temperature. The nickel was separated by filtration and washed with methanol (50 ml.). The filtrate and washings were evaporated at reduced pressure, and the resulting residue was recrystallized from methanol to give 0.14 g. (41%) of **5-pregnene-3β,20β-diol diacetate** (10), m.p. 127–128°. Subsequent crops gave an additional 0.15 g. (45%) of 10 that had m.p. 127–129°. Recrystallization of the first crop from methanol gave a pure sample, m.p. 129–130°.[26] A mixture of this material with a sample of 5-pregnene-3β,20β-diol diacetate, prepared *via* sodium borohydride reduction of 3β-hydroxy-5-pregnen-20-one and acetylation, showed no depression in melting point (infrared spectra identical).

Desulfurization of 16β-Acetylthio-3β-acetoxy-5-pregnen-20-one (3). A. Lithium Aluminum Hydride Reduction.—A solution of 16β-acetylthio-3β-acetoxy-5-pregnen-20-one (3, 1.78 g., 4.12 mmoles) in dry tetrahydrofuran (20 ml.) was added over a period of 15 min. to a slurry of lithium aluminum hydride (0.50 g.) and dry tetrahydrofuran (5.0 ml.). Dry ether (75 ml.) was added and the mixture was stirred at room temperature for 21.5 hr. After the excess lithium aluminum hydride was destroyed with ethyl acetate, the mixture was poured into dilute hydrochloric acid (3 *N*, 100 ml.) and extracted with ether (three 25-ml. portions). The combined organic phase was washed with water (two 30-ml. portions), dried (magnesium sulfate), and evaporated at reduced pressure.

The residue (1.55 g., m.p. *ca.* 65–200°) was acetylated by heating with acetic anhydride (20 ml.) and pyridine (20 ml.) for 1 hr. on a steam bath. The product was precipitated with ice-water (150 ml.) and extracted from the mixture with methylene chloride (three 25-ml. portions). The methylene chloride extracts were washed with dilute hydrochloric acid (3 *N*, two 25-ml. portions), saturated sodium bicarbonate solution (two 25-ml. portions), and water (two 25-ml. portions), dried (magnesium sulfate), and evaporated at reduced pressure to an oil. The oil was dissolved in methanol and fractionally crystallized. From the head fractions was obtained 0.18 g. of **16β-acetylthio-5-pregnene-3β,20α-diol diacetate** (13): m.p. 187–188°; $[\alpha]_D$ −56° (*c* 0.78); n.m.r. (7% in CCl_4) τ 9.24 (C-18), 8.99 (C-19), 8.73 (C-21, doublet, J = 6.5 c.p.s.), 8.12 (AcO at C-20), 7.98 (AcO at C-3), 7.74 (AcS), and 4.63 (C-6).

Anal. Calcd. for $C_{27}H_{40}O_5S$: C, 68.03; H, 8.46. Found: C, 68.24; H, 8.38.

From the tail fractions was isolated 0.09 g. of **16β-acetylthio-5-pregnene-3β,20β-diol diacetate** (12): m.p. 178–179°; $[\alpha]_D$ −32° (*c* 0.87); n.m.r. (7% in CCl_4) τ 9.31 (C-18), 9.01 (C-19), 9.06 (C-21, doublet, J = 6 c.p.s.), 8.06 (AcO at C-3 and C-20), 7.73 (AcS), and 4.68 (C-6).

Anal. Calcd. for $C_{27}H_{40}O_5S$: C, 68.03; H, 8.46. Found: C, 67.85; H, 8.31.

Investigation of the mother liquors yielded an additional trace (*ca.* 3 mg.) of 13 and 0.11 g. of 12. No new material could be found.

B. Desulfurization of 16β-Acetylthio-5-pregnene-3β,20α-diol Diacetate (13).—Deactivated (by refluxing for 1 hr. in acetone) Raney nickel (0.25 teaspoon) was stirred for 16 hr. with 13 (0.09 g., 0.2 mmole) in acetone (40 ml.). Unchanged starting material, m.p. 186–188°, m.m.p. 186–188°, was isolated from the filtrate after separation of the nickel. This material was retreated for 4 hr. with deactivated Raney nickel (0.25 teaspoon) in refluxing ethanol. Isolation as above gave an oil that crystallized from aqueous methanol to give 0.01 g. of **5-pregnene-3β,20α-diol diacetate** (14), m.p. 139–142°, $[\alpha]_D$ −54° (*c* 0.43) (lit.[26] m.p. 142–143°, $[\alpha]_D$ −56°). Later crops gave material melting over a wide range.

The identity was confirmed by saponification of the above 0.01 g. to 5-pregnene-3β,20α-diol which was identical with an authentic sample (mixture melting point) provided by Dr. Mihina.

C. Desulfurization of 16β-Acetylthio-5-pregnene-3β,20β-diol Diacetate (12).—The triacetate 12 (0.25 g., 0.52 mmole) and Raney nickel (*ca.* 0.5 teaspoon) were suspended in ethanol (95%, 100 ml.) and refluxed gently with stirring for 15 hr. The nickel was separated by filtration and washed with ethanol (100 ml.). Concentration of the filtrate and then chilling afforded 0.20 g., m.p. 122–127°. After attempts to purify the sample by crystallization were unsuccessful, the 0.20 g. was chromatographed on silica gel (10.0 g.). The product (0.13 g.) eluted with a 2% (v./v.) solution of ethyl acetate and benzene was recrystallized from methanol to give 0.09 g. of **5-pregnene-3β,20β-diol diacetate**, m.p. 128–130°, identical with the authentic sample (mixture melting point and infrared spectrum).

3β-Acetoxy-5α-pregnan-20-one (8).—6β,16α-Diacetylthio-3β-acetoxy-5α-pregnan-20-one (6, 0.10 g., 0.20 mmoles) was heated under reflux in acetone (100 ml.) for 1 hr. with deactivated Raney nickel (0.5 teaspoon, refluxed 1 hr. with 100 ml. of acetone). The nickel was separated by filtration and washed with methanol (100 ml.). Evaporation of the filtrate gave *ca.* 0.09 g. of an amorphous solid. The solid was dissolved in benzene and chromatographed on silica gel (4 g.). A 2% (v./v.) solution of ethyl acetate in benzene eluted the crude product. Recrystallization from aqueous methanol and then aqueous acetone gave 0.02 g. of the 3β-acetoxy-5α-pregnan-20-one, m.p. 147–148°, m.m.p. 147–149° with an authentic sample.

Reduction of Organic Compounds by Carbon Monoxide. I. The Reductive Coupling of Aromatic Nitro Compounds[1]

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The reductive coupling of several aromatic nitro compounds to the corresponding azo derivatives was effected in the presence of carbon monoxide and catalytic quantities of iron pentacarbonyl. Azoxybenzene was isolated as an intermediate in the transformation of nitrobenzene to azobenzene. Carbon monoxide is the reductant and is oxidized to carbon dioxide in the process.

The conversion of nitrobenzene to azobenzene has been effected in numerous ways since the uses of iron and acetic acid[2] or zinc and aqueous sodium hydroxide[3] were described. The latter system has since become the method of choice for laboratory-scale syntheses. Other interesting and novel methods of producing azobenzene and its derivatives include reduction of the corresponding nitro aromatic by carbohydrates,[4,5] electrolytically produced amalgams,[6] sodium aluminum hydride,[7] silicon,[8] and carbon monoxide.[9]

Carbon monoxide has been used to effect the reduction of many inorganic compounds, but its use in reduction of organic compounds has not been widely explored. Murahashi and co-workers[10] obtained a low

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[1] Presented at the 20th Southwest Regional Meeting of the American Chemical Society, Shreveport, La., Dec. 1964.

[2] A. Noble, *Ann.*, **98**, 253 (1856).

[3] P. Alexeyeff, *Z. Chem.*, **3**, 33 (1867).

[4] Chemikalienwerk Griesheim, German Patent 225,245 (April 24, 1908); *Chem. Abstr.*, **5**, 592 (1911).

[5] N. Oponolick, *Ind. Eng. Chem.*, **27**, 1045 (1935).

[6] (a) R. B. MacMullin, *Chem. Ind.* (London), **61**, 41 (1947); (b) R. B. MacMullin, *Chem. Eng. Progr.*, **46**, 440 (1950).

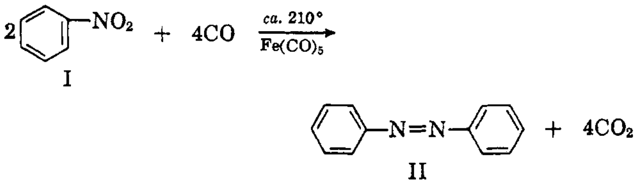
[7] A. E. Finholt, E. C. Jacobson, A. E. Ogard, and P. Thompson, *J. Am. Chem. Soc.*, **77**, 4163 (1955).

[8] R. Meier and F. Bohler, *Chem. Ber.*, **89**, 2301 (1956).

[9] G. D. Buckley and N. H. Ray, *J. Chem. Soc.*, 1154 (1949).

[10] S. Murahashi, S. Horie, and F. Jo, *Nippon Kagaku Zasshi*, **79**, 499 (1958).

yield of 1,3-diphenylurea when nitrobenzene was treated with a mixture composed of 100 atm. each of carbon monoxide and hydrogen in the presence of a catalytic amount of dicobalt octacarbonyl. Azobenzene is reportedly produced in 97.5% yield when nitrobenzene is heated at 250° under 3000 atm. of carbon monoxide.[9] We have found that carbon monoxide, initially in the presence of catalytic quantities of iron pentacarbonyl, effects the reductive coupling of nitrobenzene and certain *para*-substituted nitrobenzenes to the corresponding azobenzenes, the carbon monoxide undergoing oxidation to carbon dioxide. Anhydrous benzene served as the solvent. The use of iron pentacarbonyl allows the reaction to proceed under a carbon monoxide pressure much lower than that employed by Buckley and Ray.[9] Although ferrous oxalate effects the coupling of aromatic nitro compounds,[11] the use of finely divided iron powder[11b] and carbon monoxide allowed quantitative recovery of nitrobenzene.



Yields of azobenzene amounting to 79–80% could be obtained under optimum conditions as specified in Table I, which sets forth the gross effects of temperature, carbon monoxide pressure, reaction time, and substrate–catalyst ratio on yield. Of the two variables, temperature and carbon monoxide pressure, the former is more important, as is shown in runs 1 and 9 in Table I and by the entries in Table II.

Table I

Effect of Reaction Parameters on the Synthesis of Azobenzene from Nitrobenzene and Carbon Monoxide in the Presence of Iron Pentacarbonyl[a]

Run no.	Temp., °C.	Pressure, p.s.i.g.	Reaction time, hr.[b]	$PhNO_2/Fe(CO)_5$, mole ratio	Azobenzene yield, %[c]
1	93–102	2000–2425	3.25	10	No reaction
2	204–210	2975–3000	1.3	10	79.0
3	202–207	3100–3150	3.0	10	57.2
4	202–208	3100–3150	3.0	20	80.0
5	147–160	2700–2800	3.0	10	Trace
6	202–204	3100–3125	1.0	20	2.7
7	203–208	3075–3150	1.0	10	67.5
8	188–200	3000–3075	3.0	10	79.0
9	221–228	3300–3350	3.0	10	Black, gummy product
10	200–221	2275–2350	1.3	10	48.4
11	204–210	1575–1650	1.3	10	63.8

[a] Benzene was used as solvent; the reactor was a 1400-ml. Aminco (glass-lined) rocking autoclave. With the exception of runs 4 and 6, the reaction mixture consisted of a solution of 6.15 g. of nitrobenzene and 1.0 g. of iron pentacarbonyl in 100 ml. of benzene. Runs 4 and 6 were identical, except that 12.3 g. of nitrobenzene was used. [b] Actual rocking time at the indicated conditions. Does not include "heat-up" or cooling periods. [c] Mole % based on nitrobenzene.

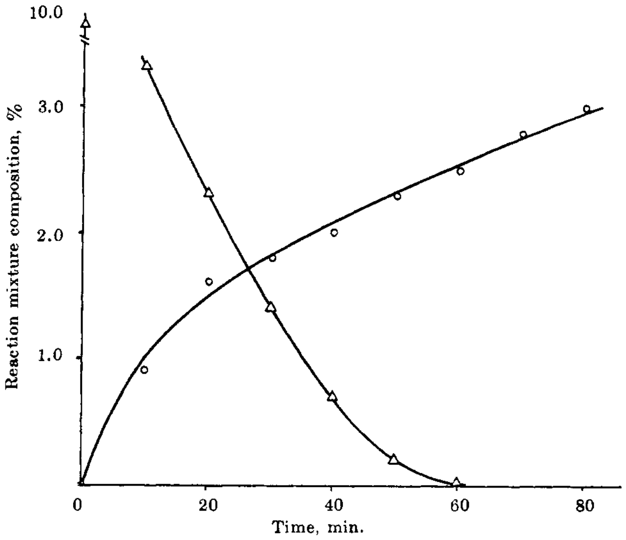


Figure 1.—Plot of the reaction mixture composition *vs.* time for the reaction of nitrobenzene with CO in the presence of $Fe(CO)_5$: nitrobenzene, △; azobenzene, ○.

Table II

Effect of Pressure and Temperature on the Carbon Monoxide–Iron Pentacarbonyl Reductive Coupling of Nitrobenzene[a]

Run	Temp., °C.	Pressure, p.s.i.g.	Azobenzene yield, %[b]
12	200–206	1100	27.4
13	198–202	1400	35.7
14	198–205	1750	35.2
15	198–202	2300	39.1
16	200	3000	35.4
17	180	3200	16.2

[a] Reaction time, 1.3 hr.; mole ratio of $PhNO_2/Fe(CO)_5$, 10; dry benzene as solvent; 300-ml. stirred autoclave. [b] Mole % based on nitrobenzene. These yields are approximately one-half those obtained when the reaction was carried out in a rocking autoclave. This decrease is apparently due to a shorter actual reaction time in the 300-ml. autoclave (water-cooled) than in the rocking autoclave (air-cooled).

The temperature effect was further demonstrated by an experiment in which samples were withdrawn from the 300-ml. autoclave at 20° intervals while the reaction mixture was heated from 20 to 200°. It was found by infrared analysis that the concentrations of nitrobenzene and iron pentacarbonyl in these samples did not vary and that a trace of azobenzene was present only in the two samples taken after the temperature reached 180°.

The reaction was followed by taking samples at 10-min. intervals during an 80-min. run at 200°. Infrared analysis of these samples showed that the formation of azobenzene was continuing after 80 min. but that nitrobenzene was absent from the reaction mixture after *ca.* 60 min.; iron pentacarbonyl was absent after *ca.* 25 min. These observations, shown graphically in Figure 1 for a run at 200°, 3000-p.s.i.g. CO pressure, revealed the presence of a relatively long-lived intermediate. The infrared analyses which furnished the plot shown in Figure 1 also revealed the presence of a component having sharp absorption bands at 1440 and 765 cm.$^{-1}$. Figure 2 is a plot of the intensity of the 1440-cm.$^{-1}$ band *vs.* time and clearly shows a buildup followed by a decrease in concentration of the material responsible for this band. It

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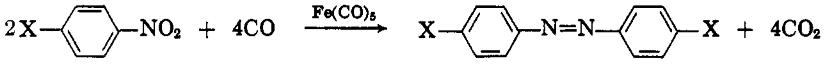
[11] (a) R. A. Abramovitch and B. A. Davis, *Chem. Rev.*, **64**, 149 (1964), and references cited therein. (b) Electrolytic iron powder, Fisher 1-62.

TABLE III

THE SYNTHESIS OF 4,4′-DISUBSTITUTED AZOBENZENES FROM *para*-SUBSTITUTED NITROBENZENES, CARBON MONOXIDE, AND IRON PENTACARBONYL[a]



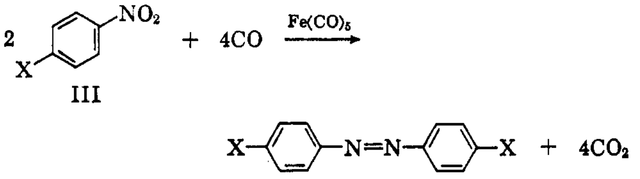
Run no.	X	Temp., °C.	Pressure, p.s.i.g.	Azo compound: Yield, %[b]	Azo compound: M.p., °C. (obsd.)[c]	Azo compound: M.p., °C. (lit.)	Nitrogen, %: Calcd.	Nitrogen, %: Found
2	H	204–210	2975–3000	79.0	67–68	68[d]	15.38	15.44
18	F	204	3000	18.1	87–89	101[e]	12.83	12.79
19	Cl	199–207	3100–3150	55.1	186–188	186[f]	11.16	11.19
20	Br	204–207	3100–3175	56.1	202–203	204–205[g]	8.23	8.19
21	I	201–203	2950	32.5	232–240	237–238[h]	6.46	6.38
22	CH_3	200–215	3250–3350	45.1	144–145	144[g]	13.32	13.11
23	OCH_3	193–204	3100–3200	44.2	160.5–161.9	162[h]	11.57	11.57
24[i]	OH	202–204	3050–3075	. . .	. . .	. . .	. . .	. . .
25	NH_2	197–205	2775	28.2	246–249	248–249[j]	26.40	26.48
26	$CO_2C_2H_5$	200–205	2850	Low	. . .	145.5[k]	. . .	. . .
27[l]	NCO	202–204	3175–3200	0	. . .	. . .	. . .	. . .
28	CN	202–204	3050–3075	0	. . .	. . .	. . .	. . .
29	$COCH_3$	199–204	2950–3000	Low	. . .	. . .	. . .	. . .

[a] Reaction time, 1.3 hr.; molar ratio of $RNO_2/Fe(CO)_5$, 10; solvent, 150 ml. of dry benzene. [b] Mole % based on nitro compound. [c] Melting points are corrected and refer to the analytical sample. [d] W. Tadros, M. S. Ishak, and E. Bassili, *J. Chem. Soc.*, 627 (1959). [e] T. Lichtenberger and R. Thermet, *Bull. soc. chim. France*, 318 (1951). [f] G. B. Barlin, K. H. Pausacker and N. V. Riggs, *J. Chem. Soc.*, 3122 (1954). [g] S. M. Mehta and M. V. Vakilwala, *J. Am. Chem. Soc.*, **74**, 563 (1952). [h] G. M. K. Hughes and B. C. Saunders, *J. Chem. Soc.*, 4630 (1954). [i] Most of starting material recovered. [j] K. Veno and S. Akiyoshi, *J. Am. Chem. Soc.*, **76**, 3667 (1954). [k] D. Vorlander and F. Meyer, *Ann.*, **320**, 122 (1902). [l] Isocyanate function destroyed by reaction conditions.

reaches a maximum after about 40-min. run time, the point at which the rate of nitrobenzene decrease begins to taper off (compare Figures 1 and 2). Thus, the absorbances at 1440 and 765 cm.$^{-1}$ were assigned to the intermediate in the nitrobenzene → azobenzene transformation.

A number of substances are known to be produced as intermediates in the reduction of nitrobenzene by systems such as zinc and aqueous sodium hydroxide. Haber[12] studied the products formed as intermediates in the electrolytic reduction of nitrobenzene. Among the established reaction intermediates are nitrosobenzene and azoxybenzene. Such compounds, therefore, seemed likely to intervene in the carbon monoxide reduction of nitrobenzene. Azoxybenzene was isolated from the reaction mixture when a reaction which had been proceeding under optimum conditions was quenched by cooling after 1 hr. at 200°. The reduction of azoxybenzene at 204–216° under a CO pressure of *ca.* 2900 p.s.i.g. proceeded smoothly to produce azobenzene in 78.5% yield.[13] The crude reaction mixture contained only a small amount of black solid by-product in contrast to the larger quantities of such materials obtained when the starting materials were nitro compounds. This observation indicates that the tarry by-products obtained from nitro compounds derived from a species intermediates in the nitro → azoxy transformation.

An obvious extension of this reaction was the synthesis of azobenzene derivatives from substituted nitrobenzenes. We chose to study *para*-substituted nitrobenzenes because it was thought that this would give insight into the electronic requirements of the reaction and because several starting materials were readily available. Accordingly, the reductive coupling was extended to *para*-substituted nitrobenzenes in which the substituents were F, Cl, Br, I, CH_3, OCH_3, OH, NH_2, $CO_2C_2H_5$, N=C=O, CN, and $COCH_3$ (acetyl). Results of these runs are shown in Table III.



III

IV

X = substituent

The data presented in Table III show the striking influence that the *para* substituent exercises on the facility with which reductive coupling occurs. Generally, one may safely conclude that substituents which are considered *ortho–para* directing in electrophilic aromatic substitution reactions allow the coupling of nitro functions to occur, although the yields are lower than those obtained from nitrobenzene itself. When the *para* substituent is one which is considered *meta* directing in electrophilic aromatic substitution, the corresponding 4,4′-disubstituted azobenzene could not be obtained in pure form. While, with *meta*-directing substituents, we believe that the coupling reaction occurred to a minor extent, yields are not shown in Table III because of difficulties encountered in isolation and purification of the desired azobenzene derivative. The results obtained with *p*-nitrobenzonitrile (Table III, run 28) may be cited as an example of typical difficulties encountered. No evidence was obtained for the presence of 4,4′-dicyanoazobenzene in the product mixture. The product was a brick red powder, m.p. 228–290°, which was practically insoluble in several solvents used in attempted recrystallizations. Infrared analysis indicated the red powder to be a mixture of *p*-nitrobenzonitrile and *p*-aminobenzonitrile (VII). Mass spectrometry revealed the presence of a large amount of starting material and traces of *p*-

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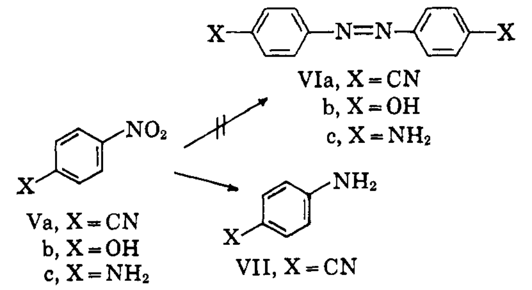
(12) F. Haber, *Z. Elektrochem.*, **4**, 506 (1898).

(13) The reaction of N-oxides of pyridine and its derivatives with metal carbonyls has been studied extensively by Hieber and co-workers; see, for example, W. Hieber and A. Lipp, *Chem. Ber.*, **92**, 2085 (1959).



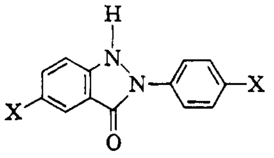
VIa, X = CN
b, X = OH
c, X = NH$_2$

Va, X = CN
b, X = OH
c, X = NH$_2$

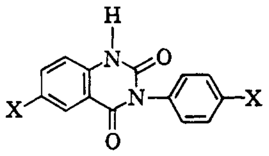
VII, X = CN

aminobenzonitrile. Both methods of analysis confirmed the virtual absence of the desired 4,4′-dicyanoazobenzene (VIa).

Run 24, using *p*-nitrophenol (Vb) as starting material, furnished no evidence for the formation of 4,4′-dihydroxyazobenzene (VIb). Most of the starting material was recovered accompanied by a small amount of black, unidentified organic material. The failure in obtaining the desired dihydroxy compound may be attributable to the acidity of the nitrophenol. Run 25, in which *p*-nitroaniline (Vc) was the starting material, gave a much lower yield of 4,4′-diaminoazobenzene than might be expected *a priori* considering the powerful activating effect of the amino function. The low yield was partially due to the formation of an appreciable amount of white, crystalline by-product which behaved as though it were a mixture of 2-(*p*-aminophenyl)-5-aminoindazolone (VIIIa) and 2,4-dioxo-3-(*p*-aminophenyl)-6-amino-1,2,3,4-tetrahydroquinazoline (IXa). Small amounts of by-products thought to be VIIIb and IXb were obtained when the starting material was *p*-nitrotoluene.[14] Such compounds have been synthesized by the reaction of azobenzene and its derivatives with carbon monoxide[10,15,16] and there is no reason to assume that a portion of the azo compound produced by the reactions described in this paper would not undergo a secondary reaction with carbon monoxide.



VIIIa, X = NH$_2$
b, X = CH$_3$



IXa, X = NH$_2$
b, X = CH$_3$

Application of the coupling reaction to dinitro compounds presumed capable of undergoing intramolecular ring closure was successful in the case of 2,2′-dinitrobiphenyl (X). This compound gave a 15.5% yield of crude benzo[*c*]cinnoline (XI), which was difficult to obtain in a pure state by recrystallization because of the presence of a small amount of amino compound which derived from reduction of the nitro function.

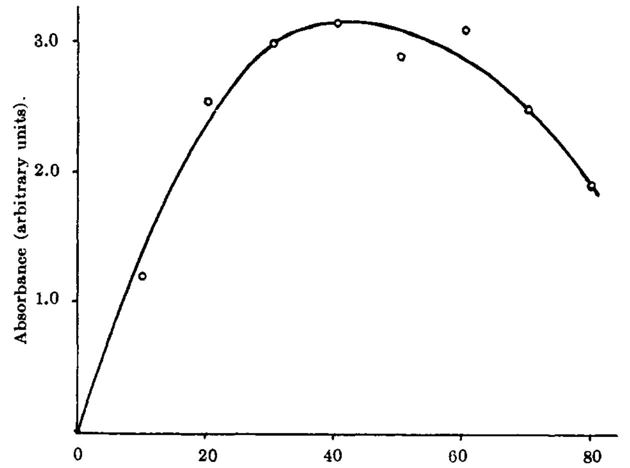
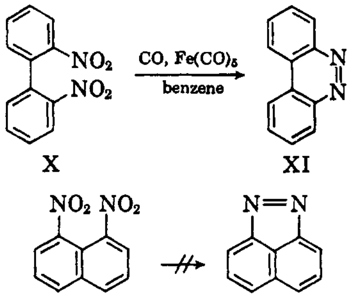


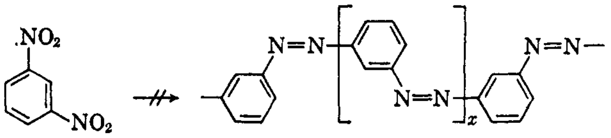
Figure 2.—Absorbance at 1440 cm.$^{-1}$ *vs.* time for the intermediate in reaction of nitrobenzene with CO in the presence of Fe(CO)$_5$.



X XI

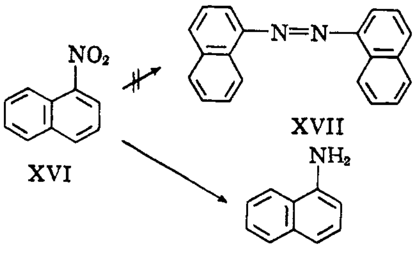
XII XIII

A considerable amount of intractable tar accompanied XI. Neither the attempted conversion of 1,8-dinitronaphthalene (XII) to benz[*c,d*]indazole (XIII) nor the conversion of *m*-dinitrobenzene (XIV) to a polyazo polymer (XV) were successful. Black, amorphous, tarry materials were obtained in both instances. Infrared analyses of the products from these reactions indicated the presence of large quantities of amines.



XIV XV

When the reaction was attempted with 1-nitronaphthalene, the sole isolable product (by vacuum sublimation) was 1-aminonaphthalene. Again, the majority of the starting material decomposed to a black, viscous tar.



XVI XVII XVIII

We are not presently in a position to propose, with any certainty, a reasonable mechanism for this re-

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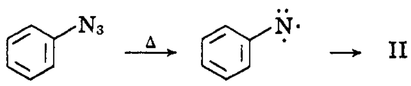
[14] A referee suggested that low yields from the *para*-substituted nitrobenzenes could, to some extent, have been due to displacement reactions at the *para* substituent by carbon monoxide. No attempt was made to establish the presence of such by-products in our crude reaction mixtures.

[15] (a) S. Horie and S. Murahashi, *Bull. Chem. Soc. Japan*, **33**, 88 (1960); (b) S. Murahashi and S. Horie, *J. Am. Chem. Soc.*, **78**, 4816 (1956); (c) S. Murahashi and S. Horie (Sunitomo Chemical Co., Ltd.), U. S. Patent 2,944,056 (July 5, 1960); (d) S. Murahashi and S. Horie, Japanese Patent 9133 (Oct. 14, 1958); (e) S. Murahashi and S. Horie, Japanese Patent 3366 (May 7, 1959); (f) S. Horie, *Nippon Kagaku Zasshi*, **80**, 1038 (1959); (g) *ibid.*, 1040 (1959); (h) *ibid.*, 1043 (1959); (i) W. W. Prichard (Du Pont); U. S. Patent 2,769,003 (Oct. 30, 1956).

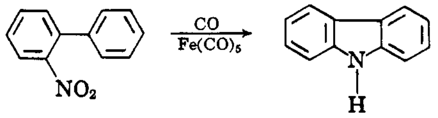
[16] C. W. Bird, *Chem. Rev.*, **62**, 283 (1962).

ductive coupling. However, the intervention of a nitrene intermediate is not an impossibility and, in fact, such a species might explain several observations in this work.

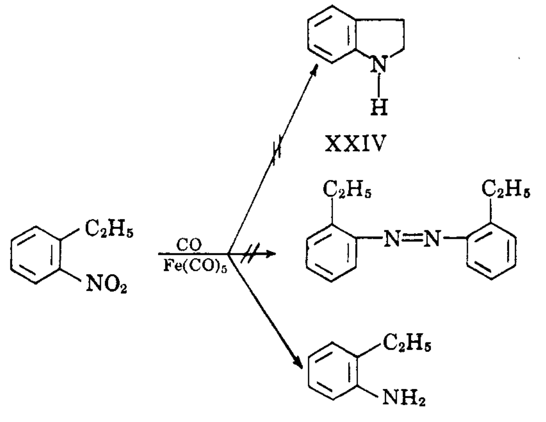
Phenylnitrene (XX) could produce azobenzene by coupling, azoxybenzene by a rapid reaction with nitrosobenzene (derived by reduction of nitrobenzene), amines by hydrogen abstraction, and polymeric tars by decomposition. Smolinsky,[17] as well as Lwowski and co-workers,[18] have presented convincing evidence for the formation of such active intermediates in the thermal decomposition of azides. Cadogan and co-workers[19] recently invoked nitrene intermediates to explain certain cyclization reactions which occur when nitro compounds are treated with triethyl phosphite. Among their findings was the formation of carbazole when 2-nitrobiphenyl was treated with triethyl phosphite.[19a]



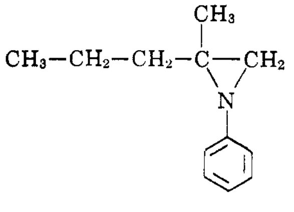
The conversion of 2-nitrobiphenyl to carbazole proceeded in the presence of carbon monoxide and iron pentacarbonyl giving a 37.5% yield of the amine. Again, a large quantity of black tarry material accompanied the desired product. The attempted conversion of *o*-nitroethylbenzene to 2,3-dihydroindole or 2,2′-diethylazobenzene was unsuccessful. The only isolable product of this reaction was *o*-ethylaniline obtained in 30% yield.



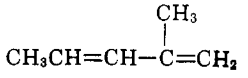
XXI XXII



Although the addition of nitrenes to olefins has not been reported, the coupling of nitrobenzene was carried out in the presence of 2-methylpentene-1 in an attempt to trap a suspected nitrene intermediate. When an anhydrous benzene solution of equimolar amounts of nitrobenzene and 2-methylpentene-1 was subjected to the action of carbon monoxide and iron pentacarbonyl under reaction conditions similar to those of run 2, Table I, the aziridine XXVII could not be isolated from the reaction mixture. This reaction produced a 30% yield of aniline; approximately half of the starting olefin was recovered but no evidence



XXVII



$CH_3CH{=}CH{-}\overset{\overset{CH_3}{|}}{C}{=}CH_2$

XXVIII

for the presence of 2-methyl-1,3-pentadiene (XXVIII) was obtained. The relatively large aniline yield caused by introduction of the aliphatic hydrocarbon might be considered as derived from phenyl nitrene abstracting hydrogen atoms more readily from an aliphatic than from an aromatic (benzene solvent) molecule. Furthermore, the absence of XXVIII indicates that hydrogen atom abstraction from 2-methylpentene-1 occurred in a random manner.

Experimental[20]

Materials.—The *para*-substituted nitrobenzenes were obtained from Distillation Products Industries, Matheson Coleman and Bell, or the Aldrich Chemical Co. and were used as received. 2-Nitrobiphenyl and 2,2′-dinitrobiphenyl were obtained from the Aldrich Chemical Co. and were recrystallized (benzene) twice before use. Azoxybenzene and 1,8-dinitronaphthalene were obtained from Chemicals Procurement Laboratories, Inc., and were recrystallized (benzene) twice before use. The benzene was Mallinckrodt thiophene-free analytical grade which was distilled from and stored over sodium. The carbon monoxide was commercial grade (98% min.) obtained from the Matheson Co.

Equipment.—All preparative reactions involving *para*-substituted nitrobenzenes were carried out in a 1400-ml., glass-lined rocking autoclave.[21] Runs shown in Table II and those concerned with isolation of the azoxybenzene intermediate formed in the coupling of nitrobenzene were conducted in an Autoclave Engineers 300-ml. stirred 316 stainless steel autoclave.

Reductive Coupling of Nitrobenzene.—A solution of 12.3 g. (0.10 mole) of nitrobenzene and 1.0 g. (0.005 mole) of iron pentacarbonyl in 100 ml. of anhydrous benzene[22] was charged to the rocking autoclave which was then sealed and flushed thoroughly with carbon monoxide. The system was pressured to 2000 p.s.i.g. with CO and the temperature was raised to 204°. After rocking the mixture at 204–219° for 3.0 hr. under a total pressure of 3350–3475 p.s.i.g., the heat and rocker were turned off and the autoclave and contents were allowed to cool overnight.

The excess gases were vented slowly through 1600 ml. of vigorously stirred 0.334 *N* barium hydroxide solution. The autoclave was flushed twice by pressuring to 300 p.s.i.g. with CO; this gas was also bubbled through the barium hydroxide solution. After this procedure the normality of the hydroxide solution (barium carbonate removed by rapid filtration) was 0.092. After substracting a blank which measured the amount of carbon dioxide in the starting carbon monoxide and in that used to flush the system after the reaction, this corresponded to the production of

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(17) (a) G. Smolinsky, *J. Am. Chem. Soc.*, **82**, 4717 (1960); (b) *ibid.*, **83**, 2489 (1961); (c) *J. Org. Chem.*, **27**, 3557 (1962); (d) *ibid.*, **26**, 4108 (1961); (e) G. Smolinsky, E. Wasserman, and W. A. Yager, *J. Am. Chem. Soc.*, **84**, 3220 (1962).

(18) (a) W. Lwowski and T. W. Mattingly, *Tetrahedron Letters*, 277 (1962); (b) W. Lwowski, T. J. Maricich, and T. W. Mattingly, Jr., *J. Am. Chem. Soc.*, **85**, 1200 (1963).

(19) (a) J. I. G. Cadogan and M. Cameron-Wood, *Proc. Chem. Soc.*, 361 (1962); (b) P. J. Bunyan and J. I. G. Cadogan, *J. Chem. Soc.*, 42 (1963); (c) J. I. G. Cadogan and R. J. G. Searle, *Chem. Ind.* (London), 1434 (1963).

(20) All melting points are corrected.

(21) American Instrument Co., Silver Spring, Md.

(22) In one instance in which the solvent was omitted, a violent detonation occurred when the temperature reached 166°. No problems were encountered when the reaction was carried out in benzene solvent.

0.184 mole of carbon dioxide in the nitrobenzene reduction (theoretical is 0.20 mole assuming 100% conversion of nitrobenzene and yield of azobenzene). The autoclave contents were removed and filtered, and the black solid on the filter was washed thoroughly with benzene. This solid, after drying, amounted to 1.2 g., contained iron, and showed a correct analysis for 56.0% carbon. The X-ray diffraction pattern of this material gave d-spacings (in order of decreasing intensity) of 4.57, 4.28, 3.33, 15.85, 5.34, and 5.40.

The combined filtrate and washings were treated twice with decolorizing charcoal and the orange solution was evaporated at 40 mm. to *ca.* 25 ml. The orange crystals which formed on cooling were removed by filtration, and the filtrate was allowed to evaporate overnight on a watch glass. The two crops of crystals were combined and after recrystallization from 95% aqueous ethanol and drying amounted to 7.0 g. (76.8%), m.p. 67–68°, undepressed on admixture with authentic azobenzene.

Isolation of Azoxybenzene.—The coupling reaction, as described above, was quenched after 1 hr. at 200° and the crude reaction mixture was freed of dark color bodies by adsorption chromatography on a 3.5 × 20 cm., 200-mesh silica gel column. Elution with benzene gave a bright orange solution containing azobenzene, the intermediate, and residual nitrobenzene. The benzene was removed by distillation and the residue was subjected to vacuum distillation to remove nitrobenzene an a second fraction, b.p. 150–160° (4 mm.), which solidified as bright orange crystals, m.p. 46–65°, and was shown, by infrared analysis, to be azobenzene containing a small amount of the intermediate (band at 1440 and 765 cm.$^{-1}$). A benzene solution of the distillation bottoms showed a very strong absorbance at 1440 and 765 cm.$^{-1}$ and the infrared spectrum of this solution was practically identical with that of a benzene solution of authentic azoxybenzene—the spectra were superimposable in the 1700–650-cm.$^{-1}$ region. Steam distillation of the bottoms gave fractions ranging in color from yellow to orange. The yellow fractions were combined and extracted with ether. Removal of the ether by distillation gave a viscous, orange-yellow residue which would not solidify at room temperature. This was dissolved in 1 ml. of methanol and the yellow solution, on cooling in ice–water, deposited yellow needles which were filtered off and air dried. The melting point of the yellow solid was 35–36°, undepressed on admixture with authentic azoxybenzene. The infrared spectra of the yellow solid and of azoxybenzene (both in benzene solution) were identical.

Anal. Calcd. for azoxybenzene, $C_{12}H_{10}N_2O$: C, 72.71; H, 5.09; N, 14.13. Found: C, 72.81; H, 5.03; N, 14.23.

Reduction of Azoxybenzene to Azobenzene.—The 1400-ml. rocking autoclave was charged with a solution of 19.8 g. (0.10 mole) of azoxybenzene and 1.0 g. (0.005 mole) of iron pentacarbonyl in 100 ml. of anhydrous benzene. After flushing the system and pressuring to 2000 p.s.i.g. with carbon monoxide, the mixture was heated at 204–216° under a total pressure of 2875–2925 p.s.i.g. for 3.0 hr. and allowed to cool overnight. The crude product was filtered to remove a small amount of black solid which was washed with hot benzene and discarded. Following the isolation procedure described for the nitrobenzene coupling, there was obtained 14.3 g. (78.5%) of azobenzene, m.p. 67–68° undepressed on admixture with authentic azobenzene.

4,4′-Disubstituted Azobenzenes.—The general procedure for the coupling of nitrobenzene was used in all cases with reaction conditions as shown in Table III. The amount of starting nitro compound was, in all instances, 0.10 or 0.20 mole. Product isolation was identical with that used in the nitrobenzene case and all products were purified by crystallization from 95% aqueous ethanol.

Intramolecular Cyclization of 2,2′-Dinitrobiphenyl.—The 1400-ml. rocking autoclave was charged with a solution of 12.2 g. (0.05 mole) of 2,2′-dinitrobiphenyl and 1.0 g. (0.005 mole) of iron pentacarbonyl in 150 ml. of dry benzene. The reactor was flushed and then pressured to 2000 p.s.i.g. with CO. While rocking, the reaction mixture was heated at 204–216° (pressure was 3325–3430 p.s.i.g.) for 3.0 hr. and allowed to cool overnight.

The reaction mixture was filtered to remove a black solid which was washed thoroughly with hot benzene and discarded. The combined washings and filtrate were evaporated to *ca.* 20 ml. and cooled to give 2.8 g. (15.5%) of yellow solid, m.p. 135–140°. Recrystallization from 50% aqueous methanol, 50% aqueous ethanol, or cyclohexane did not give a sharp melting point. The crude product was sublimed at 100–110° (2 mm.) to give a yellow crystalline sublimate, m.p. 156–157.5°.[23] The ultraviolet spectrum of the sublimate was identical with that reported for benzo[*c*]cinnoline.[24]

Anal. Calcd. for benzo[*c*]cinnoline, $C_{12}H_8N_2$: C, 79.98; H, 4.48; N, 15.57. Found: C, 79.89; H, 4.50; N, 15.63.

Conversion of 2-Nitrobiphenyl to Carbazole.—The 1400-ml. rocking autoclave was charged with a solution of 40.0 g. (0.20 mole) of 2-nitrobiphenyl and 3.9 g. (0.02 mole) of iron pentacarbonyl in 150 ml. of anhydrous benzene. The reactor was flushed and pressured to 2000 p.s.i.g. with CO. After heating the reaction mixture, while rocking, at 201–205° (pressure was 3275–3300 p.s.i.g.) for 2.0 hr., the reactor was allowed to cool overnight. The reaction mixture was filtered to remove a black-tan crystalline solid which, after washing with hot 95% aqueous ethanol, left only a small amount of black residue which was discarded. The ethanol washings and benzene filtrate were combined and evaporated to *ca.* 20 ml. The tan solid which formed on cooling in ice water was removed by filtration and after recrystallization from 95% aqueous ethanol amounted to 12.5 g. (37.5%), m.p. 246–248° undepressed on admixture with authentic carbazole. The infared spectrum of the product was identical with that of authentic carbazole.

Anal. Calcd. for carbazole, $C_{12}H_9N$: C, 86.18; H, 5.43; N, 8.38. Found: C, 85.98; H, 5.41; N, 8.30.

Attempted Synthesis of 2,3-Dihydroindole from *o*-Nitroethylbenzene.—The 1400-ml. rocking autoclave was charged with a solution of 30.2 g. (0.20 mole) of *o*-ethylnitrobenzene and 3.9 g. (0.02 mole) of iron pentacarbonyl in 150 ml. of anhydrous benzene. The system was flushed and pressured to 2000 p.s.i.g. with CO. After heating, with rocking, at 193–216° (pressure was 3225–3450 p.s.i.g.) for 2.5 hr., the reaction mixture was allowed to cool overnight. The product was filtered to remove a small amount of black solid which was discarded. Treatment of the dark filtrate with decolorizing charcoal had no visible effect. Removal of most of the benzene at *ca.* 20 mm. left a black residue which would not solidify on cooling in ice-water. After removal of the remaining benzene, distillation at 3 mm. furnished 9.2 g. (30.4%) of slightly impure *o*-ethylaniline: b.p. 60–62°, n^{20}D 1.5620, benzamide m.p. 147–148°; lit. b.p. 108° (30 mm.) and n^{20}D 1.5588,[25] benzamide m.p. 147°.[26]

Chromatography of the distillation bottoms on a 37 × 200 mm. F-20 Alcoa activated alumina column (eluted with 1:1 benzene–chloroform) resulted in no rectification of the black, tarry material.

Attempted Isolation of an Aziridine.—The rocking autoclave was charged with a solution of 12.3 g. (0.10 mole) of nitrobenzene, 8.4 g. (0.10 mole) of 2-methylpentene-1, and 2.0 g. (0.01 mole) of iron pentacarbonyl in 100 ml. of anhydrous benzene. The system was flushed and pressured to 2000 p.s.i.g. with CO. After heating, with rocking, at 202–236° (pressure was 3100–3425 p.s.i.g.) for 1.5 hr., the mixture was allowed to cool overnight.

The dark product had a strong amine-like odor and was not visibly affected by treatment with decolorizing charcoal at room temperature. Distillation at atmospheric pressure resulted in the recovery of 3.9 g. (46.5% of charge) of 2-methylpentene-1, b.p. 61–63°, followed by the benzene solvent. The last traces of benzene were removed at 40 mm. leaving *ca.* 25 ml. of dark, viscous residue. Distillation of this material in a semimicro apparatus resulted in the isolation of 2.85 g. (30.6% yield based on nitrobenzene) of aniline, b.p. 95–96° (41 mm.), n^{20}D 1.5832, benzamide m.p. 158.5–159.5°, undepressed on admixture with authentic benzanilide.

After removal of the aniline, the distillation bottoms were introduced onto a 12 × 270 mm. F-20 Alcoa activated alumina column. Elution with *n*-hexane, hexane-benzene (3:1, 1:1, 1:3), and benzene (in the order given) resulted in no separation. On evaporation of the solvents, black viscous gums that had an amine-like odor were obtained. These were not investigated further.

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Anchimeric Assistance by Benzyloxy Groups and the Effect of Configuration on an Intramolecular Displacement Reaction of the Pentitols[1]

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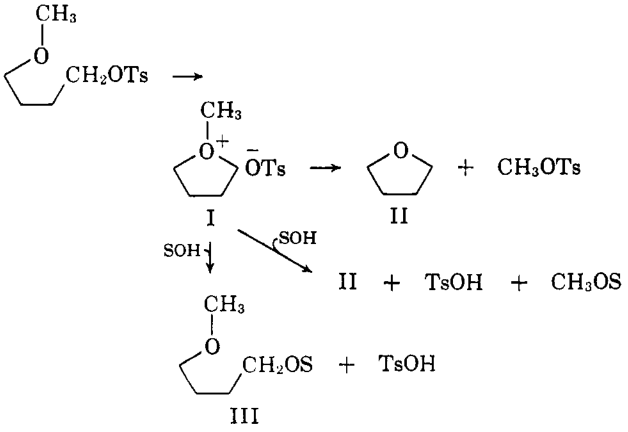
A 4-benzyloxy group renders powerful anchimeric assistance in the displacement of a 1-*p*-tolylsulfonyloxy group. The products are the corresponding tetrahydrofuran and benzyl tosylate. The rate of the reaction is greatest when the substituents on the tetrahydrofuran ring in the product are *trans*.

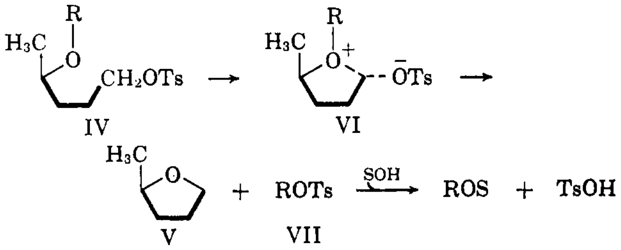
In the absence of a neighboring group capable of rendering anchimeric assistance alkyl *p*-tolylsulfonyl esters are reasonably stable under both acidic and alkaline conditions.[5] The presence of an alkoxyl group adjacent (β) to an ester function usually increases its stability[6] (by induction), although the presence of β-substituents in addition to the alkoxyl group tends to reverse the stabilizing effect[7] and it is probable that β-alkoxyl functions assist in solvolysis of arylsulfonic acid esters. The resultant of inductive and anchimeric forces is a net decrease in rate for β-alkoxyl solvolyses compared with those of unsubstituted esters.

The presence of a methoxyl group δ to an arylsulfonic acid ester increases the rate of ethanolysis of the ester by a factor of 20 at 75°[8] indicating a vigorous anchimeric assistance. The products of the displacement reaction point to the occurence of a cyclic oxonium ion intermediate (I) which can decompose in different ways[8] (Scheme I). From *n*-alkyl esters the only product is the corresponding acyclic derivative III. However, under similar conditions, 2-*o*-anisyl-2-methyl-1-propyl bromobenzenesulfonate gives a cyclic product exclusively. The cyclization appears to be due to a steric effect of the *gem*-methyl groups, since from 2-*o*-anisylethyl bromobenzenesulfonate only the acyclic solvolysis product is obtained.

SCHEME I



SCHEME II



R = $CH_2C_6H_5$

We find that 4-*O*-benzyl-1-*O*-*p*-tolylsulfonylpentanediol (IV) in ethanol at 75° is rapidly decomposed to give 2-methyltetrahydrofuran (V), *p*-toluenesulfonic acid, and benzyl ethyl ether. When the reaction is followed by intermittent titration of the acid produced, the rate constant is found to increase with time (Figure 1). This finding is reasonable if acid production is the resultant of two first-order processes in which the rate constant of one step does not differ from that of the other step by more than a factor of 100.[9] Since all of the compounds studied (see below) evinced similar behavior, and since a good fit of the experimental data could be obtained in each case if the second step was assigned a value of 6.6×10^{-3} sec.$^{-1}$, we propose that the process involves the formation of an ion pair (VI) which collapses to give 2-methyltetrahydrofuran and benzyl *p*-toluenesulfonate (VII). Solvolysis of VII, $k = 6.6 \times 10^{-3}$ sec.$^{-1}$, then yields *p*-toluenesulfonic acid and benzyl ethyl ether (Scheme II). If the reaction is carried out in ethanol–water (3:2, v./v.), benzyl alcohol is obtained rather than benzyl ethyl ether. Under the conditions used (95% ethyl alcohol at 75°) benzyl *p*-toluenesulfonate[10] has $k = (1.0 \pm 0.4) \times 10^{-2}$ sec.$^{-1}$ and gives an 80% yield of benzyl ethyl ether.

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