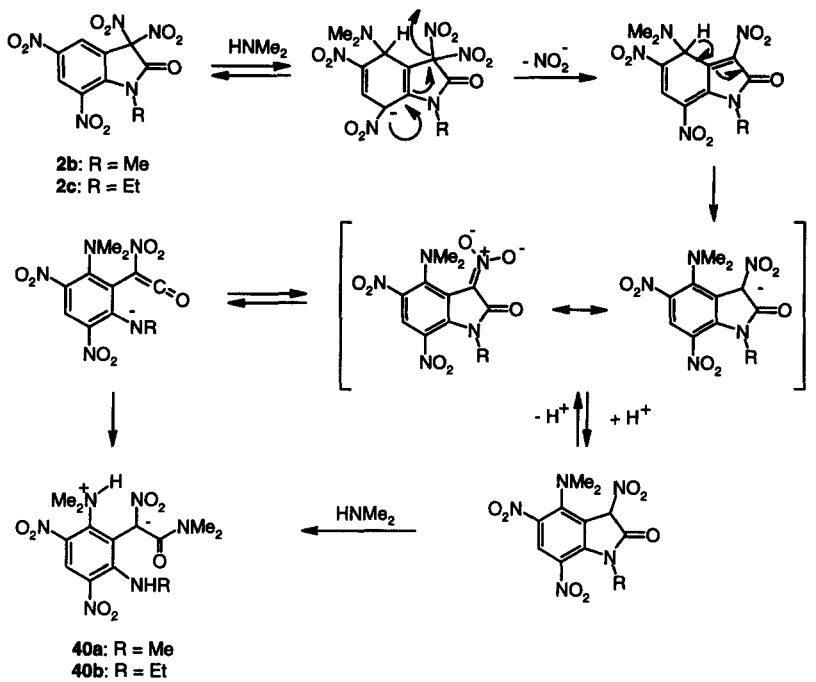
The ring-opening reaction of **2a** with amines could readily be extended using *N,N*-diethylamine, morpholine, methylamine and ammonia. The corresponding cyclisation reactions worked well with the secondary amine adducts, whereas the ureido derivatives **37a** and **37b**, from the reaction of **2a** with ammonia and methylamine respectively, failed to give such derivatives. Instead 3,5-dinitroanthranilic acid was obtained. This outcome could be explained (as shown in Scheme 6) by the tautomerisation and subsequent hydrolysis of the benzoxazinones formed. It seemed not unlikely that *e.g.* **37a** could alternatively cyclise yielding 6,8-dinitroquinazoline-2,4-dione, a known compound.[44] However, no quinazoline derivatives were observed in this or any other related experiments.

An attempt to prepare the proposed intermediate 5,7-dinitroisatoic anhydride **38** by nitration of isatoic anhydride failed, because of the ready decarboxylation of this compound. However, the 5-nitroisatoic anhydride could be prepared easily (by mono-nitration of isatoic anhydride followed by aqueous work-up).

Attempts to prepare the benzoxazinone **29a** directly from 3,5-dinitroanthranilic acid and Viehe's reagent using the conditions originally given by Bitter (a few minutes at ambient temperature in CH_2Cl_2)[45] failed.

Heating of 3,5-dinitroanthranilic acid with Viehe's reagent in acetonitrile (reflux 1 h) also failed, whereas 5-nitroanthranilic acid quickly (reflux 3 min) gave the anticipated product 2-dimethylamino-6-nitrobenzoxazinone. Even harsher conditions (reflux 30 min in trichloroethylene) resulted in complete consumption of the 3,5-dinitroanthranilic acid. However the product formed (after aqueous work-up) was not the benzoxazinone **29a** but an uncharacterized product was obtained.

The mechanism for the formation of the salts **14a** and **27** involves an initial abstraction of the acidic proton on the ring nitrogen atom (*cf.* Scheme 2). Hence it was of interest to study the interaction of amines such as dimethylamine with *N*-methyl-3,3,5,7-tetranitrooxindole **2b**, where the possibility of anion formation at position 1 is blocked.



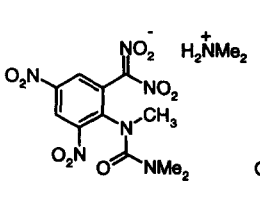
Scheme 7.

Formation of compound **39** would have been expected, however, the ^{1}H NMR spectrum of the product **40a**, obtained as a precipitate, revealed that two dimethylamino groups had been introduced, δ 2.9 (6H, s), 2.5 (6H, s), and one of them is obviously in the aromatic ring (only one aromatic resonance in the ^{1}H NMR spectrum, also evident in the ^{13}C DEPT spectrum as one single aromatic CH).

A rationalisation of the events leading to the product, involving the formation of a Meisenheimer complex, is given in Scheme 7. Heavily nitrated heterocycles are known to form Meisenheimer complexes readily. For instance, dissolution of 4,6-dinitrobenzofurazan 1-oxide (**41**) in methanol gives highly acidic complexes.[46,47]

Reaction of **2b** with morpholine similarly gave **42**. The ^{1}H NMR spectrum of **42** at 25 °C exhibited partly hindered rotation of one the morpholine rings (presumably around the amide bond) whose methylenes were broadened. However a spectrum recorded at 80 °C gave two well resolved triplets, each integrating as 4H. Also the *N*-ethyl tetranitrooxindole **2c** reacted in the same manner with dimethylamine to form the corresponding compound **40b**.

Nucleophilic attack of ethoxide on **2a** followed a similar pattern, *i.e.* initial formation of an anion, leading after acidic work-up to the final product **23**, which upon heating in acetic acid was converted, possibly *via* 2-ethoxy-6,8-dinitrobenzoxazinone, to the ethyl carbamate **43**. As a minor coproduct with **23**, the isatin ketal **44**, was formed via an -NO_2 -OEt exchange reaction (related exchange reactions have been recorded by Bowman).[48]



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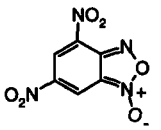

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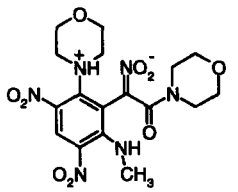
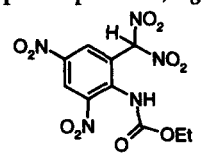


42

The potassium salt **14a** reacted with formaldehyde in acetic acid yielding 3,5,7-trinitroindole (**45a**). Attempts to extend this reaction to less reactive aldehydes gave meagre results. Acetaldehyde gave a poor yield of 2-methyl-3,5,7-trinitroindole (**45b**), whereas benzaldehyde failed to give any products, thus illustrating the poor nucleophilicity of the amino group strongly influenced by the electron-withdrawing nitro groups, as well as the $CH(NO_2)_2$ group in **17**. This low nucleophilicity is also illustrated by the fact that attempts to react the potassium salt **14a** with *N,N*-dimethylcarbamoyl chloride or ethyl chloroformate failed and the expected products, *e.g.* **23** and **28a**, were not observed.



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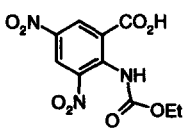

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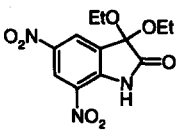
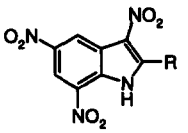


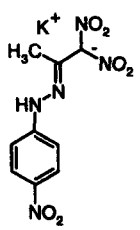
44



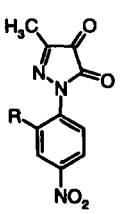
45a: R = H
45b: R = Me

The pyrazolone derivative **3a** had similar chemical properties as 3,3,5,7-tetranitrooxindole and underwent facile ring-cleavage when treated with *e.g.* potassium hydroxide in water, producing the decarboxylated 1,1-dinitroacetone derivative **46**. Thermal decomposition of **3a** and **3b** (in analogy with Scheme 1) also ocurred in hot acetic acid or acetonitrile yielding the ruby-red compounds **47a** and **47b** respectively. Compound **47b** readily formed a hydrate and was isolated as such (*i.e.* **48b**). However, heating (140 °C) converted **48b** into **47b**. The corresponding conversion of **48a** to **47a** had previously been observed by Zeine.[9]

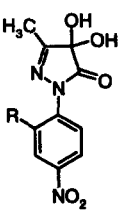
Reaction of **3a** with dimethylamine resulted in ring-opening leading to **49**, which in DMSO-d_6 existed as the tautomer **49a** but in CD_3CN it existed as a mixture of **49a** and **49b** in the ratio 9:8.



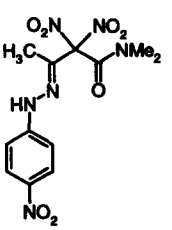
46



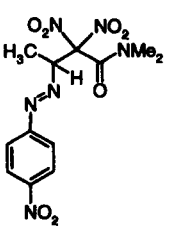
47a: R = H
47b: R = NO_2



48a: R = H
48b: R = NO_2



49a



49b

The corresponding experiments with **3b** were generally more complex and gave a range of products that were difficult to isolate and characterize. To account for this we speculate that the dinitrophenyl ring in **3b** readily reacts with nucleophiles to form relatively stable Meisenheimer complexes which subsequently might undergo various secondary reactions, a phenomenon that has been observed by Kovar *et al.* who studied the behavior of some 2-(2,4-dinitrophenyl)-3-pyrazolones towards acetone/potassium hydroxide.[48]

Experimental. Melting points were measured on a *Reichert VME Kofler bench*, IR-spectra recorded with a *Perkin Elmer 1600 FTIR*, NMR-spectra with a *Bruker AM400* or *DPX300* spectrometer and mass spectra with a *Masslynx Platform II* instrument with direct inlet at 70 eV. CAUTION Most of the compounds described below are potentially explosive materials and appropriate precautions should be taken in their preparation and handling.

3,3,5,7-Tetranitrooxindole (2a):

Method A: Oxindole (13.1 g 100 mmol) was dissolved in sulfuric acid (100 ml, *d* 1.82) and the solution cooled to 0-5 °C, whereupon nitric acid (25 ml, *d* 1.52) was added dropwise to the stirred solution keeping the temperature at 0-5 °C. After completed addition the solution was stirred 2 h at 5-10 °C and during that period the product appeared as a precipitate (which can be collected by filtration on a glass-filter). After completed reaction the whole mixture was poured into a stirred solution of sodium acetate (30 g, aq, 300 ml) at 10-15 °C. The precipitate was washed with water and dried. Yield 24.6 g (79 %) of an off-white solid. An analytical sample was recrystallized from acetonitrile/diisopropyl ether.

Method B: Oxindole (13.3 g 100 mmol) was dissolved in trifluoroacetic acid (100 ml) and stirred at 5-10 °C. To this solution, sulfuric acid (15 ml, *d* 1.88) and then nitric acid (20 ml, *d* 1.52) was added dropwise. The resulting solution was stirred and slowly allowed to rise in temperature to 15 °C whereupon the product crystallized as a yellowish powder which was collected by filtration and washed with trifluoroacetic acid. Yield 20.9 g (74 %).

Mp (dec. with explosion) 140 °C. IR (KBr): 3226, 3093, 1779, 1634, 1590, 1535, 1466, 1341, 1300, 1189, 1091, 934, 806 cm^{-1}. ^1H NMR (TFA-d_1): 9.48 (1H, d, J 1.9 Hz), 9.06 (1H, d, J 2.0 Hz) ppm. ^{13}C NMR (DMSO-d_6): 160.1 (s), 146.4 (s), 142.1 (s), 131.9 (d), 128.9 (s), 126.1 (s), 120.4 (d), 106.5 (s) ppm. ^{15}N NMR (DMSO-d_6): -17.0 (1N), -18.8 (1N), -23.1 (2N) ppm (relative to CH_3NO_2).

N-Methyl-3,3,5,7-tetranitrooxindole (2b):

Method A: *N*-Methyloxindole (5.8 g, 40 mmol) was nitrated following the procedure for 3,3,5,7-tetranitrooxindole (Method A) to give 8.52 g (65 %) as a pale beige powder.

Method B: *N*-Methyloxindole (1.47 g, 10 mmol) was nitrated following the procedure for 3,3,5,7-tetranitrooxindole (Method B) to give 2.78 g (85 %).

Method C: 3,3,5,7-Tetranitrooxindole **2a** (316 mg) was added to ether (10 ml) containing 1.3 eq. of diazomethane at 0 °C, which resulted in a quick dissolution and brisk evolution of nitrogen. The solvent was evaporated and the residue crystallized from 2-propanol giving 320 mg (97 %) of the product.

Mp (dec. with explosion) 150 °C. IR(KBr): 1775, 1625, 1594, 1579, 1537, 1344, 1319, 1262, 1092, 805, 739 cm^{-1}. ^1H NMR (CD_3CN): 8.90 (1H, d, J 2.3 Hz), 8.80 (1H, d, J 2.2 Hz), 3.32 (3H, s) ppm. ^{13}C NMR (CD_3CN): 160.6 (s), 145.7 (s), 144.4 (s), 136.6 (s), 128.5 (d), 128.2 (d), 120.9 (s), 110.0 (s), 32 .6 (q) ppm.

MS (*m/z*): 327 (1 %), 281 (12 %), 251 (70 %), 149 (49 %), 148 (47 %), 144 (55 %), 102 (61 %), 103 (61 %), 88 (99 %), 75 (100 %), 62 (77 %).

N-*Ethyl-3,3,5,7-tetranitrooxindole* (2c): *N*-Ethyloxindole (1.61 g, 10 mmol) was nitrated following the procedure for 3,3,5,7-tetranitrooxindole **2a** (Method B). Yield 1.50 g (44 %) of a pale beige solid. Mp (dec.) 100-101 °C. IR (KBr): 1772, 1618, 1585, 1541, 1340, 1314, 1232, 1094, 820, 806, 744 cm^{-1}. ^1H NMR (DMSO-d_6): 9.08 (1H, d, J 2.3 Hz), 8.97 (1H, d, J 2.3 Hz), 3.77 (2H, q), 1.22 (3H, t) ppm. ^{13}C NMR (DMSO-d_6): 159.3 (s), 143.1 (s), 142.2 (s), 134.5 (s), 127.2 (d), 127.2 (d), 119.9 (s), 105.7 (s), 40.3 (t), 12.4 (q) ppm.

3-Methyl-4,4-dinitro-1-(4-nitrophenyl)pyrazol-5-one (3a): 3-Methyl-1-phenylpyrazol-5-one (17.4 g, 100 mmol) was added in portions at 10-15 °C to a stirred solution of nitric acid (60 ml, *d* 1.52) and water (10 ml). During this operation the product started to separate. After completed addition, the mixture was stirred for 30 min at 15 °C, cooled and the white precipitate collected on a glass filter, washed with trifluoroacetic acid and dried, 29.1 g (90 %). Mp (dec.) 150 °C. IR (KBr): 1757, 1582, 1514, 1496, 1341, 1300, 1267, 858, 816 cm^{-1}. ^1H NMR ($CDCl_3$): 8.33 (2H, d, J 9.3 Hz), 8.07 (2H, d, J 9.3 Hz), 2.48 (3H, s) ppm. ^{13}C NMR ($CDCl_3$): 153.7 (s), 148.0 (s), 145.6 (s), 140.4 (s), 125.1 (d), 118.8 (d), 117.1 (s), 13.9 (q) ppm.

3-Methyl-4,4-dinitro-1-(2,4-dinitrophenyl)pyrazol-5-one (3b): 3-Methyl-1-phenylpyrazol-5-one (17.4 g, 100 mmol) was dissolved in sulfuric acid (100 ml, *d* 1.84) whereupon nitric acid (30 ml, *d* 1.52) was added at 10 °C to the solution, which was allowed to assume 25 °C and then cooled again to 5-12 °C. The mixture was now diluted with trifluoroacetic acid (30 ml) and the solid collected, washed with trifluoroacetic acid and dried, 30.5 g (86 %). Mp (dec.) 130 °C. IR (KBr): 1767, 1594, 1574, 1534, 1345, 1299, 1267, 817 cm^{-1}. ^1H NMR ($CDCl_3$): 8.91 (1H, d, J 2.5 Hz), 8.62 (1H, dd, J 8.9, J' 2.5 Hz), 8.01 (1H, d, J 8.9 Hz), 2.46 (3H, s) ppm. ^{13}C NMR ($CDCl_3$): 162.3 (s), 153.9 (s), 148.9 (s), 146.7 (s), 142.7 (s), 131.9 (s), 128.4 (d), 127.1 (d), 121.7 (d), 14.0 (q) ppm.

Picrolonic acid (4):

^1H NMR ($CDCl_3$): 8.37 (2H, d, J 9.3 Hz), 8.09 (2H, d, J 9.3 Hz), 2.58 (3H, s) ppm. ^1H NMR (DMSO-d_6):9.18 (1H, s), 8.29 (0.32H, d, J 9.3 Hz), 8.22 (3.12H, s), 8.04 (0.32H, d, J 9.3 Hz), 2.35 (2.34H, s), 2.11 (0.48H, s), 2.10 (0.18H, s) ppm. ^{13}C NMR (DMSO-d_6): 170.2 (s), 162.6 (s), 157.6 (s), 146.9 (s), 144.7 (s), 143.2 (s), 142.7 (s), 142.3 (s), 125.3 (d), 124.8 (d), 117.7 (d), 117.3 (d), 116.3 (d), 92.2 (s), 16.3 (q), 11.8 (q) ppm (*cf.* ^{13}C NMR data given by Kovar *et al.*[49]).

5,7-Dinitrooxindole: This compound was prepared as described by Coutts *et al.*[17] Yield 60 %. IR (KBr): 3040, 1746, 1626, 1531, 1340, 1070, 740, 642 cm^{-1}. ^1H NMR (DMSO-d_6): 11.73 (1H, s), 8.69 (1H, d, J 2.3 Hz), 8.38 (1H, d, J 2.3 Hz), 3.77 (2H, s) ppm. ^{13}C NMR (DMSO-d_6): 176.6 (s), 145.4 (s), 140.5 (s), 131.4 (s), 129.2 (s), 123.8 (d), 119.4 (d), 34.8 (t) ppm.

3-Acetonyl-3-hydroxy-5,7-dinitrooxindole (6): 3,3,5,7-Tetranitrooxindole (**2a**) (313 mg, 1 mmol) was refluxed with acetone (10 ml) for 30 min. Concentration of the solution gave white crystals, which were collected, washed with acetone and dried, 250 mg (84%). Mp 170 °C. ^1H NMR (DMSO-d_6): 11.73 (1H, s), 8.76 (1H, d, J 2.3 Hz), 8.50 (1H, d, J 2.3 Hz), 6.58 (1H, s), 3.79 (1H, d, J 18.3 Hz), 3.32 (1H, d, J 18.2 Hz),

2.03 (3H, s) ppm. ^{13}C NMR (DMSO-d_6): 205.9, (s), 178.6 (s), 144.6, (s), 140.9 (s), 137.0 (s), 129.4 (s), 123. 4 (d), 121.1 (d), 70.6 (s), 49.9 (t), 29.6 (q) ppm.

3-Methyl-3,5,7-trinitrooxindole (7a): The Method A, as for **2a** was used. Mp (dec.) 170 °C. IR (KBr): 3233, 3098, 1770, 1633, 1568, 1534, 1340, 1297, 1211, 1139, 736 cm^{-1}. ^{1}H NMR (DMSO-d_6): 9.95 (1H, d), 9.88 (1H, d), 2.09 (3H, s) ppm. ^{13}C NMR (DMSO-d_6): 170.5 (s), 144.4 (s), 141.8 (s), 131.0 (s), 130.2 (s), 125.4 (d), 122.8 (d), 87.8 (s), 19.0 (q) ppm.

N,3-Dimethyl-3,5,7-trinitrooxindole (7b): The Method A, as for **2a** was used. Mp (dec.) 110 °C. IR (KBr):1756, 1622, 1540, 1345, 1260, 1065 cm^{-1}. ^{1}H NMR (DMSO-d_6): 8.81 (1H, d, J 3.5 Hz), 8.80 (1H. d, J 3.4 Hz), 3.26 (3H, s), 1.79 (3H, s) ppm.

3,5-Dinitroanthranilic acid:

Method A: 2-Chloro-3,5-dinitrobenzoic acid (12.3 g, 50 mmol) was dissolved in conc. ammonia (55 ml) at 25 °C. The solution thus obtained was heated on a waterbath for 30 min. The mixture was then cooled and the ammonium salt of 3,5-dinitroanthranilic acid (13.3 g) as a dihydrate was collected. This ammonium salt was reported 1874 by Salkowski,[50] who used a different procedure. The ammonium salt was stirred in water and conc. hydrochloric acid was added at 35 °C. After stirring for 30 min, the mixture was cooled and the free acid formed was collected, 10.8 g (95 %).

Method B: Isatoic anhydride (16.3 g, 100 mmol) was dissolved in sulfuric acid (80 ml, *d* 1.84) and potassium nitrate (23.0 g, 220 mmol) was added in portions at 25-30 °C to the stirred solution. After completed addition, the temperature was raised to 60 °C for 30 min and then cooled and poured into water. After stirring for 30 min at 35 °C, this mixture was cooled and the yellow solid collected and recrystallised from ethanol. Yield 19.5 g (86 %).

Mp 268-272 °C (lit. Mp 256 °C).[51] IR (KBr): 3440, 3316, 3076, 1674, 1616, 1594, 1523, 1436, 1325, 1249, 1162, 1096, 894, 744, 720, 699, 584 cm^{-1}. ^{1}H NMR (DMSO-d_6): 8.94 (1H, d, J 2.2 Hz), 8.79 (1H, d, J 2.2 Hz), ppm. ^{13}C NMR (DMSO-d_6): 167.4 (s), 149.6 (s), 133.4 (d), 132.9 (s), 131.7 (s), 127.2 (d), 114.9 (s) ppm.

3,3,5-Trinitrooxindole (10): Isatin-3-oxime (1.62 g, 10 mmol) was dissolved in hot acetonitrile (35 ml), and a brisk stream of nitrogen dioxide was introduced. After completed reaction and evaporation of the solvent, the residue was crystallised from methyl acetate, yield 1.82 g (72 %). Mp (dec.) 160 °C. ^{1}H NMR (DMSO-d_6): 12.1 (1H, s), 7.98 (1H, d, J 1.8 Hz), 7.79 (1H, dd, J 8.0, J' 1.8 Hz), 7.04 (1H, d, J 8.0 Hz) ppm. ^{13}C NMR (DMSO-d_6) 158.9 (s), 144.1 (s), 138.2 (d), 133.6 (s), 129.9 (d), 118.4 (s), 114.9 (s), 114.0 (d) ppm.

N-Methyl-3-nitrooxindole, potassium salt (12): *N*-Methyloxindole (1.50 g, 10 mmol), dissolved in dry THF (10 ml) was added to a cooled (-50 - -40 °C) and stirred suspension of potassium *t*-butoxide (1.9 g, 16.5 mmol) in dry THF (10 ml), immediately followed by freshly distilled *n*-butyl nitrate[26] (1.31 g, 11 mmol). The mixture was allowed to warm to 0 °C, causing precipitation of a yellow solid that was collected by filtration and thoroughly washed with THF. Yield 1.80 g (78 %). Mp (dec.) 380 °C. IR (KBr): 1654, 1608, 1464, 1439, 1213, 1095, 998, 856, 768, 742, 549 cm^{-1}. ^{1}H NMR (DMSO-d_6): 7.79 (1H, d, J 7.2 Hz), 6.97-6.82 (3H, m),

3.13 (3H, s) ppm. ^{13}C NMR (DMSO-d_6): 161.0 (s), 133.6 (s), 121.9 (s), 121.7 (d), 120.1 (d), 118.0 (d), 110.7 (s), 106.1 (d), 25.3 (q) ppm.

(2-Amino-3,5-dinitrophenyl)dinitromethane, potassium salt (14a):

3,3,5,7-Tetranitrooxindole (**2a**, 3.11 g, 10 mmol) was added in portions to a stirred solution of potassium hydroxide (1.0 g) in water (35 ml) at 15 °C, causing a transient red colouration. Within one minute gas evolution was observed and the title compound started to precipitate. The solution was stirred 1 h at room temperature and then cooled to 5 °C before the potassium salt was collected, 3.25 g as a dihydrate (100 %). The analytical sample was recrystallized from water and dried to give red-brown needles. Mp (dec.) ca 150 °C. IR (KBr): 3394, 3303, 1628, 1586, 1529, 1510, 1481, 1425, 1342, 1223, 1139, 1124, 745 cm^{-1}. ^{1}H NMR (DMSO-d_6): 8.82 (1H, d, J 2.3 Hz), 8.04 (3H, d, J 2.4 Hz) ppm. ^{13}C NMR (DMSO-d_6): 148.2 (s), 134.3 (s), 131.1 (d), 129.6 (s), 127.4 (s), 125.3 (s), 122.8 (d) ppm. [Found: C, 25.69; H, 1.35; N, 21.42. $C_7H_4KN_5O_8$ requires C, 25.85; H, 1.24; N, 21.53 %].

(2-Methylamino-3,5-dinitrophenyl)dinitromethane, potassium salt (14b):

The procedure given for **14a** was used, starting with *N*-methyl-3,3,5,7-tetranitrooxindole (3.27 g, 10 mmol). Yield 2.86 g (85 %) of a yellow powder. Mp (dec.) 280°C. IR (KBr) 3450, 1607, 1534, 1330, 1178, 1099 cm^{-1}. ^{1}H NMR (DMSO-d_6): 8.79 (1H, d, J 1.8 Hz), 8.74 (1H, q, J 5.5 Hz), 8.02 (1H, d, J 1.8 Hz), 2.82 (3H, d, J 5.5 Hz) ppm. ^{13}C NMR (DMSO-d_6): 148.7 (s), 133.8 (s), 132.6 (d), 132.0 (s), 130.0 (s), 123.2 (d), 122.5 (s), 29.8 (q) ppm.

(2-Amino-3,5-dinitrophenyl)dinitromethane (17): The potassium salt **14a** was treated with aqueous sulfuric acid (*d* 1.18). Mp (dec.) 30 °C. IR (KBr): 3467, 3347, 3112, 2995, 1630, 1591, 1575, 1529, 1431, 1332, 1287, 1116, 785, 707 cm^{-1}. ^{1}H NMR ($CDCl_3$): 9.37 (1H, d, J 2.6 Hz), 9.54 (1H, d, J 2.6 Hz), 7.53 (2H, s, br.), 7.31 (1H, s) ppm. ^{13}C NMR ($CDCl_3$): 147.4 (s), 136.4 (s), 135.1 (d), 133.4 (s), 127.8 (d), 113.2 (d), 111.2 (s) ppm. ^{13}C NMR (DMSO-d_6): 148.3 (s), 134.4 (s), 131.2 (d), 129.6 (s), 127.4 (s), 125.5 (s), 122.9 (d) ppm. MS (*m/z*): 287 (7 %), 241 (100 %), 194 (63 %), 164 (50 %), 103 (89 %).

(2-Methylamino-3,5-dinitrophenyl)dinitromethane: The potassium salt **14b** was stirred with aqueous sulfuric acid (*d* 1.18) for 10 min at 20 °C and the yellow precipitate formed collected and dried. Yield 75 %. Mp (dec.) 135 °C. IR (KBr): 3299, 3107, 1621, 1596, 1571, 1533, 1350, 1325, 1307, 1052, 740 cm^{-1}. ^{1}H NMR ($CDCl_3$): 9.27 (1H, d, J 2.7 Hz), 8.63 (1H, d, J 2.7 Hz), 8.50 (1H, s, br.), 7.67 (1H, s) 3.35 (3H, d, J 5.7 Hz), ppm. ^{13}C NMR (DMSO-d_6): 149.0 (s), 134.2 (s), 132.9 (d), 132.3 (s), 130.3 (s), 123.5 (d), 122.7 (s), 30.0 (q) ppm. MS (*m/z*): 301 (2 %), 283 (100 %), 115 (51 %).

3,5,7-Trinitroindazole (19):

Method A: Oxindole (6.55 g, 50 mmol) was dissolved in sulfuric acid (50 ml, *d* 1.82) and the solution cooled to 0-5 °C, wherupon nitric acid (12.5 ml, *d* 1.52) was added dropwise keeping the temperature at 0-5 °C. After a stirring period for 2 h at 5-10 °C, water (8 ml) was added at 5-10 °C. After completed addition the temperature was increased to 35 °C for 0.5 h, wherupon the solution was poured into ice and water. The crystals formed were collected, washed with water and recrystallized from MeCN/DMA to give white needles.

Method B: 5-Nitroindazole (6.52 g, 40 mmol) was added in portions to a stirred solution of nitric acid (11 ml, *d* 1.52) in sulfuric acid (50 ml, *d* 1.82) at 0-5 °C. After completed addition the reaction mixture was allowed to reach room temperature. After 2 h the mixture was heated (100 °C) for 24 h, whereupon the solution was cooled and poured into ice/water. The crude solid formed was washed with water, dried and recrystallized from ethanol/water giving 7.62 g (76 %). Mp 227-228 °C (lit. mp 227-228 °C)[31] IR (KBr): 3287, 3101, 1644, 1561, 1538, 1496, 1392, 1357, 1301, 1168, 1134, 976, 799 cm^{-1}. ^1H NMR (DMSO-d_6): 12.10 (1H, s), 9.62 (1H, d, J 1.9 Hz), 9.36 (1H, d, J 1.9 Hz) ppm. MS (*m/z*): 253 (100 %), 195 (10 %), 149 (10 %), 88 (12 %), 30 (63 %), 28 (17 %).

Ethyl 3-chloro-3-hydroxy-5,7-dinitro-2,3-dihydroindazol-2-yl carbonate (22):

Method A: The potassium salt **14a**, a dihydrate (365 mg, 1 mmol) was dissolved in DMF (5 ml) at 60 °C and ethyl chloroformate (432 mg, 4 mmol) was added to the stirred solution, which was subsequently heated to 105 °C for 15 min. The reaction mixture was cooled, concentrated and poured into water, which gave a yellow precipitate of the product as the covalent hydrate **22**, which was purified by recrystallisation from 2-propanol.

Method B: The potassium salt **14a**, a dihydrate (365 mg, 1 mmol) was stirred in $CHCl_3$ (15 ml) at 80 °C and ethyl chloroformate (432 mg, 4 mmol) was added to the stirred solution, whereupon HCl gas was bubbled through during 30 min. After the mixture was cooled to RT, a yellow precipitate could be collected. This crude product contained approximately 50 % of the hydrate **22** as estimated from ^1H NMR and was not further purified.

Mp (viol. dec.) 180 °C. IR (KBr): 3394, 3304, 1795, 1626, 1590, 1529, 1328, 1232, 989, 744 cm^{-1}. ^1H NMR (DMSO-d_6): 9.28 (1H, d, J 2.4 Hz), 9.09 (1H, d, J 2.4 Hz), 4.45 (2H, q), 1.45 (3H, t) ppm. ^{13}C NMR (DMSO-d_6): 152.0 (s), 147.2 (s), 144.0 (s), 135.1 (s), 132.4 (s), 126.5 (d), 116.7 (d), 66.6 (t), 14.1 (q) ppm.

Transformation of 22 to 3-morphlino-5,7-dinitro-1H-indazole 24: The hydrate **22** (348 mg, 1 mmol) was dissolved in dioxane (6 ml) containing morpholine (261 mg, 1 mmol) and heated at reflux for 45 min. After cooling to 25 °C, triethyl phosphite (166 mg, 1 mmol) was added and the solution stirred for 24 h, whereupon the solution was concentrated. Water was added and the precipitate collected, washed with water and recrystallized from 2-propanol. Yield 165 mg (50 %). Mp 175-176 °C. The product was identical with 3-morphlino-5,7-dinitro-*1H*-indazole **24** as described below.

3-Chloro-5,7-dinitroindazole: 3-Chloro-5-nitroindazole (19.7 g, 100 mmol) was dissolved in sulfuric acid (65 ml, *d* 1.84) containing nitric acid (18 ml, *d* 1.52) at 25 °C, whereupon the solution was heated (65 °C/2 h), cooled and poured into ice/water to give a pure product directly, 22.8 g (94 %). Mp 172-173 °C (lit. mp 179-180 °C).[52] IR (KBr): 3299, 1634, 1591, 1538, 1458, 1338, 1286, 1116, 953, 799, 735, 691cm^{-1}. ^1H NMR (DMSO-d_6): 14.66 (1H, s), 8.94 (1H, d, J 1.6 Hz), 8.92 (1H, d, J 1.6 Hz) ppm. ^{13}C NMR (DMSO-d_6): 140.9 (s), 137.8 (s), 134.7 (s), 131.8 (s), 123.4 (s), 123.1 (d), 119.3 (d) ppm.

3-Morphlino-5,7-dinitro-1H-indazole (24): A solution of 3-chloro-5,7-dinitroindazole (2.43 g, 10 mmol) and morpholine (2.1 ml, 22 mmol) was heated in dioxane (40 ml) on a water bath for 2 h, after which the solution was concentrated and poured into water. The solid formed was collected and dried, 2.70 g (92 %). Mp 175-176 °C. IR (KBr): 1614, 1520, 1456, 1338, 1280, 1118, 797, 728, 689 cm^{-1}. ^1H NMR (DMSO-d_6):

8.67 (1H, d, J 2.0 Hz), 8.62 (1H, s, br), 3.75 (4H, t, J 4.8 Hz), 3.05 (4H, t, J 4.6 Hz) ppm. ^{13}C NMR (DMSO-d_6): 139.8 (s), 137.7 (s), 136.7 (s); 132.3 (s), 123.6 (s), 122.3 (d), 116.9 (d), 64.4 (t), 43.7 (t) ppm.

Dimethylammonium salt (27): 3,3,5,7-Tetranitrooxindole (**2a**, 0.626 g, 2 mmol) was dissolved in ethanol (65 ml) and then dimethylamine (2.50 g, aq. 40 %) was added, whereupon a yellow precipitate quickly formed. The reaction mixture was allowed to stand 5 min and then the yellow solid was collected by filtration. Yield 6.30 g (78 %). Mp (dec.) 168-169 °C. IR (KBr): 3273, 3099, 2798, 1670, 1542, 1499, 1339, 1245, 1134, 1114, 745, 732, 714 cm^{-1}. ^{1}H NMR (DMSO-d_6): 8.52 (1H, d, J 2.7 Hz), 8.37 (1H, d, J 2,7 Hz), 8.2 (2H, br. s), 2.85 (6H, s), 2.54 (6H, s) ppm. ^{13}C NMR (DMSO-d_6): 154.4 (s), 142.5, (s), 140.7 (s), 138.0 (s), 130.7 (d), 129.9 (s), 129.3 (s), 119.9 (d), 36.3 (q) ppm. MS (*m/z*): 312 (4 %), 295 (2 %), 280 (7 %), 266 (100 %), 72 (10 %). [Found: C, 35.38; H, 4.32; N, 24.26. $C_{12}H_{17}N_7O_9$ requires C, 35.74; H, 4.25; N, 24.31 %].

3-(2-Dinitromethyl-4,6-dinitrophenyl)-1,1-dimethylurea (28a): The salt **27** (2.5 g, 6.2 mmol) was mixed with water (10 ml) at 60 °C. The mixture obtained was cooled, conc. hydrochloric acid (5 ml) added at 25 °C and the stirring continued for 30 min. Collection of the yellow solid formed gave 2.1 g (95 %). IR (KBr): 3381, 1690, 1592, 1578, 1474, 1347, 1169 cm^{-1}. ^{1}H NMR (DMSO-d_6): 8.52 (1H, d, J 2.7 Hz), 8.47 (1H, s), 8.38 (1H, d, J 2.7 Hz), 2.85 (6H, s) ppm. ^{13}C NMR (DMSO-d_6): 154.3 (s), 142.5 (s), 140.7 (s), 138.0 (s), 130.8 (s), 130.0 (d), 129.3 (s), 119.9 (d), 36.4 (q), 34.4 (q) ppm.

Morpholine-4-carboxylic acid (2-dinitromethyl-4,6-dinitrophenyl)amide (28c): The same procedure as above was used, starting with 1.57 g 3,3,5,7-tetranitrooxindole (5 mmol) gave 1.37 g (56 %) of the yellow morpholinium salt. Mp (dec.) 130-150 °C. IR (KBr): 1664, 1543, 1488, 1425, 1344, 1235, 1110, 873 cm^{-1}. ^{1}H NMR (DMSO-d_6): 8.53 (1H, d, J 2.7 Hz), 8.33 (1H, d, J 2.7 Hz), 3.74 (4H, t, J 4.9 Hz), 3.57 (4H, t, J 4.5 Hz), 3.67 (4H, t, J 4.5 Hz), 3.07 (4H, t, J 4.9 Hz) ppm. ^{13}C NMR (DMSO-d_6): 154.3 (s), 142.2 (s), 140.7 (d), 138.6 (s), 130.7 (s), 130.3 (d), 128.8 (s), 120.0 (s), 66.1 (t), 63.4 (t), 45.0 (q), 43.0 (q) ppm. The salt was treated as described for the conversion **27** to **28a**. Mp (dec.) 140-150 °C. IR (KBr): 3401, 3101, 2996, 2920, 2864, 1682, 1576, 1487, 1350, 1242, 1110, 778, 744, 726, 575 cm^{-1}. ^{1}H NMR (DMSO-d_6): 9.68 (1H, s), 9.26 (1H, d, J 2.4 Hz), 8.85 (1H, d, J 2.4 Hz), 3.81 (4H, t, J 4.8 Hz), 3.59 (4H, t, J 4.8 Hz) ppm.

2-Dimethylamino-6,8-dinitro-3,1-benzoxazin-4-one (29a):

Method A: The ureido derivative **28a** (0.72 g, 2 mmol) was heated (reflux 2 min) in acetic acid (6 ml). Upon cooling the product partly precipitated. Water was added and the pale yellow product collected after 10 min. 0.335 g (60 %).

Method B: 2-(3,3-Dimethylureido)benzoic acid **34**[42] (1.49 g, 5 mmol) was nitrated with nitric acid (0.63 g, *d* 1.52, 10 mmol) in sulfuric acid (15 ml, *d* 1.84) at 75 °C for 30 min. Pouring the reaction mixture on ice/water gave 1.2 g (85 %) of the product.

Method C: 2-Dimethylaminobenzoxazinone **33** (0.38 g, 2 mmol) was nitrated at 60 °C/15 min in sulfuric acid (6 ml, *d* 1.84) containing nitric acid (1 ml, *d* 1.52). The reaction mixture was cooled and poured into ice/water.

Mp 159-160 °C. IR (KBr): 1792, 1771, 1645, 1603, 1584, 1535, 1503, 1336 cm^{-1}. ^{1}H NMR (DMSO-d_6): 8.94 (1H, d, J 2.4 Hz), 8.65 (1H, d, J 2.4 Hz), 3.18 (3H, s), 3.15 (3H, s) ppm. ^{13}C NMR (DMSO-d_6): 156.5

(s), 156.3 (s), 148.1 (s), 142.2 (s), 138.9 (s), 127.1 (d), 125.5 (d), 113.9 (s), 37.4 (q), 36.3 (q) ppm. MS (*m/z*): 280 (24 %), 263 (39 %), 220 (43 %), 190 (56 %), 144 (18 %), 116 (39 %), 88 (20 %), 72 (100 %). HRMS (*m/z*): found 280.0440 ($C_{10}H_8N_4O_6$ requires 280.0444).

2-Diethylamino-6,8-dinitro-3,1-benzoxazin-4-one (29b): Method A as above was used. Yield 0.34 g (55 %) of a yellow powder. Mp 120-121 °C. IR (KBr):1766, 1600, 1544, 1506, 1449, 1324, 1076, 1042, 794, 719 1336 cm^{-1}. ^1H NMR (DMSO-d_6): 8.91 (1H, d, J 2.5 Hz), 8.64 (1H, d, J 2.5 Hz), 3.62-3.33 (4H, m), 1.21 (6H, q, J 7.2 Hz) ppm. ^{13}C NMR (DMSO-d_6):156.6 (s), 155.6 (s), 148.2 (s), 142.2 (s), 138.8 (s), 126.9 (d), 125.3 (d), 114.3 (s), 43.5 (t), 42.3 (t), 13.2 (q), 12.3 (q) ppm. MS (*m/z*): 308 (24 %), 291 (100 %), 265 (25 %), 236 (99 %), 220 (93 %), 190 (71 %), 116 (70 %).

2-Dimethylamino-6-nitro-4H-3,1-benzoxazin-4-one (31): 5-Nitroanthranilic acid (1.82 g, 10 mmol) and dichlorodimethyliminium chloride (1.62 g, 10 mmol) were heated at reflux in acetonitrile for 10 min. The white hydrochloride formed was collected after cooling to room temperature, 2.60 g. Mp >260 °C. IR (KBr): 1798, 1682, 1607, 1356, 1285, 1042, 919, 872, 760, 666 cm^{-1}. ^1H NMR (DMSO-d_6): 14.2 (1H, s), 8.52 (2H, m), 8.14 (1H, dd, J 9.5, J' 2.8 Hz), 2.9 (6H, s) ppm. ^{13}C NMR (DMSO-d_6): 168.8 (s), 157. 7 (s), 153.7 (s), 153.6 (s), 139.2 (s), 128.6 (d), 126.7 (d), 118.2 (s), 113.6 (d) ppm.

The hydrochloride obtained was stirred with sodium carbonate (aq. 5 %, 40 ml) for 15 min at 5-10 °C, giving the free base 2.05 g, (80 %) as an yellow powder. Mp 161-162 °C. IR (KBr) 1770, 1634, 1602, 1577, 1494, 1420, 1322, 1196, 1087, 848, 518 cm^{-1}. ^1H NMR (DMSO-d_6): 8.46 (1H, d, J 2.7 Hz), 8.31 (1H, dd, J 2.7, J' 9.1 Hz), 7.20 (1H, d, J 9.1 Hz) 3.14 (3H, s), 3.11 (3H, s) ppm. ^{13}C NMR (DMSO-d_6): 157.8 (s), 155.7 (s), 155.5 (s), 141.1 (s), 130.5 (d), 124.8 (d), 124.4 (d), 111.0 (s), 37.3 (q), 36.1 (q): ppm. MS (*m/z*): 235 (100 %), 191 (91 %), 145 (96 %), 117 (38 %), 72 (71 %).

2-(3,3-Dimethylureido)benzoic acid (34): This compound was prepared as described by Bitter.[42] In our hands the older method by Staiger and Miller[53] failed. Mp (dec.) 170 °C. IR (KBr): 1684, 1636, 1602, 1584, 1538, 1450, 1300, 1236, 756 cm^{-1}. ^1H NMR (DMSO-d_6): 13.5 (1H, br), 10.84 (1H, s), 8.47 (1H, d, J 8.5 Hz), 7.94 (1H, dd, J 8.0, J' 2.3 Hz), 7.49 (1H, t, J 8.4 Hz), 6.96 (1H, t, J 7.6 Hz), 2.95 (6H, s) ppm. ^{13}C NMR (DMSO-d_6): 170.3 (s), 154.6 (s), 143.4 (s), 133.7 (d), 130.9 (d),120.2 (d), 118.5 (d), 114.2 (s), 35.7 (q) ppm.

Ammonium salt 37a: The general procedure as for **27** was used with ammonia (aq. conc.) as base. Mp (dec.) 210 °C. IR (KBr): 3461, 3365, 3310, 1700, 1545, 1508, 1486, 1420, 1344, 1245, 1111, 901, 616 cm^{-1}. ^1H NMR (DMSO-d_6): 8.50 (1H, d, J 2.3 Hz), 8.33 (1H, d, J 2.3 Hz), 7.34 (4H, s), 6.52 (2H, s) ppm. ^{13}C NMR (DMSO-d_6): 154.3 (s), 142.6 (s), 140.9 (s), 137.4 (s), 130.1 (s), 130.1 (d), 127.5 (s), 120.1 (d) ppm.

Methylammonium salt 37b: The general procedure as for **27** was used with methylamine (aq. 40 %) as base. Mp (dec.) 175 °C. IR (KBr): 3406, 3098, 1697, 1544, 1497, 1341, 1227, 1152 cm^{-1}. ^1H NMR (DMSO-d_6): 8.50 (1H, d, J 2.0 Hz), 8.32 (1H, d, J 2.0 Hz), 7.57 (3H, s), 6.92 (1H, q, J 4.6 Hz), 2.57 (3H, d, J 4.6 Hz), 2.36 (3H, s) ppm. ^{13}C NMR (DMSO-d_6): 154.0 (s), 142.1 (s), 140.7 (s), 137.3 (s), 130.1 (s), 129.8 (d), 127.4 (s), 120.3 (d), 26.3 (q), 24.6 (q) ppm.

Reaction of* N-*methyl-3,3,5,7-tetranitrooxindole with dimethylamine: Dimethylamine (6 ml, aq. 40 %, 45 mmol) was added to a stirred mixture of *N*-methyl-3,3,5,7-tetranitrooxindole (3.27 g, 10 mmol) in ethanol (35 ml) at 25 °C, which resulted in quick dissolution. Within 5 min the product **40a** started to crystallize and was collected as an yellow powder after 1 h at 5 °C. Yield 1.40 g (0.38 %). Mp (dec.) 205 °C. IR (KBr): 3014, 2798, 1698, 1537, 1426, 1334, 1237, 1219, 1086, 1031, 968, 897 cm^{-1}. ^1H NMR (DMSO-d_6): 8.33 (1H, s), 8.2 (1H, br), 3.12 (3H, s), 2.69 (6H, s), 2.55 (6H, s) ppm. ^{13}C NMR (DMSO-d_6): 159.8 (s), 140.1 (s), 133.3 (s), 133.1 (s), 126.4 (s), 122.0 (s), 113.5 (d), 108.7 (s), 43.0 (q), 34.4 (q), 24.5 (q) ppm.

Reaction of* N-*methyl-3,3,5,7-Tetranitrooxindole with morpholine: The same procedure as above was used. 1.57 g *N*-Methyltetranitrooxindole gave 1.37 g (63 %) of (**42**) as an yellow powder. Mp (dec.) 250 °C. IR (KBr): 3056, 2854, 1678, 1527, 1447, 1422, 1348, 1241, 1222, 1108, 1092 cm^{-1}. ^1H NMR (DMSO-d_6 at 80 °C): 8.31 (1H, s), 5.9 (1H, br), 3.79 (4H, t, J 4.9 Hz), 3.56 (4H, t, J 4.3 Hz), 3.14 (4H, t, J 4.9 Hz), 3.11 (3H, s), 2.99 (4H, t, J 4.3 Hz) ppm. ^{13}C NMR (DMSO-d_6): 160.1 (s), 140.3 (s), 133.4 (s), 131.0 (s), 126.3 (s), 122.3 (d), 113.5 (s), 109.0 (s), 66.9 (t), 63.4 (t), 50.4 (t), 43.0 (t), 24.7 (q) ppm.

Reaction of* N-*ethyl-3,3,5,7-tetranitrooxindole with dimethylamine: The same procedure as for **40a** was used. Starting with 0.30 g of the *N*-ethyl-3,3,5,7-tetranitrooxindole gave 60 mg (16 %) of **40b** as an yellow powder. Mp (dec.) 180 °C. IR (KBr): 3078, 2802, 1680, 1538, 1473, 1415, 1335, 1087, 1042 cm^{-1}. ^1H NMR (DMSO-d_6): 8.36 (1H, s), 3.56 (2H, q), 2.68 (6H, s), 2.55 (6H, s), 1.02 (3H, t) ppm. ^{13}C NMR (DMSO-d_6): 159.8 (s), 140.1 (s), 133.6 (s), 133.1 (s), 125.2 (s), 122.4 (s), 113.6 (d), 108.8 (s), 42.9 (q), 34.4 (q), 34.4 (t), 14.9 (q) ppm.

6-Nitro-4H-3,1-benzoxazine-2(1H),4-dione: Isatoic anhydride (16.3 g, 100 mmol) was dissolved in sulfuric acid (55 ml, *d* 1.84) and potassium nitrate (10.1 g, 100 mmol) was added in portions at 20-25 °C to this solution. After completed addition the mixture was kept at this temperature for 30 min and then poured into ice/water. The pale yellow precipitate formed was collected, washed with cold water, dried and recrystallized from dioxane. Mp 260 °C (lit. mp 220 °C)[54]. IR (KBr): 1778, 1697, 1629, 1354, 1334, 1094, 1036, 856, 659 cm^{-1}. ^1H NMR (DMSO-d_6): 12.32 (1H, s), 8.54 (1H, d, J 2.5 Hz), 8.49 (1H, dd, J 9.0, J' 2.5 Hz), 7.28 (1H, d, J 8.9 Hz) ppm. ^{13}C NMR (DMSO-d_6): 158.6 (s), 146.5 (s), 146.1 (s), 142.5 (s), 131.3 (d), 124.6 (d), 116.7 (d), 111.1 (s) ppm.

(2-Dinitromethyl-4,6-dinitrophenyl)carbamic acid ethyl ester (23):

3,3,5,7-Tetranitrooxindole (3.13 g, 10 mmol) was added to ethanol (20 ml) wherein sodium (0.5 g, 0.13 mol) had been dissolved. A dark-red solution was quickly obtained and after 20 min at 30 °C, the solution was cooled and water (20 ml) and acetic acid (2 ml) was added. After 30 min the white needles formed (0.40 g, 13 %) was collected and identified as 3,3-diethoxy-5,7-dinitrooxindole **44**. Acidification with hydrochloric acid of the mother-liquor gave a pale yellow precipitate of the carbamic ester **23** 2.50 g, (70 %). Mp (dec.) 120 °C. IR (KBr) 3351, 1736, 1573, 1496, 1349, 1229, 1054, 772, 733, 599 cm^{-1}. ^1H NMR (DMSO-d_6): 10.07 (1H, s), 8.54 (1H, d, J 2.6 Hz), 8.37 (1H, d, J 2.6 Hz), 4.01 (2H, q, J 7.1 Hz), 1.16 (3H, t, J 7.1 Hz) ppm. ^{13}C NMR (DMSO-d_6): 153.6 (s), 144.0 (s), 142.6 (s), 136.0 (s), 132.4 (s), 130.8 (d), 128.3 (d), 119.8 (s), 61.4 (t), 14.3 (q) ppm.

3,3-Diethoxy-5,7-dinitrooxindole (44): See the preceding procedure. Mp 179-180 °C. IR (KBr): 3312, 3102, 2985, 1759, 1625, 1544, 1530, 1342, 1119, 1072 cm^{-1}. ^1H NMR (DMSO-d_6): 11.93 (1H, s), 8.80 (1H, d, J 2.2 Hz), 8.41 (1H, d, J 2.2 Hz), 3.94 (2H, m), 3.71 (2H, m), 1.16 (6H, t, J 7 Hz) ppm. ^{13}C NMR (DMSO-d_6): 172.3 (s), 143.1 (s), 141.4 (s), 131.0 (s), 129.7 (s), 124.2 (d), 122.3 (d), 93.77 (s), 58.7 (t), 15.0 (q) ppm.

Reaction of the potassium salt 14a with formaldehyde: The potassium salt ***14a*** (3 mmol) was refluxed for 30 min in acetic acid (10 ml) containing formaldehyde (4 mmol) as formalin (aq, 40 %). The reaction mixture was concentrated, poured into water and the precipitate collected and recrystallized form ethanol/water, yield 70 % of 3,5,7-trinitroindole **45a**, identical with a sample prepared as described by Noland *et al.*[51]

1,1-Dinitroacetone 2,4-dinitrophenylhydrazone, potassium salt (46): The trinitro compound **3a** (2.55 g, 8 mmol) and potassium hydroxide (3.0 g) was refluxed in water (15 ml) for 1 h. The orange solid of the potassium salt **46** was collected after cooling, 1.40 g (53 %). Mp (dec.) 220 °C. IR (KBr): 3285, 1596, 1473, 1350, 1306, 1273, 1192, 1112, 1085, 834, 751 cm^{-1}. ^1H NMR (DMSO-d_6): 10.14 (1H, s), 8.04 (2H, d, J 9.4 Hz), 7.17 (2H, d, J 9.4 Hz), 2.09 (3H, s) ppm. ^{13}C NMR (DMSO-d_6): 151.2 (s), 139.3 (s), 137.6 (s), 126.9 (s), 125.9 (d), 111.4 (d), 20.7 (q) ppm.

3-Methyl-1-(4-Nitrophenyl)-1H-pyrazole-4,5-dione (47a): The trinitro compound **3a** (3.09 g, 10 mmol) was refluxed in acetic acid (18 ml) for 10 min, whereby nitrogen oxides were formed. Upon cooling, ruby red needles of the product formed 2.1 g (88 %). Mp 200-201 °C (lit. mp 201 °C).[9] IR (KBr): 1777, 1737, 1593, 1510, 1496, 1337, 1283, 1161, 1110, 855, 842, 754 cm^{-1}. ^1H NMR (DMSO-d_6): 8.35 (2H, d, J 7.2 Hz), 8.07 (2H, d, J 7.2 Hz), 2.13 (3H, s) ppm. ^{13}C NMR (DMSO-d_6): 180.1 (s), 152.4 (s), 147.5 (s), 143.4 (s), 142.5 (s), 125.3 (d), 116.5 (d), 11.1 (q) ppm. MS (*m/z*): 233 (6 %), 177 (47 %), 136 (43 %), 134 (19 %), 106 (14 %), 90 (100 %), 64 (40 %), 63 (94 %). HRMS (*m/z*): found 233.0422 ($C_{10}H_7N_3O_4$ requires 233.0437).

4,4-Dihydroxy-3-methyl-1-(4-nitrophenyl)-1,4-dihydropyrazol-5-one (48a):

The tetranitro compound **3b** (3.54 g, 10 mmol) was refluxed in acetic acid (18 ml) for 10 min, whereby nitrogen oxides were formed. Evaporation gave a thick oil which, when dissolved in diisopropyl ether containing 2 % acetonitrile, crystallized yielding the hydrate **48b** as a yellow solid, 2.3 g (77 %). The compound loses water at *ca* 140 °C (**47a** is formed) and then melts at 202-203 °C. IR (KBr): 3354, 1737, 1597, 1517, 1501, 1335, 1116, 1096, 853, 837, 755 754 cm^{-1}. ^1H NMR (DMSO-d_6): 8.27 (2H, d, J 9.3 Hz), 8.03 (2H, d, J 9.3 Hz), 7.84 (2H, s), 2.12 (3H, s) ppm. ^{13}C NMR (DMSO-d_6): 170.2 (s), 162.5 (s), 143.2 (s), 142.7 (s), 125.2 (d), 117.3 (d), 92.2 (s), 11.8 (q) ppm. MS (m/z): 233 (32 %), 177 (98 %), 136 (60 %), 90 (100 %), 63 (73 %).

4,4-Dihydroxy-3-methyl-1-(2,4-dinitrophenyl)-1,4-dihydropyrazol-5-one (48b):

Prepared as described by Zeine.[9] Mp 120 °C. IR (KBr): 3443, 3355, 1742, 1606, 1546, 1530, 1490, 1351, 1128, 1102, 1083, 836, 750, 736, 664754 cm^{-1}. ^1H NMR (DMSO-d_6): 8.73 (1H, d, J 2.5 Hz), 8.58 (1H, dd, J 9.0, J' 2.5 Hz), 7.97 (1H, d, J 9.0 Hz) 2.10 (3H, s) ppm. ^{13}C NMR (DMSO-d_6): 169.2 (s), 163.2 (s), 144.3 (s), 141.1 (s), 133.4 (s), 128.5 (d), 124.7 (d), 121.3 (d), 91.6 (s), 11.8 (q) ppm.

N,N-*Dimethyl-2,2-dinitro-3-(4-nitrophenylhydrazono)butyramide (49):*

To a solution of the the trinitro compound **3a** (1.55 g, 5 mmol) in acetonitrile (15 ml) was added dimethylamine (1.3 ml, 40 % aq., 10 mmol). A yellow solid was collected by filtration after 5 min, 0.36 g (20 %). Mp (dec.) 250 °C. IR (KBr): 3117, 2791, 1660, 1593, 1498, 1375, 1317, 1246, 1101, 856, 804 664, 754 cm^{-1}. ^1H NMR (DMSO-d_6): 8.29 (2H, d, J 2.2 Hz), 8.21 (2H, d, J 2.2 Hz), 2.58 (6H, s), 2.35 (3H, s) ppm. ^{13}C NMR (DMSO-d_6): 159.2 (s), 146.8 (s), 145.3 (s), 141.6 (s), 124.7 (d), 116.7 (d), 115.8 (s), 34.5 (q), 16.7 (q) ppm.

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