tassium permanganate per mole of the base had been consumed. The excess permanganate was decolorized with formic acid and the mixture heated to 75° and filtered. The acid was precipitated as the copper salt and liberated in hot water by means of hydrogen sulfide. The copper sulfide was filtered off and the filtrate yielded 32 mg. (5.4%) of white crystals which melted at 258° after recrystallization from water. A mixed melting point with an authentic sample of 2,5-pyridinedicarboxylic acid showed no depression.

Anal. Calcd. for $C_7H_5NO_4$: N, 8.39. Found: N, 8.50.

Experimental

A $C_{10}H_{15}N$ base has been isolated from California petroleum. By a series of degradation reactions it has been shown to be 2,3-dimethyl-6-isopropylpyridine.

AUSTIN 12, TEXAS RECEIVED OCTOBER 24, 1949

[CONTRIBUTION FROM THE INSTITUTE OF ORGANIC AND PHARMACEUTICAL CHEMISTRY, UNIVERSITY OF BUDAPEST, HUNGARY]

On Disalicylideneacetone and Analogs

BY PETER T. MORA[1] AND TIBOR SZÉKI

It is well known that *o*-hydroxy aromatic aldehydes will condense with acetone and other ketones to form compounds structurally related to the anthocyanidins and to the dicoumarins. It was suggested[2,3,4] that the mechanism of the condensation involves, in the case of equimolar proportions of acetone and salicylaldehyde, an unsaturated intermediate, *viz.*, *o*-hydroxystyryl methyl ketone. The condensation of salicylaldehyde and various homologs with some ketones in alkaline solution has now been studied in detail. This work is part of a program to study the anticoagulant and antibacterial activity of compounds of related structure.

Salicylaldehyde (2 moles) reacts with 1 mole of acetone and certain other ketones in the presence of sodium hydroxide furnishing the disodium salt of disalicylideneacetone (I, X = Na, X′ = Na).[5,6,7] Under acidic conditions or when the above disodium salt is subsequently treated with dilute acids, colored substituted benzopyrylium salts (II) are formed and these have been isolated as the chloride,[2,7,8] sulfate[7] and perchlorate.[8] Treatment of the disodium salt (I, X = Na, X′ = Na) with carbon dioxide resulted in the elimination of the sodium as sodium carbonate and a phenolic compound was obtained which was assumed formerly to have the structure I (X = H, X′ = H), *i.e.*, 2,2′-dihydroxydistyryl ketone. Dehydration of this compound or of the benzopyrylium salts (II) derived from it, yielded the same diphenospiropyran (IV)[7,9] the structure of which is known. Whilst the literature[5,7,10,11] describes the free phenolic disalicylideneacetone as 2,2′-dihydroxydistyryl ketone (I, X = H, X′ = H) there is some evidence in analogous cases[3,8,10] that ring closure to a 2-chromenol of the type III structure can occur, the resulting compound being a monophenol. The same or a similar substance is formed also by neutralization of the corresponding benzopyrylium derivatives (II).

Methylation of this free phenolic disalicylideneacetone with methyl iodide resulted in the formation of a dimethyl ether (I, X = CH_3, X′ = CH_3), *i.e.*, the ring, if present, had been opened. Similarly, attempts to acetylate, benzoylate or to form an oxime from the initial phenolic substance resulted in the "open" form, giving a diacetate and a dibenzoate (I, X = Ac, X′ = Ac; X = Bz, X′ = Bz) and an oxime.

On the other hand, methylation with diazomethane produced a sirupy monomethyl ether which when treated with sodium hydroxide, yielded a crystalline monosodium salt (I, X = Na, X′ = CH_3). Also, the initial monomethyl ether could be converted into crystalline monobenzoyl and mono-*p*-nitrobenzoyl derivatives.

This result shows that there is some difference in the reactivity of the two hydroxyl groups in the molecule. Because the carbonyl group is located in any reasonable molecular model close to one of the hydroxyl group, this difference can be interpreted as a result of some interaction between these two groups. However, the methods employed are not capable of giving an unequivocal solution in the problem of selecting a simple structure for this tautomeric substance.

The disodium salt of I treated with carbon dioxide under controlled conditions afforded a crystalline monosodium salt. Methylation of the latter with methyl iodide resulted in the same monosodium salt monomethyl ether (I, X = Na, X′ = CH_3) as was obtained from diazomethane methylation of III and it yielded the same benzoyl or *p*-nitrobenzoyl derivatives.

It was found that fusion above the m. p. or distillation *in vacuo* of the free disalicylidene-

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(5) Fabinyi, *Chem. Centr.*, **71**, II, 301 (1900); German Patent 110,-520.
(6) Borsche and Geyer, *Ann.*, **393**, 29 (1912).
(7) Decker and Felser, *Ber.*, **41**, 2997 (1908).
(8) Buck and Heilbron, *J. Chem. Soc.*, 1198 (1922).
(9) Dilthey, Berres, Holterhoff and Wubken, *J. prakt. Chem.*, **114**, 179 (1926).
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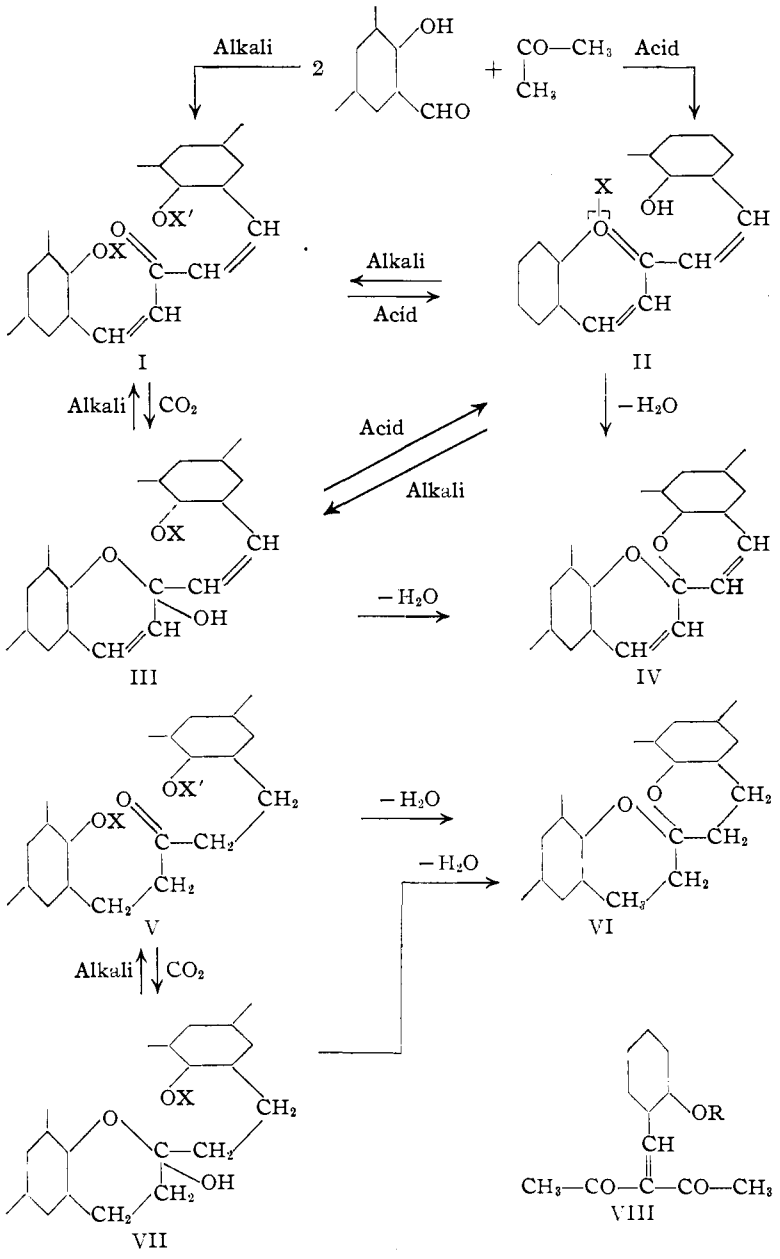
(11) Fabinyi and Széki, *Ber.*, **40**, 3455 (1907).

Fig. 1.



acetone (III, X = H) resulted in the formation of diphenospiropyran (IV) identical with the material obtained from the pyrylium chloride (II) by Decker and Felser.[7]

Hydrogenation of the disodium salt of I at room temperature with palladium–charcoal introduced four atoms of hydrogen into the molecule giving a saturated compound (VII, X = H) which was separated after neutralization with carbon dioxide. Hydrogenation of the sodium-free disalicylideneacetone was attempted by Borsche,[12] who obtained the saturated spiropyran (VI). This is attributed to the fact that Borsche distilled the product of his reaction and it has now been demonstrated that distillation suffices to bring about ring closure to a spiropyran. Under non-alkaline conditions the saturated spiropyran (VI) was formed with great ease even in attempts to form derivatives of VII, *e.g.*, acetate or oxime, which involve the elimination of water. Benzoylation of tetrahydrodisalicylideneacetone (VII, X = H) under alkaline conditions, however, gave a dibenzoate (V, X = Bz, X′ = Bz).

The condensation of analogous aldehydes, 3-nitrosalicylaldehyde and 5-nitrosalicylaldehyde with acetone was investigated and in both cases the corresponding disodium salts (type I structures) and the free compounds (possibly with type III structures) were characterized. Direct nitration of disalicylideneacetone (III) yielded 6,5′-dinitro derivative (III, 6 = NO_2, 5′ = NO_2) identical with that obtained by condensation of acetone with 5-nitrosalicylaldehyde, and not the 4,4′-dinitro compound (I, 4 = NO_2, 4′ = NO_2) as previously described.[11] Further nitration of this 6,5′-dinitro compound yielded the 6,8,3′,5′-tetranitro derivative (III, 6,8,3′,5′ = NO_2) whilst nitration of tetrahydrodisalicylideneacetone (VII) was accompanied by cyclization giving 6,6′, - 8,8′ - tetranitrotetrahydrospiropyran (VI, 6,6′,8,8′ = NO_2) identical with that obtained by direct nitration of the saturated spiropyran (VI).

Similarly, condensation of *o*-vanillin with acetone resulted in the formation of the disodium salt of di-(*o*-methoxysalicylidene)-acetone, which could be converted to a free compound (III, 8 = MeO, 3′ = MeO). On hydrogenation of the disodium salt of the di-(*o*-methoxy)-compound, the tetrahydro-di-(*o*-methoxysalicylidene)-acetone (VII, 8 = MeO, 3′ = MeO) was obtained, and this was converted readily to the dimethoxytetrahydrospiropyran (VI, 8 = MeO, 8′ = MeO). Some analogous compounds were obtained starting with 5-methoxysalicylaldehyde. In each possible case the corresponding monosodium salt was isolated. The structure III type representation is preferred throughout although admittedly the

(12) Borsche, *Ber.*, **45**, 46 (1912).

TABLE I

Structure	Method of preparation: Description[e]	Method of preparation: From[d]	Yield,[b] %	Crystallized from	M. p. (uncor.), °C.	Empirical formula	Analyses, %: C or N Calcd.	C or N Found	H or Na Calcd.	H or Na Found
I, X = Na, X′ = Na	A1(a)	I, II	98	H_2O + EtOH	D.	$C_{17}H_{12}O_5Na_2 \cdot 7H_2O$				
I, X = Ac, X′ = Ac	A1(a) (i), A2[g]	1, 9[g]	92	EtOH	129	$C_{21}H_{18}O_8$	72.00	71.56	5.14	5.64
I, X = Bz, X′ = Bz	A1(b) (ii), A2[g]	1, 9[g]		EtOH	135	$C_{31}H_{22}O_5$	78.48	78.69	4.64	4.41
1, X = Me, X′ = Me	A1(b) (iii)	1		EtOH	124	$C_{19}H_{18}O_5$	76.51	76.27	7.36	7.10
1, X = Me, X′ = Na	B1, B2[g]	9, 8[g]		EtOH	D	$C_{18}H_{15}O_4Na$			7.26	7.18
1, X = Me, X′ = Bz	B1, B2[g]	9, 8[g]	15	EtOH	119–122[a]	$C_{25}H_{18}O_5$	75.52	75.22	5.20	5.51
1, X = Me, X′ = *p*-NO_2Bz	B1, B2[g]	9, 8[g]	29	EtOH	204–207[a]	$C_{25}H_{19}O_7N$			3.15	3.14
11I, X = Na	A3	1	80	H_2O + EtOH	D	$C_{17}H_{13}O_3Na$			7.98	7.89
11I, X = H	A2	1	95	EtOH	160 D[a]	$C_{17}H_{14}O_3$				
1I1, X = Me	B1, B2[g]	9, 8[g]		Syrupy						
1I1/2,[c] 8 = NO_2, 3′ = NO_2	A1(a), A2[h,f]	1, III	44	EtOH	230–232	$C_{17}H_{12}O_7N_2$	7.87	7.79		
1I1/2,[c] 6 = NO_2, 5′ = NO_2	A1(a), A2[h,f]	I, IV	48	EtOH	216–219[a]	$C_{17}H_{12}O_7N_2$	7.87	7.75		
1I1/2,[c] 8 = MeO, 3′ = MeO	A1(a), A2[h,f]	1, V	92	EtOH	179–180	$C_{19}H_{18}O_5$	70.00	69.59	5.53	5.67
1I1/2,[c] 6 = MeO, 5′ = MeO	A1(a), A2[h,f]	1, VI	93	EtOH	154	$C_{19}H_{18}O_5$	70.00	70.71	5.53	5.20
1V	A4	9	50	EtOH	106[a]	$C_{17}H_{12}O_2$				
1V, 6,6′ = NO_2; 8,8′ = NO_2	C2	9	55	$PhNO_2$	>260 D	$C_{17}H_8O_{10}N_4$	13.40	13.59		
V, X = Bz, X′ = Bz	A1(b)(ii)	22	72	EtOH	117–118	$C_{31}H_{26}O_5$	77.78	76.99	6.99	7.13
VI	A6	22	72	EtOH	108[a]	$C_{17}H_{16}O_2$				
V1, 8 = MeO, 8′ = MeO	A6	23	90	EtOH	138	$C_{19}H_{20}O_4$	73.14	72.61	6.43	6.71
V1, 6,6′ = NO_2; 8,8′ = NO_2	C4, C3[g]	18, 22[g]	64	AcOH	180–182[a]	$C_{17}H_{12}O_{10}N$	13.28	13.30		
V1I, X = Na	A3	22	36	H_2O+EtOH	D	$C_{17}H_{12}O_3Na$			7.8	7.94
V1I, X = H	A5	1	72	Benzene	89	$C_{17}H_{18}O_3$	75.55	75.29	6.66	6.94
VI1, 8 = MeO, 3′ = MeO	A5	13[f]	98	EtOH	123–123.5	$C_{19}H_{22}O_5$	69.13	68.62	6.68	7.09
V11,[c] 6 = MeO, 5′ = MeO	A5	14[f]	94	EtOH	138	$C_{17}H_{22}O_5$	69.13	68.82	6.68	6.92
	See A6	9	50	EtOH	226	$C_{17}H_{18}O_4N_2$	65.01	65.08	5.74	5.89
	See A6	13	47	EtOH	202–203	$C_{19}H_{22}O_6N_2$	60.98	60.56	5.88	6.03
V11I, R = H	A2	V11, 11[f]		Benzene	85[a]	$C_{12}H_{12}O_3$				

[a] M. p.'s and mixed m. p.'s identical with the alternatively prepared or authentic material. [b] In alternative cases the lowest. [c] III/2 indicates III, X = H; VII/2 = VII, X = H. [d] In this fourth column arabic numbers refer to the substances shown by first column of this Table; I = acetone, II = salicylaldehyde, III = 3-nitrosalicylaldehyde, IV = 5-nitrosalicylaldehyde, V = 3-methoxysalicylaldehyde, VI = 5-methoxysalicylaldehyde, VIII = acetylacetone. [e] Letters and numbers indicate appropriate subsections in the Experimental text. [f] Prepared from the corresponding disodium salt. [g] Alternatively. [h] Successively.

validity of the extension of this structure is not conclusively established. Attempts to use 4-methoxysalicylaldehyde were unsuccessful because of the instability of this substance in acidic or alkaline solution. When the aqueous alkali medium was replaced by piperidine, the condensation did not proceed as before but N,N′-salicylidene-dipiperidine was obtained.

Excess salicylaldehyde was condensed with acetylacetone and acetonylacetone, under alkaline conditions as set out before. In each case, the same disodium salt of disalicylideneacetone (I, X = Na, X′ = Na) resulted. With equimolar proportions of acetylacetone and salicylaldehyde, the compound VIII was isolated identical with that obtained by the Knoevenagel method.[13]

Experimental

A. Condensation of Salicylaldehyde and Acetone and Conversion to Free Compound

1. (a) **Formation of Disodium Salt of Disalicylideneacetone.**—Salicylaldehyde (24.4 g., 2 mole) was dissolved in ethanol (100 cc.) and acetone (6.0 g. 1 mole) and to this solution was added dropwise an aqueous solution of sodium hydroxide (16 g. in 25 cc., 4 mols.). The mixture was vigorously shaken for thirty minutes and allowed to stand at room temperature for twenty-four hours. The resulting solid was filtered rapidly and recrystallized from aqueous ethanol; 43.1 g. of the disodium salt of disalicylideneacetone was isolated. The compound was insoluble in organic solvents but soluble in water giving an intensely violet solution.

(13) Knoevenagel, *Ber.*, **37**, 4461 (1904).

(b) **Derivatives of Disodium Disalicylideneacetone.** (i) **Acetylation.**—Disodium disalicylideneacetone (4.36 g.) was suspended in acetic anhydride (40 cc.) which contained fused sodium acetate (3 g.). The mixture was refluxed for thirty minutes and poured into ice water (200 cc.). The resulting solid (2,2′-diacetoxydibenzylideneacetone) was recrystallized from ethanol; m. p. 128° (yield 3.21 g.).

Anal. Calcd. for $C_{21}H_{18}O_5$: C, 72.00; H, 5.14. Found: C, 71.56; H, 5.64.

(ii) **Benzoylation.**—Disodium disalicylideneacetone (4.36 g.) was suspended in ethanol (10 cc.) and benzyl chloride (2.8 g.) was added over a period of thirty minutes with vigorous shaking. The precipitate, in a good yield, was separated and crystallized from ethanol; m. p. 135°.

Anal. Calcd. for $C_{31}H_{22}O_5$: C, 78.48; H, 4.64. Found: C, 78.69; H, 4.41.

(iii) **Methylation.**—The disodium salt (I, X = Na, X′ = Na) (4.36 g., 0.01 mole) was suspended in ethanol (50 cc.) and methyl iodide (0.02 mole) added, and the mixture refluxed for 30 minutes. The solution was poured into ice water (200 cc.) and the precipitate recrystallized from ethanol; m. p. 124°.

Anal. Calcd. for $C_{19}H_{18}O_5$: C, 76.51; H, 7.36. Found: C, 76.27; H, 7.10.

2. **Conversion of Disodium Disalicylideneacetone to Free Compound.**—Disodium disalicylideneacetone (4.35 g.) was dissolved in water (1 l.) at room temperature and carbon dioxide was passed until the solution was completely decolorized. The resulting yellow precipitate was filtered and recrystallized from hot aqueous ethanol. The product (2.65 g.) separated as yellow needles, soluble in organic solvents but insoluble in water; m. p. 160°. The substance decomposed when heated with 10% aqueous alkali regenerating salicylaldehyde and acetone. In acid solutions, the substance yielded the well-known benzopyrylium salt.

Acetylation by the method described above, benzoylation and methylation of the substance in alkaline conditions gave crystalline derivatives identical with those obtained from the disodium salt (see Table I).

3. Formation of Monosodium Disalicylideneacetone.—Disodium disalicylideneacetone (4.36 g.) was dissolved in water (0.5 l.) and the solution was treated with carbon dioxide at 0° until the dark color turned pink. From this solution, crystals of the monosodium salt separated (yield 2.3 g.), which were recrystallized from aqueous ethanol. The product was soluble in hot water but insoluble in organic solvents. Addition of sodium hydroxide to it regenerated the starting material.

Anal. Calcd. for $C_{17}H_{13}O_3Na$: Na, 7.98. Found: Na, 7.89.

4. Formation of Diphenospiropyran. Method (a).—Free disalicylideneacetone (2.66 g. 0.01 mole) was heated above its melting point for ten minutes. The brown residual mass was mixed with water and steam distilled to remove volatile pyrolysis products. The remaining solution was extracted with ether. The etheral extract was separated, dried and evaporated. A white crystalline compound was obtained which was recrystallized from ethanol (yield 1.38 g.); m. p. 107° alone or in admixture with authentic specimen of diphenospiropyran obtained from the corresponding pyrylium chloride.[8,14]

Method (b).—The free disalicylideneacetone (2.66 g., 0.01 mole) was distilled *in vacuo* (b. p. 210–215°, at 16 mm.). The distillate (1.85 g.) was washed with ligroin and crystallized from ethanol; m. p. 106° alone or in a mixture with an authentic specimen.

5. Hydrogenation of Disodium Disalicylideneacetone.—Disodium disalicylideneacetone (10 g.) was dissolved in water (200 cc.) in the presence of palladium–charcoal (0.1) and the solution was heated to 50°. After being shaken for two hours at this temperature with hydrogen, 2 mols. had been taken up. The solution was cooled and filtered and the filtrate treated with excess carbon dioxide in order to precipitate the saturated derivative. A white solid was thus obtained which was recrystallized from benzene (yield 5.7 g.); m. p. 89°.[15]

Anal. Calcd. for $C_{17}H_{18}O_3$: C, 75.55; H, 6.6. Found: C, 75.29; H, 6.94.

6. Formation of Tetrahydrodiphenospiropyran.—The saturated compound prepared as in the previous paragraph was readily converted to tetrahydrodiphenospiropyran (VI) by the methods (a) and (b) described above in the case of the unsaturated material. Three further methods were found.

(a) The saturated compound (2.5 g.) was dissolved in acetic anhydride (20 cc.) to which was added fused sodium acetate (1.5 g.) and the mixture refluxed for thirty minutes. The resulting solution was poured into ice water and the solid (2 g.) removed and recrystallized from either ethanol–methanol or glacial acetic acid; m. p. 108° alone or in admixture with an authentic sample of tetrahydrodiphenospiropyran (VI) prepared by the method of Borsche.[12,16]

(b) The saturated material (5.9 g.) was dissolved in ethanol (20 cc.) to which was added a solution of hydroxylamine hydrochloride (2.41 g.) in ethanol (25 cc.) which was previously neutralized with the calculated amount of sodium carbonate and filtered. The mixture was refluxed for one hour, cooled, and the solid which separated (3.93 g.) was filtered and recrystallized from ethanol; m. p. 108° alone or in admixture with an authentic specimen.

(c) The saturated compound (2.5 g.) was dissolved in ethanol (30 cc.) and palladium–charcoal (0.05 g.) was added and the mixture shaken with hydrogen for thirty-six hours at a temperature 60–70°. The filtered solution was concentrated and the solid which formed (2.1 g.) was recrystallized from ethanol; m. p. 108° (alone and mixed m. p.).

(14) M. p. of diphenospiropyran is reported by Decker and Felser to be 101–102°. In our hands, the m. p. of the substance obtained by the same method was found to be 106°.

(15) Borsche[12] obtained only a sirupy product from the free disalicylideneacetone in ethanol. Repeating this, we obtained the crystalline saturated derivative.

(16) Borsche[12] by hydrogenation obtained a sirup which on distillation *in vacuo* gave material VI.

B. Evidence for a 2-Chromenol Structure (III, X = H) of the Free Disalicylideneacetone

1. Diazomethane Methylation of III.—Disalicylideneacetone (2.66 g.) was dissolved in ether (100 cc.), treated with diazomethane (0.025–0.030 mole) and allowed to stand overnight at 0°. After removal of the solvent a brown sirup was obtained which was soluble in organic solvents but insoluble in water. No crystalline material was obtained. This sirupy monomethyl ether was treated with sodium hydroxide (40 cc., 1%) at room temperature and benzoyl chloride (2.8 g.) added. After shaking for a few minutes, a solid separated which was washed and recrystallized from ethanol four times (yield 0.8 g.), m. p. 119–122° (m. p. depressed by dibenzoyl derivative of I).

Anal. Calcd. for $C_{23}H_{20}O_4$: C, 75.52; H, 5.20. Found: C, 75.22; H, 5.51.

Similarly, the methylated sirup (1.5 g.) treated with *p*-nitrobenzoyl chloride (1.85 g.) and sodium hydroxide yielded a crystalline mono-*p*-nitrobenzoate of the monomethyl ether (0.5 g.), m. p. 204–207°.

Anal. Calcd. for $C_{25}H_{19}O_7N$: N, 3.15. Found: N, 3.14.

The methylated sirup when treated with sodium hydroxide yielded a crystalline monosodium salt of the monomethyl ether (I, X = Na, X′ = CH_3).

Anal. Calcd. for $C_{18}H_{15}O_3Na$: Na, 7.26. Found: Na, 7.18.

2. Methyl Iodide Methylation of Monosodium Salt of III.—The monosodium salt of III (2.8 g.) was dissolved in ethanol (40 cc.) and methyl iodide (1.40 g.) added. After refluxing for one and one-half hours, the dark red solution had become a pale pink, and was then concentrated and the amorphous solid which separated was removed (2.5 g.). This substance was benzoylated by the method described in 1 above and the same crystalline monobenzoate monomethyl ether was obtained; m. p. 120–122° (alone or in admixture). Similarly the same *p*-nitrobenzoate was obtained as in 1 above; m. p. 205–208°. The original methylated solid, treated with sodium hydroxide, yielded a crystalline monosodium salt of the monomethyl ether (I, X = Na, X′ = CH_3).

Anal. Calcd. for $C_{18}H_{15}O_3Na$: Na, 7.26. Found: Na, 7.08.

C. Nitration of the Free Disalicylideneacetone (III)

1. 6,5′-Dinitro Derivative.—The chromenol (III, 6 g.) was dissolved in glacial acetic acid (80 cc.) and mixed with nitric acid (5 cc., 75%) diluted with four volumes of glacial acetic acid. The two solutions were mixed rapidly at 0°. After six hours at this temperature, the solution was poured into ice water, and a yellow compound separated (7.8 g., m. p., 208–214°). After recrystallization from acetone, the m. p. rose to 218–219°; mixed m. p. with a specimen of the material obtained from 5-nitrosalicylaldehyde[11] unchanged.

Anal. Calcd. for $C_{17}H_{12}O_7N_2$: N, 7.87. Found: N, 7.79.

2. 6,6′,8,8′-Tetranitro Derivative.—The chromenol (III, 5 g.) was dissolved in glacial acetic acid (75 cc.) and mixed at 0° with nitric acid (12.5 cc., d. 1.40). After six hours a crystalline solid was obtained. The flask and contents was heated at 100° for thirty minutes. On cooling, a crystalline product formed, which was recrystallized from nitrobenzene; m. p. 260° (dec.); insoluble in alkali and organic solvents.

Anal. Calcd. for $C_{17}H_8O_{10}N_4$: N, 13.40. Found: N, 13.59.

3. **Nitration of the Saturated Disalicylideneacetone (VII).**—The chromanol (VII, 1 g.) was dissolved in glacial acetic acid (20 cc.) and to it was added at 40° a solution of nitric acid (3 cc., d. 1.48) in glacial acetic acid (9 cc.). After standing for several hours at room temperature, the solution was poured into ice water (300 cc.). The resulting solid (1.7 g.) was crystallized from glacial acetic acid; m. p. 180–182°.

Anal. Calcd. for $C_{17}H_{12}O_{19}N_4$: N, 13.28. Found: N, 13.28.

4. **Nitration of Tetrahydrospiropyran (VI).**—Nitration of VI under the conditions at 40° set out above afforded a crystalline tetranitro compound, m. p. 180–182° alone or in admixture with a specimen of tetranitrotetrahydrospiropyran prepared as described above.

D. Condensation with Analogous Aldehydes

Condensations and conversions to chromenol derivatives from acetone and 3-methoxysalicylaldehyde, 5-methoxysalicylaldehyde, 3-nitrosalicylaldehyde, 5-nitrosalicylaldehyde were carried by the general methods described for salicylaldehyde and acetone. The properties of the derivatives are recorded in Table I.

E. Condensation of Salicylaldehyde with Various Ketones

1. Salicylaldehyde (3 mols) was condensed with acetylacetone (1 mol) in the presence of alkali in the same way as described for the formation of disodium disalicylideneacetone. The product in this case was also disodium disalicylideneacetone.

2. Equimolar proportions of salicylaldehyde (12.2 g.) and acetylacetone (10 g.) dissolved in ethanol (50 cc.) with sodium hydroxide (8 g. in 12 cc. water) were condensed by being shaken for thirty minutes and standing at room temperature for one day. The product was filtered rapidly and the solid recrystallized from aqueous ethanol. The red crystalline product (VIII, R = Na) was dissolved in water and treated with excess carbon dioxide until decolorization was complete. The resulting yellow precipitate was recrystallized from benzene; m. p. 85.5° (alone or mixed with an authentic specimen of salicylidene acetylacetone (VIII, R = H) prepared by the method of Knoevenagel).[14]

3. Acetonylacetone condensed with salicylaldehyde under alkaline conditions in every proportion yielded only disodium disalicylideneacetone. The method of preparation was described in A.1(a). The amount of salicylaldehyde varied from 1 mole to 3 moles. The resulting salt after conversion to the free compound by the method A.2 gave a crystalline compound, m. p. 160°. The mixed m. p. with disalicylideneacetone was unchanged.

Acknowledgment.—The authors are indebted to Dr. P. W. Kent for his advice and help in the preparation of the manuscript of this work.

Summary

1. Some evidence is given for a possible 2-chromenol structure in a model compound disalicylideneacetone.

2. Compounds, differently substituted on the phenolic hydroxyls of the model were prepared.

3. Diphenospiropyran and saturated derivatives were investigated.

4. Corresponding compounds were obtained from acetone condensed with 3-nitro- and 5-nitrosalicylaldehyde and 3-methoxy- and 5-methoxysalicylaldehyde. The condensation of acetylacetone or acetonylacetone with excess salicylaldehyde resulted in the formation of the same disodium salicylideneacetone.

PRINCETON, NEW JERSEY RECEIVED JULY 8, 1949

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

The Chemistry of Diazo Compounds. II. Evidence for a Free Radical Chain Mechanism in the Reduction of Diazonium Salts by Hypophosphorous Acid[1,2]

BY NATHAN KORNBLUM, GLENN D. COOPER[3] AND JAY E. TAYLOR

When a diazonium salt is reduced with hypophosphorous acid the diazonium group is replaced by hydrogen. Inasmuch as diazonium salts are readily obtained from aromatic primary amines, this provides a simple and effective means for replacing an aromatic primary amino group by hydrogen[4]

$$\text{Aryl-NH}_2 \xrightarrow[\text{HX}]{\text{HNO}_2} \text{Aryl-N}_2^+\,\text{X}^- \xrightarrow{\text{H}_3\text{PO}_2} \text{Aryl-H} + \text{N}_2 \quad (1)$$

Despite the widespread use of this deamination process, nothing was known about the mechanism of the second step of the above sequence when this investigation was begun.[5] As will become evident from the sequel, there now can be little doubt that the hypophosphorous acid reduction of diazonium salts is a free radical chain reaction.

After preliminary studies had shown that the hypophosphorous acid reduction of *p*-tolyldiazonium hydrogen sulfate is profoundly catalyzed[5a] by small amounts of certain oxidizing agents, among them potassium permanganate, cupric sulfate, and sodium nitrite, attention was directed to the kinetics of the uncatalyzed reaction. Although analytically pure, crystalline, *p*-tolyldiazonium hydrogen sulfate, *p*-anisyldiazonium

(1) Paper I in this series: Kornblum and Iffland, THIS JOURNAL, **71**, 2137 (1949).

(2) A portion of this paper was presented at the New York meeting of the American Chemical Society, September, 1947.

(3) X-R Fellow of the Purdue Research Foundation 1947–1949.

(4) Kornblum in Adams, "Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1944, Vol. II, pp. 277–282.

(5) Recently Alexander and Burge [THIS JOURNAL, **72**, 3100 (1950)] have found biphenyl and *p*-terphenyl among the products of the hypophosphorous acid reduction of benzenediazonium chloride and have suggested that the formation of these by-products involves free radicals.

(5a) Actually, this is an induced reaction. The distinction between catalyzed and induced reactions is not commonly made, however, and it is not invoked here.