[Contribution from the Department of Chemistry, University of Missouri]

The Effect of Nuclear Substituents on the Reactions of Styrenes. II. The Reaction of Primary and Secondary Amines With *o*- and *p*-Nitrostyrene[1]

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Various primary and secondary aliphatic amines have been observed to react readily with *o*- and *p*-nitrostyrene to give addition products. Steric factors exert a pronounced effect on the yields of adducts.

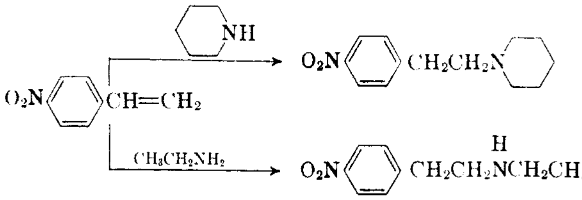
From the reactions of primary amines with *o*- and *p*-nitrostyrene, only mono-addition products resulted, with the exception of methylamine. No di-addition products were obtained from the other primary amines used, even under conditions favoring di-addition. No additions of amines could be effected to *m*-nitrostyrene under the same conditions used for successful reactions involving *o*- and *p*-nitrostyrene.

Since styrene is typically nucleophilic in its ionic reactions, the addition of amines to styrene cannot be effected without the assistance of a catalyst. Danforth[2] found sodium effective in promoting the addition of di-*n*-butylamine to styrene; a 21% yield of addition product was obtained after 50 hours at 50°. Wegler and Pieper[3] were successful in adding other amines to styrene in 10 to 81% yield, using similar conditions. The only other catalyst reported to promote this type of addition reaction between styrene and amines is an amine hydrohalide. Thus, Hickenbottom[4] obtained a mixture of both side-chain addition products and ring-substituted amines when aromatic amines were heated with styrene in the presence of aromatic amine hydrochlorides or hydrobromides. Passerini and Casini[5] observed an unusual reaction to occur between styrene and phenylhydrazine; after 9 hours at elevated temperatures, the reaction mixture yielded benzaldehyde phenylhydrazone.

Another method of promoting the addition of nucleophilic reagents to styrene is to introduce a negative group in the *ortho* or *para* position of the styrene nucleus. Thus, Hass and Bender[6] obtained 3-methyl-3-nitro-1-(*p*-nitrophenyl)butane in 72% yield from the reaction of 2-nitropropane with *p*-nitrostyrene in methanolic sodium methoxide solution. Also, Bjork and co-workers[7] observed that 2,4,6-trinitrostyrene is unreactive toward bromine in carbon tetrachloride solution but combines readily with ammonia in anhydrous ether to form bis-(2,4,6-trinitro-β-phenylethyl)-amine. Furthermore, it has been demonstrated recently[8] that various sodio enolates react readily in alcohol solution with *o*- and *p*-nitrostyrene to give Michael-type adducts, whereas no addition of enolates can be effected to *m*-nitrostyrene or to styrene itself under the same experimental conditions.

Of related interest are the reactions of β-nitrostyrene, which is also capable of uniting with amines without the assistance of catalysts. The extensive investigations, particularly those of Worrall, on the additive capacity of β-nitrostyrene and numerous derivatives are well known.[9]

In the present study, amines of both aliphatic and aromatic character and of both primary and secondary type were reacted with *o*- and *p*-nitrostyrene. The additions of aliphatic amines were accomplished with ease and in the absence of catalysts, by refluxing the amines with the nitrostyrenes in ethanol solution for a few hours. The mole ratios of the addenda to acceptors were 2:1 and 5:1 for secondary and primary amines, respectively. Even with primary amines and under conditions favoring di-addition, only mono-addition products resulted, with the exception of methylamine, *e.g.:*



In concentration experiments, the mole ratio of *n*-butylamine to *o*-nitrostyrene was varied from 5:1 to 1:3. At these extremes, the amount of mono-adduct varied from 69% to 48%, respectively, but no di-adduct was obtained. In other experiments, the mole ratio of isobutylamine to *p*-nitrostyrene was varied in the same way. The

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(1) Based on a thesis submitted by G. B. to the Graduate School of the University of Missouri in partial fulfillment of the requirements for the M.A. degree.

(2) Danforth, U. S. Patent, 2,449,644 (Sept. 21, 1948); *Chem. Abstr.*, **43**, 681 (1949).

(3) Wegler and Pieper, *Ber.*, **83**, 1 (1950).

(4) Hickenbottom, *J. Chem. Soc.*, 319 (1934).

(5) Passerini and Casini, *Gazz. chim. ital.*, **67**, 785 (1937).

(6) Hass and Bender, *J. Am. Chem. Soc.*, **71**, 3482 (1949).

(7) Bjork, Gey, Robson, and VanDolah, *J. Am. Chem. Soc.*, **75**, 1988 (1953).

(8) Dale and Strobel, *J. Am. Chem. Soc.*, **76**, 6172 (1954).

(9) (a) Worrall, *J. Am. Chem. Soc.*, **43**, 919 (1921); (b) Worrall, *J. Am. Chem. Soc.*, **49**, 1598 (1927); (c) Musante, *Gazz. chim. ital.*, **67**, 579 (1937); (d) Worrall, *J. Am. Chem. Soc.*, **60**, 2841 (1938); (e) Worrall and Benington, *J. Am. Chem. Soc.*, **60**, 2844 (1938); (f) Worrall, *J. Am. Chem. Soc.*, **60**, 2845 (1938); (g) Worrall and Finkel, *J. Am. Chem. Soc.*, **61**, 2969 (1939); (h) Hurd and Patterson, *J. Am. Chem. Soc.*, **75**, 285 (1953).

TABLE I

PRODUCTS OF THE ADDITION OF SECONDARY AMINES TO *p*-NITROSTYRENE

					Analysis			
					Calc'd		Found	
Addendum	B.p., °C.	MM.	n_D^{20}	Yield, %	C	H	C	H
Dimethylamine	142–144	1	1.5354	97	61.83	7.27	61.66	7.52
Diethylamine	136–140	1	1.5315	89	64.84	8.16	64.66	8.18
Di-*n*-propylamine	139–140	1	1.5219	64	67.17	8.86	67.02	8.75
Di-*n*-butylamine	152–157	1	1.5152	48	69.03	9.41	68.86	9.30
Diisoamylamine	130–140	1	1.5122	45	70.55	9.87	70.21	9.77
Pyrrolidine	166–173	1	1.5532	93	65.43	7.32	65.17	7.34
Piperidine	165–169	1	1.5487	95	66.64	7.74	66.41	7.95

TABLE II

PRODUCTS OF THE ADDITION OF SECONDARY AMINES TO *o*-NITROSTYRENE

					Analysis			
					Calc'd		Found	
Addendum	B.p., °C.	MM.	n_D^{20}	Yield, %	C	H	C	H
Dimethylamine	126–130	1	1.5308	89	61.83	7.27	61.70	7.50
Diethylamine	120–123	1	1.5228	64	64.84	8.16	64.72	8.19
Di-*n*-propylamine	126–127	1	1.5162	57	67.17	8.86	67.26	8.82
Di-*n*-butylamine	152–153	1	1.5100	32	69.03	9.41	68.78	9.32
Diisoamylamine	165–173	1	1.5018	31	70.55	9.87	70.82	9.94
Pyrrolidine	153–160	1	1.5481	85	65.43	7.32	65.16	7.53
Piperidine	150–155	1	1.5439	81	66.64	7.74	66.38	7.91

TABLE III

PRODUCTS OF THE ADDITION OF PRIMARY AMINES TO *p*-NITROSTYRENE

					Analysis			
					Calc'd		Found	
Addendum	M.p. or b.p., °C.	MM.	n_D^{20}	Yield, %	C	H	C	H
Methylamine	125–129	1	1.5651	25	59.98	6.71	60.19	6.63
	114–116[a,b]			7	55.81	5.51	55.73	5.42
Ethylamine	130–135	1	1.5498	86	61.83	7.27	61.96	6.93
n-Propylamine	142–143	1	1.5412	85	63.44	7.74	63.77	8.07
Isopropylamine	136–141	1	1.5360	82	63.44	7.74	63.45	7.78
n-Butylamine	141–144	1	1.5330	83	64.84	8.16	65.04	8.02
Isobutylamine	155–163	1	1.5302	82	64.84	8.16	64.79	8.11
tert-Butylamine	265–267[b]			45	55.70	7.40	55.71	7.61
Cyclohexylamine	159–163	1	1.5535	56	67.71	8.12	67.92	8.03
Benzylamine	190–195	1	1.5905	85				
	253–254[b]				61.54	5.86	61.31	5.87
	118–119[c]				73.31	5.59	73.60	5.84

[a] Di-addition product. [b] Analyzed as the hydrochloride. [c] Analyzed as the benzamide.

TABLE IV

PRODUCTS OF THE ADDITION OF PRIMARY AMINES TO *o*-NITROSTYRENE

					Analysis			
					Calc'd		Found	
Addendum	M.p. or b.p., °C.	MM.	n_D^{20}	Yield, %	C	H	C	H
Methylamine	114–117	1	1.5471	68	59.98	6.71	59.70	6.96
Ethylamine	120–123	1	1.5392	67	61.83	7.27	61.57	7.15
n-Propylamine	125–126	1	1.5339	69	63.44	7.74	63.51	7.65
Isopropylamine	130–133	1	1.5298	72	63.44	7.74	63.58	7.67
n-Butylamine	127–132	1	1.5255	69				
	157–159.5[a]				55.70	7.40	55.57	7.37
Isobutylamine	126–128	1	1.5231	71				
	188–190.5[a]				55.70	7.40	55.98	7.52
tert-Butylamine	120–122	1	1.5261	7	64.84	8.16	65.13	7.94
Cyclohexylamine	156–161	1	1.5447	65	70.29	6.29	70.42	6.52
Benzylamine	171–178	1	1.5849	75	67.71	8.12	67.88	8.36

[a] Analyzed as the hydrochloride.

yield of mono-adduct varied from 82% to 66%, but no di-adduct was isolated.

The yields and physical constants of the addition products are shown in Tables I and II for the secondary amines and in Tables III and IV for the primary amines. It is apparent that the yields of adducts are markedly dependent upon the position of the nitro group in the nitrostyrenes and also upon the steric requirements of the amines. In the reactions involving secondary amines and *p*-nitrostyrene, pyrrolidine, piperidine, and dimethylamine all gave yields of greater than 90%. The diethylamine adduct was obtained in somewhat less yield (89%) than was the dimethylamine adduct (97%) and the increased bulk in di-*n*-propylamine caused a further reduction in yield (64%). However, diisopropylamine did not give any isolable amount of adduct. Similarly, the reaction of di-*n*-butylamine with *p*-nitrostyrene gave 48% of addition product, but diisobutylamine could not be caused to react with *p*-nitrostyrene. In contrast, diisoamylamine, with branching removed to the *gamma* position in the alkyl groups, reacted with *p*-nitrostyrene to give a 45% yield of adduct. These bulk effects probably do not involve steric interaction between the amines and the *ortho*-nitro group, since the site of the reaction is the *beta* carbon of the vinyl group. They are most likely simple frontal effects between the *beta* carbon of the styrene and the amines.

The results of the reactions with secondary amines and *o*-nitrostyrene were very similar except that the yields with the same amines were all slightly lower (by 8 to 25%) than from the corresponding *p*-nitrostyrene reactions. Again, diisopropylamine and diisobutylamine, with branching close to the nitrogen, failed to react with *o*-nitrostyrene but diisoamylamine gave the expected adduct with *o*-nitrostyrene in 31% yield.

Under the conditions employed in these reactions, neither methylaniline nor ethylaniline was observed to unite with either *o*- or *p*-nitrostyrene.

As in the case of the secondary amines, the yields of adducts with primary amines were generally lower when *o*-nitrostyrene was used instead of the *para*-isomer. Under the conditions employed, cyclohexylamine was anomalous in its behavior and gave a slightly higher yield with *o*-nitrostyrene than it did with the *para*-isomer. However, the adduct of cyclohexylamine with *p*-nitrostyrene was difficult to distill without decomposition.

It is apparent that in the case of primary amines, a single branching in the alkyl group does not affect the yield greatly. Thus, the addition of ethylamine, *n*-propylamine, isopropylamine, *n*-butylamine, isobutylamine, and benzylamine all gave yields of approximately 85% with *p*-nitrostyrene. These same amines with *o*-nitrostyrene gave yields which were in the range of 67 to 75%. However, *tert*-butylamine, with double branching near the nitrogen, gave significantly lower yields with both *o*- and *p*-nitrostyrene.

Aromatic primary amines were investigated in this study, but even with *p*-anisidine, no isolable amount of addition product was obtained.

EXPERIMENTAL

All melting points and boiling points are uncorrected.

o-, m-, and p-Nitrostyrene. The three *ring*-nitrostyrenes were prepared as described earlier.[8] The *o*-nitrostyrene prepared by this method contains approximately 8% of the *para* isomer. It was found that the reaction time for the nitration of β-phenylethyl bromide could be shortened by the addition of small pieces of Dry Ice to the reaction mixture during the addition of both fuming nitric acid and the β-phenylethyl bromide. The presence of Dry Ice made it possible to maintain the temperature requirements more easily, and thus reduce the entire reaction time to 45 minutes. The yields of the nitrobromides were very similar to those obtained with the slower method of nitration.

Reaction of amines with nitrostyrenes. The reactions of the amines with the nitrostyrenes were all performed by very similar methods. The following procedures are typical of the entire series they represent. The mole ratios of the amines to the acceptors were 2:1 and 5:1 for secondary and primary amines, respectively. Absolute ethanol (30 ml.) was also present in each reaction. Reactions using dimethylamine were conducted in sealed tubes. Reactions involving ethylamine and methylamine were performed using a specially cooled condenser.

Reaction of p-nitrostyrene with diethylamine. To 30 ml. of absolute ethanol were added 7.5 g. (0.05 mole) of *p*-nitrostyrene, 7.3 g. (0.10 mole) of diethylamine, and a few milligrams of hydroquinone. The resulting solution was refluxed for 10 hours and then was allowed to remain overnight at room temperature. The solution was poured into a separatory-funnel containing 500 ml. of water and the oil which separated was extracted with ether. The ether solution was dried over sodium sulfate and the ether was removed from the dry extract by distillation. The residual oil was fractionated using a modified Claisen flask. There was obtained 9.9 g. (89%) of a red oil, b.p. 143–148° (1 mm.); n_D^{20} 1.5315.

Anal. Calc'd for $C_{12}H_{18}N_2O_2$: C, 64.84; H, 8.16. Found: C, 64.66; H, 8.18.

Reaction of o-nitrostyrene with dimethylamine. Into a Carius tube were placed 30 ml. of absolute ethanol, 7.5 g. (0.05 mole) of *o*-nitrostyrene, 4.5 g. (0.10 mole) of dimethylamine, and a few milligrams of hydroquinone. The tube, after sealing, was heated for 10 hours at 80°. The reaction product, when isolated as described above for the reaction of *p*-nitrostyrene with diethylamine, yielded 8.6 g. (89%) of a red oil, b.p. 126–130° (1 mm.); n_D^{20} 1.5308.

Anal. Calc'd for $C_{10}H_{14}N_2O_2$: C, 61.83; H, 7.27. Found: C, 61.70; H, 7.50.

Reaction of p-nitrostyrene with ethylamine. Into a 100 ml. round-bottomed flask equipped with a bulb condenser sealed with a rubber balloon and through which was circulated cold acetone from a Dry Ice-acetone bath, were placed 30 ml. of absolute ethanol, 15 g. (0.10 mole) of *p*-nitrostyrene, 22.5 g. (0.50 mole) of ethylamine, and a few milligrams of hydroquinone. The resulting solution was refluxed for 10 hours and then was allowed to remain overnight at room temperature. The ethanol and excess amine were removed by distillation and the residual oil was fractionated. There was obtained 16.6 g. (86%) of a yellow oil, b. p. 130–135° (1 mm.); n_D^{20} 1.5498.

Anal. Calc'd for $C_{10}H_{14}N_2O_2$: C, 61.83; H, 7.27. Found: C, 61.96; H, 6.93.

Reaction of p-nitrostyrene with methylamine. Absolute ethanol (30 ml.), 15 g. (0.10 mole) of *p*-nitrostyrene, 15.5 g. (0.50 mole) of methylamine (generated from its hydrochloride), and a few milligrams of hydroquinone were heated at reflux temperature for 10 hours. An acetone-cooled condenser was used, as above. The cooled reaction mixture was allowed to remain 12 hours at room temperature, during which time 0.7 g. of dark red needles separated from the solution. The solid was removed by filtration and was recrystallized from ethanol, m.p. 260–262°. Its carbon and hydrogen content did not correspond to any simple addition product and the compound was not further characterized.

The ethanol was removed from the above filtrate by distillation and, after the residual oil had cooled, a crystalline solid separated. After several days at 5°, 1.2 g. (7%) of crude di-addition product was collected on a filter. Attempted purification by recrystallization from various solvents failed and the compound was characterized as its *hydrochloride*, m.p., 114–116°.

Anal. Calc'd for $C_{17}H_{20}ClN_3O_4$: C, 55.81; H, 5.51. Found: C, 55.73; H, 5.42.

The above filtrate was fractionated using a modified Claisen flask. There was obtained 4.7 g. (26%) of a yellow oil (mono adduct), b.p. 125–129° (1 mm.); n^{20}_{D} 1.5651.

Anal. Calc'd for $C_9H_{12}N_2O_2$: C, 59.98; H, 6.71. Found: C, 60.19; H, 6.63.

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