TABLE I (*Continued*)

No.	R_2	R_3	R_4X	M.P.[a] or B.P. (Mm.)	RS[b]	Yield,[c] %	Formula	Analyses,[d] %					
								Carbon		Hydrogen		Nitrogen	
								Calcd.	Found	Calcd.	Found	Calcd.	Found
	$R_1 = (C_6H_5)_2C(OH)$—												
43	CH_3—	CH_3—	HCl	183–185	C	71	$C_{24}H_{26}ClNO_3$	70.0	70.2	6.4	6.1	3.4	3.1
44	CH_3—	CH_3—	CH_3I	176–178	C	69	$C_{25}H_{28}INO_3$	58.0	58.0	5.5	5.5	2.7	2.5
45	CH_3—	*i*-C_3H_7—	HCl	170–172	C	39	$C_{26}H_{30}ClNO_3$	71.0	70.5	6.9	7.0	3.2	2.8
46	C_2H_5—	C_2H_5—	HCl	164–165	C	80	$C_{26}H_{30}ClNO_3$	71.0	70.9	6.9	6.9	3.2	3.4
47	C_2H_5—	C_2H_5—	CH_3I	178–179	C	58	$C_{27}H_{32}INO_3$	59.5	59.3	5.9	6.1	2.6	2.6
48	CH_3—	C_6H_{11}—[f]	HCl	193–196	D	23	$C_{29}H_{34}ClNO_3$	72.6	72.7	7.1	7.2	2.9	3.1
49	CH_3—	C_6H_{11}—[f]	CH_3I	125–127	C	24	$C_{30}H_{36}INO_3$	61.5	61.9	6.2	6.6	2 4	2.8
50	—$(CH_2)_4$—		HCl	193–195	E	46	$C_{26}H_{28}ClNO_3$	71.3	71.2	6.4	6.6	3.2	2.8
51	—$(CH_2)_4$—		CH_3I	141–143	C	64	$C_{27}H_{30}INO_3$					2.6	2.7
52	—$(CH_2)_4$—		EBA[e]	168–169	D	49	$C_{30}H_{34}BrNO_5$	63.4	63.3	6.0	6.2	2.5	2.4
53	—$(CH_2)_5$—		HCl	203–205	D	49	$C_{27}H_{30}ClNO_3$	71.7	71.4	6.7	6.9	3.1	3.0
54	—$(CH_2)_5$—		CH_3I	178–181	C	43	$C_{28}H_{32}INO_3$	60.3	60.0	5.8	5.6	2.5	2.9
55	—$(CH_2)_2O(CH_2)_2$—		HCl	198–200	D	65	$C_{26}H_{28}ClNO_4$	68.8	69.1	6.2	6.2	3.1	2.8
56	*i*-C_3H_7	$C_6H_5CH_2$—	HCl	161–163	D	29	$C_{32}H_{36}ClNO_4$[j]	72.1	71.6	6.8	6.6	2.6	2.8

[a] Melting points are not corrected. [b] RS = recrystallizing solvent: A = methyl ethyl ketone; B = isopropyl alcohol-isopropyl ether; C = isopropyl alcohol; D = ethanol; E = acetonitrile; F = benzene; G = not recrystallized; H = chloroform-ether; I = *n*-propanol. [c] Yields are expressed as % of recrystallized or distilled product. [d] Analyses by Weiler and Strauss, Oxford, England. [e] EBA = ethyl bromoacetate quaternary salt. [f] C_6H_{11} = cyclohexyl. [g] Pic = picric acid. [h] Chlorine, Calcd.: 10.7. Found: 10.9. [i] The compound is derived from the isomeric 2-(1-pyrrolidino)-2-phenylethanol (described in ref. 1). [j] The formula represents a monohydrate.

2-Diethylamino-1-phenylethyl diphenylacetate (Compound 31). To a stirred solution of 23.1 g. (0.1 mol.) of diphenylacetyl chloride in 100 ml. of benzene was added 19.3 g. (0.1 mol.) of 2-diethylamino-1-phenylethanol in 100 ml. of benzene at a rate sufficient to maintain reflux. After heating under reflux for 3 hr., the benzene was removed and the residue treated with 250 ml. of water, cautiously basified with 40% aqueous sodium hydroxide and the separated free base extracted with five 60-ml. portions of ether. The combined extracts were dried (anhydrous magnesium sulfate), filtered, and distilled to give 74% of product, b.p. 194–195° (0.2 mm.).

2-Diethylamino-1-phenylethyl diphenylacetate methiodide (Compound 32). To a cooled solution of 3.9 g. (0.01 mol.) of 2-diethylamino-1-phenylethyl diphenylacetate in 20 ml. of acetonitrile was added 1 ml. (0.016 mol.) of methyl iodide. The solution was allowed to stand 20 hr. at room temperature and then poured into 150 ml. of dry ether. Trituration of the precipitated gum with several additional portions of dry ether gave 4.9 g. (93%) of product, m.p. 154–159°.

2-Piperidino-1-phenylethyl α-chloro-α,α-diphenylacetate hydrochloride (Compound 40). A solution of 19.9 g. (0.075 mol.) of α-chlorodiphenylacetyl chloride in 70 ml. of acetonitrile was added to a suspension of 14.3 g. (0.07 mol.) of 2-piperidino-1-phenylethanol in 30 ml. of acetonitrile. After storage at 20° for 24 hr. there was obtained 30.2 g. of product.

2-Diethylamino-1-phenylethyl benzilate hydrochloride (Compound 46). A suspension of 18 g. (0.039 mol.) of 2-diethylamino-1-phenylethyl α-chloro-α,α-diphenylacetate hydrochloride in 900 ml. of water upon warming on a steam bath for 20 min., yielded a clear solution. Sodium chloride (180 g.) was then added and the precipitate and solution extracted with a total of 2 l. of chloroform. The chloroform was removed and the residue recrystallized (isopropyl alcohol) to give 13.8 g. (80%) of product; m.p. 164–165°.

2-Diethylamino-1-phenylethyl benzilate methiodide (Compound 47). Methyl iodide (2.9 g., 0.02 mol.) was added to a cooled solution of 5.4 g. (0.013 mol.) of 2-diethylamino-1-phenylethyl benzilate in 26 ml. of acetonitrile. Upon storage for 20 hr. at 20° and scratching, the product crystallized, and was separated and recrystallized (isopropyl alcohol) to give 4.1 g. (58%) of product; m.p. 178–179°.

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Bicarbonate-catalyzed Displacement of a Nitro Group of 1,3,5-Trinitrobenzene

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During an investigation of methods for the selective reduction of one of the nitro groups of *sym*-trinitrobenzene, reduction by means of sodium sulfide and sodium bicarbonate in aqueous methanol was tried.[1] Among the reaction products none of the desired 3,5-dinitroaniline could be detected, but 3-amino-5-nitroanisole was isolated in 20% yield. Since the displacement of aromatic nitro groups by alcohols has previously been reported to occur only in strongly alkaline media,[2,3] this result was unexpected. The conditions for this displacement were then investigated and at the same

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(1) H. H. Hodgson and E. R. Ward, *J. Chem. Soc.*, 794 (1945) used this method for the mono-reduction of dinitro- and trinitronaphthalenes.

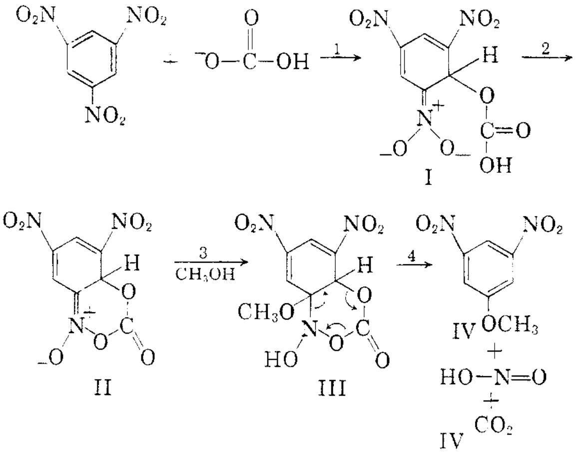
(2) C. A. Lobry de Bruyn and F. H. van Leent, *Rec. trav. chim.*, 14, 150 (1895).

(3) F. Reverdin, *Org. Syntheses*, Coll. Vol. I, 219 (1941).

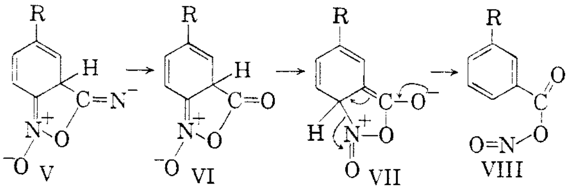
time the sequence of the substitution and reduction reactions was readily demonstrated. It was found that heating *sym*-trinitrobenzene in 76% aqueous methanol in the presence of either sodium or potassium bicarbonate or sodium carbonate in the absence of sulfide likewise resulted in the displacement of a nitro group, 3,5-dinitroanisole being obtained in 60–80% yield. In contrast, 3,5-dinitroaniline was inert under these conditions and since the mono-reduction of 3,5-dinitroanisole to 3-amino-5-nitroanisole under similar conditions had been observed previously,[4] the sequence of steps were clearly established as substitution followed by reduction.

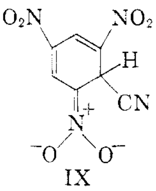
Attempts were made to effect the displacement of a nitro group in *sym*-trinitrobenzene by treatment in aqueous methanolic solutions with other catalysts such as sodium acetate, dibasic sodium phosphate, sodium iodide, ammonium carbonate, and carbon dioxide. Starting trinitrobenzene was recovered in each case in 70–100% yields. In contrast heating *sym*-trinitrobenzene in $0.6N$ aqueous methanolic sodium hydroxide solution gave only dark-colored, amorphous substances. When the bicarbonate-catalyzed substitution was carried out in aqueous ethanol, the reaction likewise gave tarry, dark-colored substances from which no 3,5-dinitrophenetole could be isolated. In this case, it appeared that the prevailing reactions were those brought about by the reducing action of ethanol.[2] On the supposition that the displacement might be the result of a weakly alkaline effect, the trinitrobenzene was boiled with 76% aqueous methanol containing sufficient sodium hydroxide to give it an initial *p*H of 11. But in this case also, no 3,5-dinitroanisole was obtained, the only identifiable substance at the end of the reaction being starting material. In contrast to trinitrobenzene, *m*-dinitrobenzene was totally inert to aqueous methanol and sodium bicarbonate.

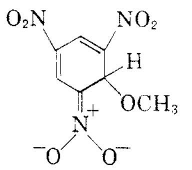
The above experiments seem to point up a rather unique specificity of the bicarbonate and carbonate anions in their roles as catalysts in the displacement of the nitro group. A mechanism that seems reasonable for these conditions and which is in harmony with the chemical behavior of trinitrobenzene and the bicarbonate anion is shown in the scheme top of column 2:



This mechanism, through the formation of the intermediates I and II, is analogous to that presented by Bunnett and Rauhut[5] for the von Richter reaction. Their mechanism is characterized by cyanide attack on the position *ortho*- to the nitro group, followed by local interaction of the two groups to give rise to V which upon hydrolysis becomes VI. The transition complex III resembles VII to a degree, an essential difference between the two being that in III, the position occupied by the nitro group bears a methoxyl group instead of a proton. The presence of the methoxyl group in III is the expected result of a nucleophilic attack on II by methanol from the basic medium. In an attempt to substantiate a nucleophilic attack at this point, a bicarbonate-catalyzed reaction was conducted in the presence of potassium iodide in the hope that iodide might compete with methanol to give rise to some 3,5-dinitroiodobenzene. Only 3,5-dinitroanisole was isolated. The addition of bicarbonate ion to give I finds further analogy in structures IX and X which were assigned by Meisenheimer[6] to the stable adducts of *sym*-trinitrobenzene with potassium cyanide and potassium methylate respectively. These compounds are responsible for the deep red colors developed when trinitrobenzene comes in contact with bases, bicarbonates included.




IX


X

EXPERIMENTAL[7]

3-Amino-5-nitroanisole. To a refluxing solution of 10 g. (0.047 mol.) of 1,3,5-trinitrobenzene in 150 ml. of methanol was added 2.4 g. (0.028 mol.) of sodium bicarbonate. This was followed by the dropwise addition of a solution com-

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(4) J. J. Blanksma, *Rec. trav. chim.*, **28**, 105 (1909).

(5) J. F. Bunnett and M. M. Rauhut, *J. Org. Chem.*, **21**, 944 (1956).

(6) J. Meisenheimer, *Ann.*, **323**, 205 (1902).

(7) Melting points are uncorrected. The microanalyses were carried out under the direction of Dr. J. A. Kuck, Stamford Laboratories, American Cyanamid Company, Stamford, Conn.

posed of 25 g. (0.10 mol.) of sodium sulfide nonahydrate, 8 g. (0.1 mol.) of sodium bicarbonate, 60 ml. of water, and 40 ml. of methanol. When one half of this mixture had been added, another 2.4 g. (0.028 mol.) of sodium bicarbonate was added to the reaction mixture in one lot. The addition of the sulfide-bicarbonate solution was carried out over a 1.5 hr. period. After that, the reaction was refluxed for an additional 0.5 hr. and allowed to cool. A rust-colored material precipitated from the dark solution. It weighed 1.4 g. (20%). Recrystallization from 40% aqueous ethanol gave material of m.p. 119–120°. Another recrystallization from 50% aqueous ethanol gave matted, orange needles melting at 118.5–119°. A mixed m.p. with an authentic sample of 3-amino-5-nitroanisole (Lit. m.p. 118°)[8] was not depressed.

Anal. Calcd. for $C_7H_8N_2O_3$: C, 50.00; H, 4.84; N, 16.66. Found: C, 49.75; H, 4.79; N, 16.95.

Another crop of crystalline material weighing 2.1 g. was obtained from the original reaction solution. This substance melted at 100–115° after a recrystallization from water containing a small amount of ethanol. Further recrystallizations from other solvents did not change this m.p. The material appeared to be a mixture of two or more compounds, one of which is probably the aminonitroanisole. It was not purified further.

3,5-Dinitroanisole. To a hot solution of 10 g. (0.047 mol.) of 1,3,5-trinitrobenzene in 150 ml. of methanol, was added a slurry of 12.8 g. (0.15 mol.) of sodium bicarbonate in a mixture of 60 ml. of water and 40 ml. of methanol. The red mixture was refluxed and stirred for 2.5 hr. and allowed to cool over a period of several hours. The tan crystals which precipitated were filtered and dried in a desiccator. Recrystallization from 200 ml. of hot methanol gave 5.5 g. (60%) of nearly colorless product, m.p. 104–106°. This melting point was not depressed by admixture with an authentic sample of 3,5-dinitroanisole (Lit. m.p. 105°).[3] Additional crystalline fractions were obtained from the mother liquors indicating a higher yield of product. These fractions, however, were not brought to a constant melting point.

When the reaction was run with potassium bicarbonate a more easily purified product melting at 104–106° was obtained in 86% yield, while sodium carbonate (0.15 mol. under the same conditions as described above) gave the product in 70% yield.

Attempted reactions with sodium acetate, dibasic sodium phosphate dodecahydrate, sodium iodide, ammonium carbonate, and carbon dioxide. A mixture of 0.05 mol. of 1,3,5-trinitrobenzene, 0.15 mol. of the requisite salt, and 250 ml. of 76% aqueous methanol was refluxed for 3 hr. In all cases, at least 70% of the trinitrobenzene was easily recovered by cooling the reaction mixture and washing the pale yellow crystals with water and cold methanol. The identity of starting material was shown by mixed m.p.'s.

In the case of the carbon dioxide experiment, this gas was bubbled through a boiling 76% aqueous methanol solution of trinitrobenzene for 3 hr. The recovery of the starting material was quantitative.

Behavior of 1,3,5-trinitrobenzene with strong alkali. To a hot solution of 10 g. (0.05 mol.) of 1,3,5-trinitrobenzene in 150 ml. of methanol was added 6 g. (0.15 mol.) of sodium hydroxide dissolved in a mixture of 60 ml. of water and 40 ml. of methanol. The dark red solution was stirred under reflux for 3 hr. No crystalline product was obtained from the black, amorphous reaction product.

Behavior of 1,3,5-trinitrobenzene with sodium bicarbonate in the presence of potassium iodide. To a hot solution of 10 g. (0.05 mol.) of 1,3,5-trinitrobenzene in 150 ml. of methanol was added a slurry of 12.8 g. (0.15 mol.) of sodium bicarbonate and 16.6 g. (0.1 mol.) of potassium iodide in a mixture of 60 ml. of water and 40 ml. of methanol. The red mixture was stirred under reflux for 2.5 hr., and cooled. A crystalline material precipitated which was filtered and recrystallized from 100 ml. of methanol. The crystals weighed 3.7 g. and melted at 104–106°. A mixed m.p. with an authentic sample of 3,5-dinitroanisole was not depressed. The original reaction solution was evaporated to about one-half volume whereupon another 1.6 g. of crude crystals was obtained. Two recrystallizations from ethanol gave a compound melting at 120–122°, which by mixed m.p. was shown to be unreacted 1,3,5-trinitrobenzene. The mother liquor was concentrated further to a small, dark, aqueous solution, which was extracted with ether several times. Evaporation of the ether gave a negligible amount of solid which was recrystallized from ethanol and melted at 120–122°. A mixed m.p. with 1,3,5-trinitrobenzene was not depressed. The yield of 3,5-dinitroanisole calculated on recovered TNB was 47%.

Attempted reaction of m-dinitrobenzene with sodium carbonate. To a solution of 4 g. (0.024 mol.) of *m*-dinitrobenzene in 75 ml. of methanol was added a suspension of 8 g. of sodium carbonate (0.075 mol.) in a mixture of 30 ml. of water and 20 ml. of methanol. No color change occurred. The mixture was stirred under reflux for 2.5 hr. and cooled in ice. The precipitated crystals were filtered and recrystallized from aqueous ethanol giving 4 g. of crystals melting at 89–90°. This m.p. remained undepressed by admixture with authentic *m*-dinitrobenzene.

Attempted reaction of 3,5-dinitroaniline with sodium bicarbonate. A 1 g. (0.005 mol.) sample of 3,5-dinitroaniline (m.p. 161–162°)[9] was dissolved in 15 ml. of not methanol. A slurry of 1.3 g. (0.015 mol.) of sodium bicarbonate in a mixture of 6 ml. of water and 7 ml. of methanol was added, and the reaction was refluxed for 3 hr. On cooling, yellow crystals precipitated. These were filtered and air-dried, giving 0.9 g. of material melting at 159–161°. A mixed m.p. with 3,5-dinitroaniline was not depressed.

Acknowledgment. The author wishes to thank Dr. E. F. Ullman for his interest and helpful suggestions.

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[8] J. J. Blanksma, *Rec. trav. chim.*, **24**, 40 (1905).

[9] Prepared by the method of J. J. Blanksma and G. Verberg, *Rec. trav. chim.*, **53**, 988 (1934).

Synthesis of 2,4,5-Trichloro-Cl^{36}-phenol

Richard W. Meikle and Elinor A. Williams

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2,4,5-Trichlorophenol is a versatile compound in agricultural pest control, appearing in many products either as such, or as an integral part of some other chemical molecule. Our investigations required the use of the chlorine-36 labeled compound; since it was not available, its synthesis was undertaken.

Because we had a quantity of the compound[1] 1,2,4,5-tetrachloro-*1-*Cl^{36}-benzene, the obvious

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[1] R. W. Meikle, *J. Org. Chem.*, **24**, 277 (1959).