Supplementary Material Available.—A table of analysis results for 1-methylacenaphthene and three figures will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 20× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D. C. 20036. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche, referring to code number JOC-73-3122.

A Novel Reaction between 3,5-Dinitroacetophenone–Acetone and Secondary Amines Yielding Naphthalenic Structures

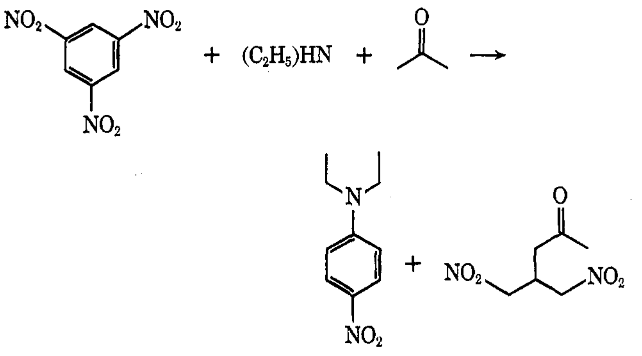
SIGMA R. ALPHA

Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

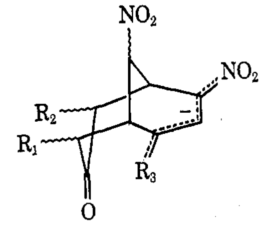
Received March 16, 1973

The exothermic reaction which occurs upon the addition of a secondary amine to a mixture of 3,5-dinitroacetophenone and acetone was investigated to determine the nature of the products. Instead of the expected Meisenheimer addition product, a new compound, 1-methyl-3-diethylamino-5,7-dinitronaphthalene, was formed. Employing 3,5-dinitrobenzaldehyde as the starting material resulted in the formation of the analogous 1,3-dinitro-7-diethylaminonaphthalene. The scope of the reaction is investigated.

The chemistry of complexes arising from the interaction of electron-deficient aromatics with organic bases has received considerable attention during the last 10 years and has been reviewed.[1,2] These so-called Meisenheimer complexes in which the negative charge is delocalized over a pentadienide system have been observed under certain conditions to undergo an internal cyclization to form a second bond and a stable bicyclic anion. An example is the reaction between trinitrobenzene, acetone, and diethylamine.



Although, as shown above, the products usually isolated are *N*,*N*-diethyl-*p*-nitroaniline and 2-acetonyl-1,3-dinitropropane,[3] the intermediate complex Ia can be isolated under special conditions.[4] Such structures with electron-withdrawing substituents other than nitro and ketones other than acetone have been isolated (Ib, Ic).[5]



Ia, $R_1 = R_2 = H$; $R_3 = NO_2$
b, $R_1 = COCH_3$; $R_2 = H$; $R_3 = NO_2$
c, $R_1 = CO_2Et$; $R_2 = H$; $R_3 = CN$

Analogous products and intermediates might be expected from the reaction of 3,5-dinitroacetophenone, acetone, and alkylamines. It was hoped to obtain some otherwise difficultly available acetophenones by means of this reaction.

In fact, when diethylamine is added to an acetone solution of 3,5-dinitroacetophenone, the mixture immediately turns black and a mildly exothermic reaction takes place. After a few minutes at room temperature black crystals begin to appear, their formation being complete within 1 hr, yielding a compound (mp 178–180° from dioxane–water) hereafter referred to as compound Y (Table I).

TABLE I

COMPOUND Y

Nmr (CF_3CO_2D)				Uv (MeOH)		Uv (66% H_2SO_4)	
δ	H	Multiplicity	*J*	λ	ε	λ	ε
0.8	6	Triplet	7.0 Hz				
3.4	4	Quartet	7.0 Hz	235	27,000	210	40,000
2.5	3	Singlet		260	48,000	255	21,000
7.4[a]	1	Broad singlet		350	5,800	295	14,000
8.4[a]	1	Broad singlet		415	24,000	360	2,700
8.6[a]	1	Doublet	2.0 Hz	470	25,000	430	80
8.9[a]	1	Doublet	2.0 Hz	620	~0	550	~0

[a] The chemical shifts of these four protons are extremely solvent dependent, being well separated in trichloroacetic acid and mineral acids but having totally different positions in other solvents. For example, in chloroform or methylene chloride the two downfield protons accidentally overlap (2 H, δ 8.36), the two upfield protons now appearing at δ 7.5 and 7.1; while in dimethyl sulfoxide both the two downfield protons as well as the two upfield protons are accidentally overlapping at δ 8.7 and 7.3, respectively.

Elemental analysis established the empirical formula as $C_{15}H_{17}N_3O_4$ and a mass spectrum of the compound confirms it to have a molecular weight of 303. This corresponds to the combination of 1 equiv each of diethylamine, acetone, and 3,5-dinitroacetophenone, together with the loss of 1 molar equiv of hydrogen and water. The ir of Y shows the presence of acidic hydrogens or C═N multiple bonds. The uv of Y shows it not to be of the dinitropropenyl class, as such

---

(1) R. Foster and C. A. Fyfe, *Rev. Pure Appl. Chem.*, **16**, 61 (1966).

(2) E. Bunchel, A. R. Norris, and K. E. Russel, *Quart. Rev., Chem. Soc.*, 123 (1963).

(3) R. Foster and C. A. Fyfe, *Tetrahedron*, **22**, 1831 (1962).

(4) H. Schran and M. J. Strauss, *J. Org. Chem.*, **36**, 856 (1971).

(5) M. J. Strauss, T. C. Jensen, H. Schran, and D. O'Conner, *J. Org. Chem.*, **35**, 383 (1970).

compounds have an absorption peak at 510 nm (ϵ 30,000–50,000).

Discussion

Reduction of Y with tin in hydrochloric acid resulted in a compound having a similar nmr except for the presence of amine hydrogens (4 H) at δ 3.8 and a shift of the aromatic peaks to δ 6.1, 6.5, 6.7, and 7.0. Treatment of this compound with acetic anhydride gave a diacetyl derivative with two methyl peaks at δ 1.8 and 2.0. These results are consistent with the presence of *two* nitro groups in Y.

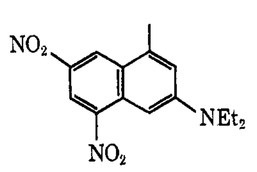
The intensely red colored Y is insoluble in water, but dissolves in concentrated mineral acids to give clear yellow solutions which yield unchanged Y upon dilution with water. Estimations of basicity of the compound in aqueous sulfuric acid solutions show it to have approximately the basicity of 3,5-dinitroaniline ($pK_a = 0.23$) but to be much more basic than 2,4-dinitroaniline. This finding suggests the presence of an amine nitrogen substituent on an aromatic ring bearing two meta nitro groups, or a direct through-conjugation with the nitro groups but across a much larger aromatic system. Such long-range conjugative effects have been observed previously, for example in the basicity of aminoquinolines.[6]

Subtracting the elements due to the methyl, diethylamino, and nitro moieties from the empirical formula $C_{15}H_{17}N_3O_4$, one is left with a skeletal formula of $C_{10}H_4$ which corresponds to a parent hydrocarbon, $C_{10}H_8$. All four of the protons not on side chains appear in the aromatic region of the nmr spectrum and show a meta coupling between the two downfield peaks. The only possible $C_{10}H_4$ aromatic skeletons consistent with these facts are naphthalenic and azulene structures containing meta-positioned hydrogens.[7]

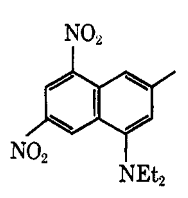
The results of a deuterium exchange experiment allow the exclusion of the azulene structures. The compound Y exchanges *one* of its four ring protons (that at δ 8.4) for deuterium in trifluoroacetic acid-*O-d* with a half-life of *ca.* 30 min. This result is consistent with the naphthalenic structures, since naphthalene is electrophilically attacked at the α position an order of magnitude faster than at the β position.[8] Azulenes, on the other hand, exchange in the 1 and 3 positions in both acidic and basic media.[9] Neither of the protons in the 1 or 3 positions could exchange faster than the other owing to resonance influences of substituents on the azulene seven-membered ring, since in acidic exchange, the plus charge of the carbonium ion intermediate is delocalized equally onto all of the carbon atoms of the seven-membered ring. A two-proton exchange is thus obligatory and we are left only with naphthalenic backbone structures to consider.

The nmr aromatic region can always be divided into two meta-coupled downfield peaks and two meta-coupled upfield peaks. From known dependences of aromatic chemical shifts on ring substitution, the former set of protons can be assigned to the nitrated ring of a naphthalene structure, and the latter set of protons to the ring derived from acetone.

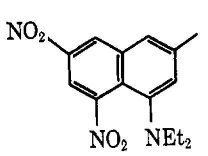
There are thus four remaining positional isomers of the remaining naphthalene possibilities, which are given below.



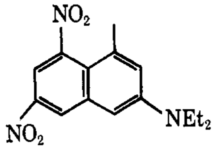
II



III



IV



V

Models show one feature which distinguishes between structures III–V and structure II. In II the hydrogens of the methyl group are in intimate contact with the peri hydrogen on the nitrated ring. Space-filling models indicate that this hydrogen ought to actually restrict the rotational motion of the methyl group. This close spatial proximity combined with the lack of through-bond coupling between the two sets of protons is what is required for the transfer of spin relaxation energy from one set of nuclei to the other, *i.e.*, a nuclear Overhauser effect.[10]

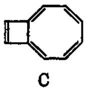
In fact, saturation of the methyl protons in either the field or frequency sweep modes produced a marked reduction in the intensity of the δ 8.6 hydrogen. From known chemical shift dependences the hydrogen between the two nitro groups ought to be furthest downfield. Therefore the hydrogen in the α position of the nitrated ring ought to be the next upfield peak (that at δ 8.6). Reduction of the intensity of this peak with respect to the other aromatic peaks was observed as high as 50%. Overhauser effects of this magnitude can be unambiguously interpreted, and this fact, along with the other evidence presented above, clearly establishes the compound Y as having structure II.[11]

Structure II can be formed through a reasonable mechanism *via* an intermediate such as VI, which is known to be formed in the interaction of 3,5-dinitro-substituted aromatics with bases.[12] However, in this case, instead of another Michael attack on the benzene ring by the acetone enamine to form bicyclic structures like I, one obtains reactions with the active car-

---

(6) R. M. Acheson, "An Introduction to the Chemistry of Heterocyclic Compounds," 2nd ed, Interscience, New York, N. Y., 1967, p 258.

(7) The pronounced stability of Y under a variety of vigorous reaction conditions renders an 8:4 system such as C unlikely.



C

(8) L. Fieser and M. Fieser, "Advanced Organic Chemistry," Reinhold, New York, N. Y., 1961, p 879.

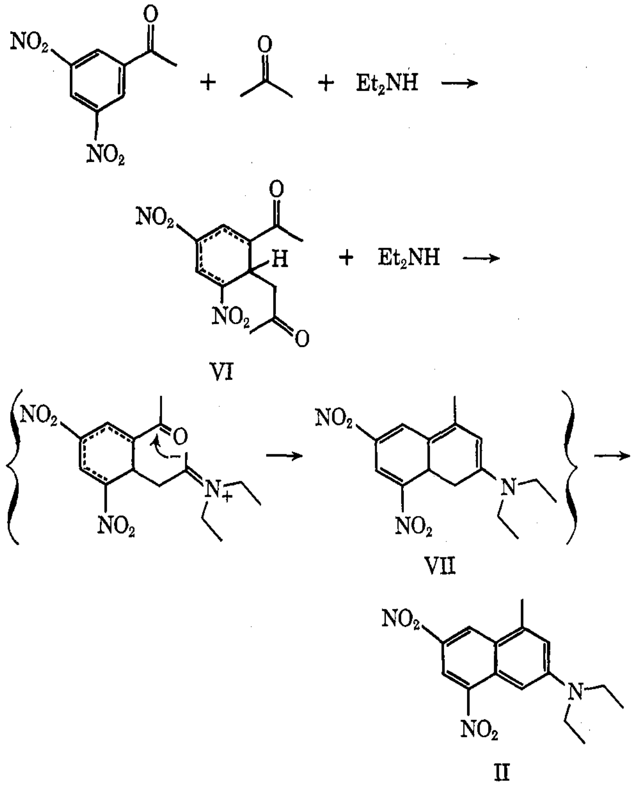
(9) B. C. Challis and F. A. Long, *J. Amer. Chem. Soc.*, **87**, 1196 (1965).

(10) R. A. Bell and J. K. Saunders, *Can. J. Chem.*, **46**, 3421 (1968).

(11) Attempts to use acetone-d_6 to distinguish among the naphthalene structures proved to be futile, as there was complete exchange of deuterium between acetone-d_6 and the acetophenone methyl prior to product formation.

(12) M. J. Foreman, R. Foster, and M. J. Strauss, *J. Chem. Soc. B*, 147 (1970).

bonyl position to yield a dihydronaphthalene structure like VII, which then aromatizes to form the product II.



Attempts were made to make derivatives of Y by treating 3,5-dinitroacetophenone and diethylamine with 1-phenylacetone, acetylacetone, or 2-butanone. However, all of these compounds failed to give isolable products. This inability to obtain products from ketones other than acetone can be rationalized in terms of structure II in that there must be too great a steric interaction in the 1,2,3- or 3,4,5-trisubstituted naphthalenes to allow the reaction to go to completion in the presence of competing side ractions.

In order to investigate the generality of the reaction it was decided to change the nature of the aromatic starting material.

When an acetone solution of 3,5-dinitrobenzaldehyde (prepared from the acid chloride and lithium tributoxyaluminum hydride[13]) was treated with diethylamine, an instant black color formed and a mildly exothermic reaction proceeded. Within a few minutes black crystals were growing from the solution, which after recrystallization gave a material with mp 183.5–185.6° in a yield of 47%.

Similarly to the original compound Y, this material was soluble in polar media to give dark red solutions. It was not soluble in water but gave a pale yellow solution in mineral acids. The molecular weight was 289, which corresponds to one CH_2 group less than Y. Analysis of the compound gave an empirical formula of $C_{14}H_{15}N_3O_4$.

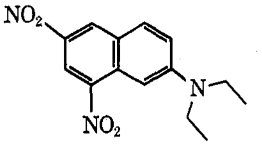
The uv and visible spectra show a series of peaks with an envelope identical in essential features with that of Y, indicating that the substance belongs to the same structural class as II.

The nmr of the material shows the presence of two ethyl moieties and *five* aromatic peaks. By analogy with structure assignment II for compound Y, there is now an expected definite AB pattern in the aromatic region of this new material ($J = 9$ cps).

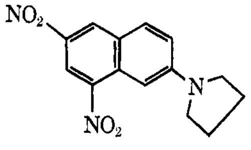
Synthesis of the material from acetone-d_6 produced a spectrum whose AB pattern was partially collapsed (incompletely owing to prereaction exchange between acetone-d_6 and diethylamine), which reveals that one of the protons in the AB pattern is derived from acetone and the other is a proton originating from the benzaldehyde.

As in the original compound II, this material exchanges *only one proton in trifluoroacetic acid-O-d,* which is the third upfield proton.

All of these findings are consistent with structure VIII for this second compound.



VIII

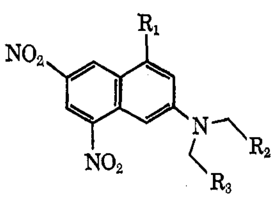


IX

As a check on the generality of the reaction, pyrrolidine was allowed to react with acetone and 3,5-dinitrobenzaldehyde. The reaction mixture proved to be very exothermic and had to be kept on ice for the first few minutes to prevent boiling to dryness. This reactivity might be expected, as pyrrolidine has a much higher propensity to form enamines than diethylamine. After crystallization from dioxane a 30% yield of black crystals was obtained, mp 229–231°.

The compound had a molecular weight of 287 and an nmr analogous to that of VIII. It was found that exchange of one of the aromatic protons in the pyrrolidine derivative was very fast (half-life in minutes) in trifluoroacetic acid-*O-d*, which is again consistent with pyrrolidine's greater stability in the iminium form than diethylamine. Also, this material exchanges the single aromtic proton in 75% D_2SO_4–D_2O with a half-life of *ca.* 1 hr. These findings are all consistent with structure IX.[14]

It thus appears that compounds of the general structure X can be made through the reaction of the



X

appropriate alkylphenone, acetone, and secondary amine.[15]

---

[13] R. N. Zaxapkah, A. H. Mosach, and R. B. Raepurecko, *Zh. Org. Khim.*, **2**, 2197 (1966).

[14] As can be seen from the structures II and III–V, the acetophenone methyl is an inherent part of the aromatic structure in compounds III–V, but is only a side chain in compound II. Thus observation of products VIII and IX with 3,5-dinitrobenzaldehyde is an independent proof of structure II *vs.* III–V.

[15] No attempts have been made to improve yields. However, as it is probable that 1 equiv of starting material is used in accepting the 1 equiv of hydrogen liberated in forming product, an oxidizing agent in the reaction mixture might considerably increase yields.

Experimental Section

3,5-Dinitroacetophenone.—Though this compound has been reported in the literature[16,17] from the reaction of 3,5 dinitrobenzoyl chloride and diethylmagnesium malonate, in our hands ethyl 3,5-dinitrobenzoate was always the major product. Included here, therefore, is a procedure which was patterned after that for the synthesis of *m*-nitroacetophenone.[18]

A three-necked 2-l. flask fitted with an addition funnel, a condenser with a nitrogen inlet, and a mechanical stirrer was charged with 16 g of magnesium turnings, and purged with nitrogen. To the flask was added 14.7 ml of absolute ethanol and 3 ml of carbon tetrachloride. After the reaction had subsided, 440 ml of anhydrous ether was added and then a solution of 103 ml (0.55 mol) of diethyl malonate, 59 ml (1.0 mol) of absolute ethanol, and 73 ml of ether was dropped in at a rate sufficient to cause rapid boiling. After refluxing for 4 hr, the ether was distilled off and approximately 200 ml of benzene was added. A continuous process of benzene addition and benzene–ethanol azeotropic distillation was carried out until the temperature was ~75° to remove the last of the ethanol. At this point, 1 l. of benzene was added to the pot, and the addition funnel was charged with a solution of 500 ml of benzene containing 135 g (0.59 mol) of 3,5-dinitrobenzoyl chloride. The stirring motor was placed on high speed, and the acid chloride solution was allowed to run into the pot as rapidly as possible. If the addition funnel has a sufficiently large bore stopcock, the addition takes approximately 15 sec, which gives the solution about 5 sec of high-speed stirring before the entire contents suddenly jell into a solid mass.

This material was then isolated and decarboxylated as in ref 18. The solid material so obtained was recrystallized from methanol, ethanol, or a 1:1 mixture of methanol–carbon tetrachloride to give 88 g (71%) of material, mp 81–83° (lit.[16] mp 80–81°).

In the following procedures high-quality 3,5-dinitroacetophenone must be used (commercial material fails to react without extensive purification) and the diethylamine and acetone must be dry. No attempts to maximize yields were undertaken other than to observe that excess amine decreases yields as does allowing the amine and acetone to mix before reaction with the aromatic compound.

1-Methyl-3-diethylamino-5,7-dinitronaphthalene (II).—To a solution of 1.5 g (0.007 mol) of 3,5-dinitroacetophenone in 4 ml of acetone was added 0.5 g (0.007 mol) of diethylamine. The solution was swirled and set aside. After 1 hr the solution was cooled in the refrigerator and then filtered. The black crystals thus obtained were washed (quickly) with acetone and then with ether. Crystallization from a 5:1 mixture of dioxane–water gave 0.7 g (32%) of II, mp 178–180°. *Anal.* Calcd for $C_{15}H_{17}N_3O_4$: C, 59.40; H, 5.61; N, 13.85. Found: C, 59.42; H, 5.71; N, 14.16. Further data can be found in the text.

1,3-Dinitro-7-pyrrolidinonaphthalene (IX).—To an ice-cold solution of 0.75 g (0.0037 mol) of 3,5-dinitrobenzaldehyde in 3 ml of acetone was added 0.27 g (0.0037 mol) of pyrrolidine. The solution was swirled and kept on ice for 15 min, whereupon it was filtered and the collected solid was rapidly washed with acetone. The crystals were taken up in 45 ml of boiling dioxane, which was then filtered. Cooling of the solution yielded 0.27 g of crystals. Addition of water to the hot, concentrated dioxane mother liquor until turbidity yielded on cooling another 0.07 g of material to give a total of 0.33 g (30%) of IX, mp 229–231°. *Anal.* Calcd for $C_{14}H_{13}N_3O_4$: C, 58.10; H, 5.19; N, 14.52. Found: C, 58.10; H, 5.22; N, 14.73. Nmr in CF_3CO_2D showed a broad singlet (4 H) at δ 2.6 and similarly (4 H) at δ 4.2, an AB pattern (2 H, $J = 9$ Hz) centered at δ 8.4, and two singlets (1 H, 1 H) at δ 9.5.

1,3-Dinitro-7-diethylaminonaphthalene (VIII).—To a solution of 1.0 g (0.0048 mol) of 3,5-dinitrobenzaldehyde in 3 ml of acetone was added 0.37 g (0.0048 mol) of diethylamine. The solution was swirled and set aside at room temperature for 30 min and worked up as above. The yield was 0.58 g (47%) of material, mp 183.5–185.6°. Nmr (CF_3CO_2D) showed a triplet (6 H, $J = 7.5$ Hz) at δ 1.48, a quartet (4 H, $J = 7.5$ Hz) at δ 4.08, an AB pattern (2 H, $J = 9.0$ Hz) at δ 8.6, a singlet (1 H) at δ 9.4, and a singlet (2 H) at δ 9.6.

Reduction of II.—To a steam-heated solution of 2 g of III in 150 ml of 38% HCl and 20 ml of concentrated sulfuric acid was added portionwise 4 g of tin with shaking over a period of 1 hr. The solution was basified with 50% aqueous NaOH and extracted with ether. After drying and treatment with activated charcoal, yellow crystals were obtained (0.5 g), mp 96–97°. Nmr ($CDCl_3$) showed a triplet (6 H, $J = 8$ Hz) at δ 1.18, a singlet (3 H) at δ 2.68, a quartet (4 H, $J = 8$ Hz) at δ 3.4, a singlet (4 H) at δ 3.88, a doublet (2 H, $J = 0.5$ Hz) at δ 6.08, a singlet (1 H, broad) at δ 6.5, a singlet (1 H) at δ 6.7, and a singlet (1 H) at δ 7.0.

To 0.35 g of this material in 20 ml of ether was added 1 ml of acetic anhydride. After 0.5 hr of stirring the solution was poured into water, neutralized with sodium bicarbonate, and extracted with methylene chloride. The methylene chloride solution was stirred with ammonium hydroxide for 0.5 hr and extracted with water and the solvent was evaporated. The residue was crystallized from methanol to give 0.25 g of material, mp 139.5–141.0°. Nmr ($CDCl_3$) showed a triplet (3 H, $J = 8$ Hz) at δ 1.18, a singlet (3 H) at 1.88, two singlets (3 H, 3 H) at δ 2.3 and 2.08, a quartet (4 H, $J = 8$ Hz) at δ 3.2, and singlets (1 H, 1 H, 2 H, 1 H, 2 H) at δ 6.48, 6.78, 7.10, 8.08, and 8.28, respectively.

Acknowledgments.—The author would like to acknowledge Professor C. G. Swain for financial support and the National Science Foundation for a predoctoral fellowship, 1970–1971. He would also like to express his indebtedness to Professor D. Kemp for many helpful discussions during the course of this work.

Registry No.—II, 40792-03-8; VIII, 40792-04-9; IX, 40792-05-0; II reduction product, 40792-22-1; II reduction product, diacetyl derivative, 40792-23-2; 3,5-dinitroacetophenone, 14401-75-3; diethyl malonate, 105-53-3; 3,5-dinitrobenzoyl chloride, 99-33-2; acetone, 67-64-1; diethylamine, 109-89-7; 3,5-dinitrobenzaldehyde, 14193-18-1; pyrrolidine, 123-75-1.

---

[16] M. Suzuki and B. Shimizu, *J. Pharm. Soc. Jap.*, **73**, 392 (1953).

[17] N. S. Kyachoc, *Zh. Obshch. Khim.*, **32**, 293 (1962).

[18] G. A. Reynolds and C. R. Hauser, "Organic Syntheses," Collect. Vol. IV, Wiley, New York, N. Y., 1963, p 708.