and 0.22 mole of potassium amide, in 500 ml. of liquid ammonia, was added during 40 min., 8.9 g. (0.04 mole) of *t*-butyl cinnamate in 100 ml. of dry ether. After 20 min., 15 g. of ammonium chloride was added and the ammonia replaced by ether. The resulting ethereal suspension was shaken with 300 ml. of water and the two layers were separated. The ethereal layer was washed with water, then extracted with saturated sodium bicarbonate solution, and washed again with water. After drying over anhydrous magnesium sulfate and filtering, the solvent was removed *in vacuo* to leave 9.8 g. of light red oil. Trituration of this oil with hexane left a small amount of suspended solid, which was removed by filtration (later text). The oil was recovered by evaporation of the hexane filtrate and dissolved in 200 ml. of 95% ethanol. Water was added dropwise to the solution to produce, initially, some red oil that was removed, and, finally, slight cloudiness. After standing several days, there was obtained a fluffy precipitate, which was removed by filtration and to give 5.6 g. (40%) of XIIc, m.p. 47–48.5° (see Table VI).

The solid that was removed from the hexane suspension mentioned earlier was recrystallized from hexane to give crystals, m.p. 114–115°, the analysis of which fitted XIII (4%).

Anal. Calcd. for $C_{31}H_{40}O_6$: C, 73.20; H, 7.93. Found: C, 73.22; H, 7.78.

The infrared spectrum of this product was essentially identical with that of XIIc (see Table VII), though the relative intensity of the β-diketone absorption compared to that of the carbonyl band was lower for the former compound.

Cleavage of Conjugate Addition Product XIIa.—A solution of 3 g. of XIIa in 60 ml. of freshly purified dioxane[15] containing 1.4 ml. of concentrated hydrochloric acid was refluxed for 4 hr. After cooling, the mixture was shaken with ether and water, and the two layers were separated. The ethereal layer was extracted with several small quantities of saturated sodium bicarbonate solution and the combined bicarbonate extract was acidified carefully with dilute hydrochloric acid. The acid solution was extracted several times with ether and the combined ethereal extract was evaporated *in vacuo*. The residue was recrystallized from ethanol–water to give 1.2 g. (72%; this yield is corrected as a large quantity of unchanged XIIa was recovered) of diketo acid XIV, 5,7-dioxo-3,7-diphenylheptanoic acid, m.p. 148.5–149°. This acid gave a bright red enol test with ethanolic ferric chloride. Its infrared spectrum showed a broad band at 3.45 μ and strong bands at 5.87 and 6.20 μ.

Anal. Calcd. for $C_{19}H_{18}O_4$: C, 73.53; H, 5.85. Found: C, 73.24; H, 5.77.

The pyrazole XV was prepared by dropwise addition of excess hydrazine to a solution of 0.2 g. of XIV in 30 ml. of 95% ethanol, the resulting solution being gently heated on the steam bath for 1 hr. After cooling, water was added, followed by dilute hydrochloric acid until the solution became cloudy. On standing, there was obtained 0.19 g. (96%) of the white crystalline product XV, m.p. 155.5–157°. It gave a negative enol test. Its infrared spectrum showed bands at 3.05 and 5.87 μ, but no absorption in the region 6.1–6.3 μ.

Anal. Calcd. for $C_{19}H_{18}O_2N_2$: C, 74.49; H, 5.92; N, 9.15. Found: C, 74.74; H, 5.88; N, 9.38.

Further cleavage of acid XIV was accomplished by heating a solution of 0.5 g. of it in 100 ml. of 0.1 *N* potassium hydroxide in 50% ethanol–water on the steam bath for 11 hr. After cooling, the mixture was shaken with ether and water, and the two layers were separated. The ethereal layer was dried over anhydrous magnesium sulfate. After filtering, most of the solvent was removed *in vacuo*. A vapor phase chromatogram of a sample of the remaining solution exhibited one peak, the retention time of which corresponded to that of authentic acetophenone. This ketone was isolated as its 2,4-dinitrophenylhydrazone (0.26 g., 54%), which, after recrystallization from ethanol–ethyl acetate, melted at 249–250° (lit.[16] m.p. 250°).

The alkaline layer containing the cleavage product (see text) was acidified and the acidic solution then extracted with ether. The solvent was removed from the ethereal extract and the residue was recrystallized from benzene to give 0.3 g. (90%) of β-phenylglutaric acid (mVI), m.p. 139.5–140.5°. This melting point was not depressed on admixture with an authentic sample of this diacid prepared as described previously.[10] The infrared spectra of the two samples of XVI were identical.

Cleavage of Conjugate Addition Product XIIb.—A solution of 0.5 g. of XIIb in 100 ml. of 50% ethanol containing 0.6 g. of potassium hydroxide was heated on the steam bath for 4 hr. After cooling, the solution was shaken with water and ether, and the two layers were separated. Most of the solvent was removed from the ethereal layer *in vacuo*. A vapor phase chromatogram on a sample of the remaining solution exhibited a peak, the retention time of which corresponded to that of *p*-methoxyacetophenone. This ketone was isolated as its 2,4-dinitrophenylhydrazone (0.28 g., 67%), m.p. 225–226° (lit.[17] m.p. 226–227°).

The alkaline layer containing cleavage product XVI (see text) was acidified with dilute hydrochloric acid and the acidic solution was then extracted with ether. The solvent was removed from the ether extract and the residue was recrystallized from benzene to give 0.28 g. (58%) of β-phenylglutaric acid (XVI), m.p. 135–138°. Its infrared spectrum was identical with that of authentic XVI.

(15) See L. F. Fieser, "Experiments in Organic Chemistry," 3rd Ed., D. C. Heath and Co., Boston, Mass., 1957, p. 284.

(16) See R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th Ed., John Wiley and Sons, Inc., New York, N. Y., p. 317.

(17) E. Buchta and G. Schaeffer, *Ann.*, **597**, 129 (1955).

The Stereochemistry of the Neber Rearrangement

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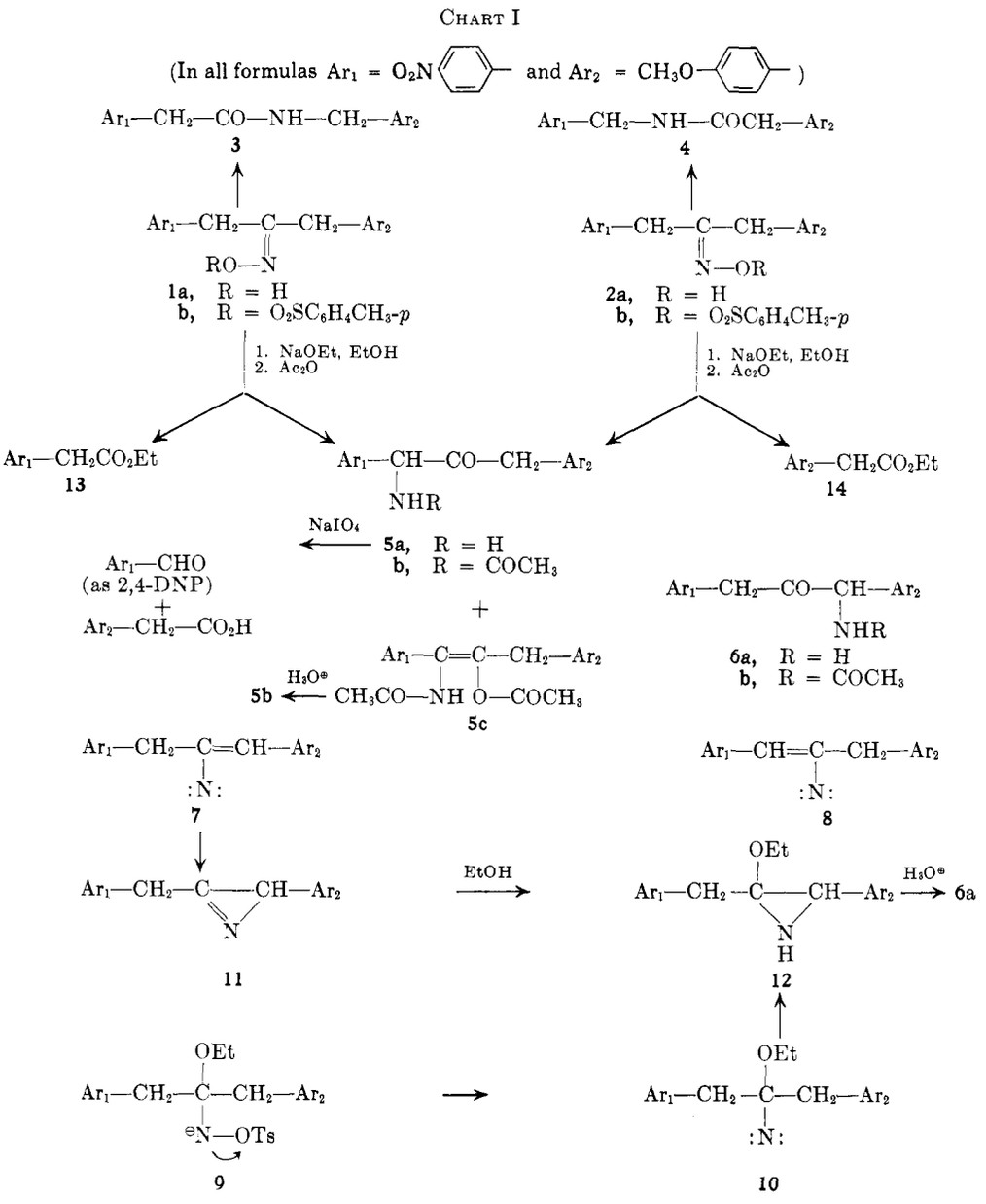
The Neber reaction with the tosyl esters of either *syn*-*p*-methoxybenzyl *p*-nitrobenzyl ketoxime or *anti*-*p*-methoxybenzyl *p*-nitrobenzyl ketoxime produced essentially the same mixture of α-amino ketones in which the major product, after acetylation, was 1-acetamido-3-*p*-methoxyphenyl-1-*p*-nitrophenyl-2-propanone. The composition of the by-product, either ethyl *p*-nitrophenylacetate or ethyl *p*-methoxyphenylacetate, from a competing Beckmann rearrangement in each of the reaction mixtures provided evidence that the two stereoisomeric oxime tosylates were not interconverted prior to the Neber rearrangement. Consequently, the major product from the Neber rearrangement is determined by the relative acidities of the α protons and not by the stereochemistry of the oxime or by the insertion of an electron-deficient nitrogen species into a C–H bond.

Previous studies of the Neber rearrangement of an oxime tosylate (*e.g.*, **1b** or **2b**) to an α-amino ketone (*e.g.*, **5a** or **6a**)[2] have not provided an unambiguous answer to the questions of what influence the stereochemistry of the oxime function and the electronic influence of substituents play in determining the structure of the product. From these studies, two general mechanistic paths appeared possible. Either the reaction is initiated by removal of an α proton followed (or accompanied) by loss of the tosyloxy group (*e.g.*, **1** → **7** or **1** →

(1) Massachusetts Institute of Technology Solar Energy Fellow, 1961–1962; Fellow of the U. S. Rubber Co. Post Graduate Foundation in Physical and Engineering Sciences, 1960–1961.

(2) (a) D. J. Cram and M. J. Hatch, *J. Am. Chem. Soc.*, **75**, 33 (1953); (b) M. J. Hatch and D. J. Cram, *ibid.*, **75**, 38 (1953); (c) H. O. House and W. F. Berkowitz, *J. Org. Chem.*, **28**, 307 (1963).

CHART I

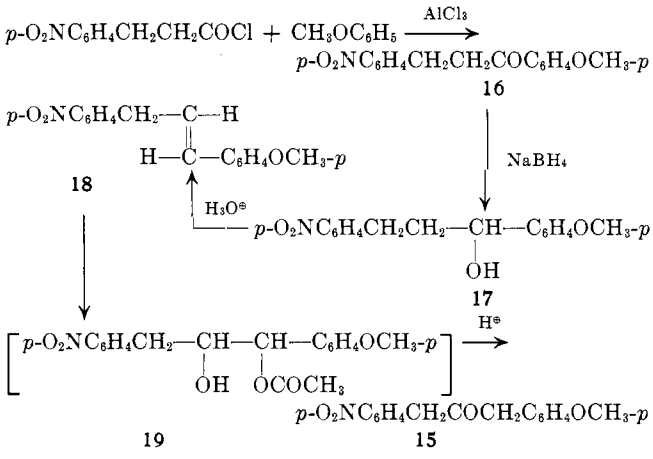


8) or the reaction proceeds by the initial addition of an alkoxide ion to the carbon–nitrogen double bond followed by loss of the tosyloxy group (*e.g.*, **1** or **2** → **9** → **10**). The further transformations of these intermediates to the reaction product are illustrated in Chart I wherein either the unsaturated nitrene **7** is converted to an azirine **11**[3a] in a process which may either be stepwise or concerted with the loss of the tosyloxy function or the saturated nitrene **10** inserts itself into an adjacent C–H bond to form the aziridine **12**.[3b] In the event that the pathway involving initial elimination (*e.g.*, *via* **7** or **8**) is followed, the further question arises whether the stereochemistry of the oxime function exerts any control over the direction (*i.e.*, *cis*, *trans*, or either) of elimination. The question arises whether the usual conditions of the Neber rearrangement (ethanolic sodium ethoxide) will rapidly equilibrate oxime tosylates by the reversible formation of intermediate **9** in which case the initial stereochemistry of the oxime tosylate becomes irrelevant.

To answer these questions, each of the stereoisomeric oxime tosylates **1b** and **2b** was prepared from the ketone **15** (see Chart II for preparation) and subjected to reaction with ethanolic sodium ethoxide (Chart I). After acetylation the major Neber product from each oxime derivative was the acetamido ketone **5b** accompanied by small amounts of the enol acetate **5c**. Although we were unable to isolate any of the pure isomeric acetamido ketone **6b** from either of these Neber rearrangements, it is possible that a small amount of this material may have been present (see Experimental). In addition, each reaction mixture contained the ester (**13** from **1b**, **14** from **2b**) corresponding to a stereospecific Beckmann rearrangement of the type previously observed[2c] when oxime tosylates are solvolyzed in ethanol or methanol. Although the reaction mixture from **1b** did contain a small amount of the ester **14**, the ester **13** was clearly the predominant Beckmann product from this reaction. From these facts one can conclude that the oxime tosylates **1b** and **2b** are not being equilibrated more rapidly than they undergo Neber rearrangement, since such an event would have led to comparable

(3) (a) G. Smolinsky, *J. Org. Chem.*, **27**, 3557 (1962); (b) D. H. R. Barton and L. R. Morgan, *J. Chem. Soc.*, 622 (1962).

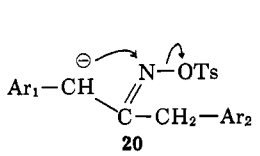
CHART II



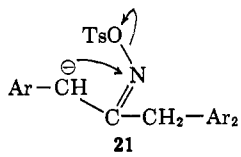
mixtures of ester **13** and **14** from either stereoisomeric oxime derivative. Consequently, the major product obtained from these Neber rearrangements (and presumably others) is not determined by the stereochemistry of the oxime function.

Our data also indicate that the saturated nitrene **10** is not an intermediate since, by analogy with the behavior of carbenes,[3b,4a] it would be expected to show little selectivity between insertion at either of the two possible benzylic positions, and, consequently, to produce comparable amounts of both Neber products **5** and **6**. Further, if any selectivity were to be observed, the predominant insertion of the electron-deficient nitrene **10** would be expected to occur at the C–H bond adjacent to the electron-donating *p*-methoxyphenyl group[4b] with the consequent formation of **12** and, subsequently, **6**, rather than the observed product **5**. Thus, the presently available data are in best agreement with a mechanism for the Neber rearrangement in which the more acidic α proton (in the present case the α proton of the *p*-nitrobenzyl group) is removed, followed or accompanied by loss of a tosyloxy group to form an unsaturated nitrene (**8** in the present case). These product-determining steps are followed by the previously discussed transformations of the unsaturated nitrene.

However, it must be noted that although the presently available data are consistent with the presence of an unsaturated nitrene intermediate (*e.g.*, **3**), they do not require the formulation of this species as a discrete intermediate. For example, the loss of the tosyloxy function and closure of the three-membered ring could be concerted processes as illustrated in structures **20**



20



21

(4) (a) J. Hine, "Physical Organic Chemistry," 2nd Ed., McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp. 484–503. (b) the question of whether the formation of an ethylenimine from a nitrene involves a true insertion reaction (with retention of stereochemistry) or a radical intermediate resulting from transfer of hydrogen atom to the nitrene (and consequent loss of stereochemical integrity) can not be answered at the present time (*cf.* ref. 3b). However, the pronounced electrophilic character of carbenes in addition to multiple bonds (ref. 4a) suggests that, even if a radical intermediate is involved, the transition state for hydrogen transfer to the nitrene will be favored by electron-donating substituents. A similar situation exists in the abstraction of hydrogen by halogen atoms. See C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, pp. 356–369, 375–376, 384.

(from **2b**) and **21** (from **1b**). Although we considered these processes unlikely, both because they involve displacements at multiple bonded atoms and because the frontside displacement **21** (from **1b**) appears particularly unfavorable, our data do not exclude this possibility.

Experimental[5]

β-(*p*-Nitrophenyl)-*p*-methoxypropiophenone (16).—A solution of crude *p*-nitrohydrocinnamoyl chloride, prepared from 58.55 g. (0.30 mole) of *p*-nitrohydrocinnamic acid[6,7] and excess thionyl chloride,[7] in 150 ml. of anisole was added, dropwise and with stirring over a 20-min. period, to a solution of 44.0 g. (0.330 mole) of aluminum chloride in 175 ml. of anisole while the reaction temperature was maintained at 30–35°. The resulting dark red solution was stirred for 1.5 hr. at room temperature and then poured into a mixture 750 ml. of 4 *N* aqueous hydrochloric acid and 600 ml. of *n*-hexane with stirring. The organic product which separated was collected and combined with the solid obtained from the organic layer. The total yield of the crude ketone **16**, m.p. 125–127°, was 70.33 g. (81%). Recrystallization from an ether–benzene mixture afforded the pure ketone **16** as pale yellow prisms, m.p. 126.3–128°, with infrared absorption[8] at 1675 cm.$^{-1}$ (conj. C=O), ultraviolet maxima[9] at 218 mμ (ε 16,800) and 279 mμ (ε 24,000), and a series of n.m.r. peaks[10] in the region 1.6–3.2 τ (8H, aryl C—H) as well as a singlet at 6.12 τ (3H, CH_3O) and two overlapping triplets ($J \sim 4$ c.p.s.) centered at 6.75 τ (4H, $ArCH_2CH_2CO$).

Anal. Calcd. for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.43; H, 5.40; N, 4.88.

1-(4-Methoxyphenyl)-3-(4-nitrophenyl)-1-propanol (17).—To a solution of 57.06 g. (0.20 mole) of the ketone **16** in 1.2 l. of methanol was added, portionwise with stirring over a 20-min. period, 15.14 g. (0.40 mole) of sodium borohydride. After the reaction mixture had been stirred for an additional 1.5 hr., it was concentrated under reduced pressure to a total volume of 300 ml. and then diluted with 900 ml. of water. The resulting mixture was extracted with ether and the ethereal extract was washed with aqueous sodium bicarbonate, dried, and concentrated to leave 52.93 g. (92%) of the crude alcohol **17**, m.p. 71–74°. Recrystallization from an ether–hexane mixture separated the pure alcohol **17** as pale yellow needles, m.p. 74.4–76°. The product has infrared absorption[8] at 3595 and 3400 cm.$^{-1}$ (unassoc. and assoc. OH) with no absorption in the 6-μ region attributable to a carbonyl function, ultraviolet maxima[9] at 221 mμ (ε 14,500), 276 mμ (ε 13,700), and 282 mμ (ε 13,300), and a series of n.m.r. peaks[10] in the region 1.6–3.3 τ (8H, aryl C—H) as well as a triplet ($J \sim 7$ c.p.s.) at 5.37 τ (1H, >CH—O), a singlet at 6.18 τ (3H, CH_3O), and complex absorption in the region 7.0–8.2 τ (5H, CH_2 and O—H).

Anal. Calcd. for $C_{16}H_{17}NO_4$: C, 66.88; H, 5.96; N, 4.88. Found: C, 66.78; H, 5.96; N, 4.88.

1-(4-Methoxyphenyl)-3-(4-nitrophenyl)-*trans*-1-propene (18).—A solution of 85 g. (0.27 mole) of the alcohol **17** and 94 mg. of anilinium *p*-toluenesulfonate in 750 ml. of benzene was refluxed for 13 hr. with continuous separation of the water which was formed. After this period of time the solution was concentrated to 450 ml. and, after the addition of 5 drops of sulfuric acid, refluxing was continued for an additional 5 hr. Since the crude product obtained from this reaction mixture still contained two major components,[11] it was chromatographed on 1.6 kg. of

(5) All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated magnesium sulfate was employed as a drying agent. The infrared spectra were determined with either a Baird Model B, or a Perkin-Elmer Model 21 infrared recording spectrophotometer fitted with a sodium chloride prism. The ultraviolet spectra were determined with a Cary recording spectrophotometer Model 14. The n.m.r. spectra were determined at 60 Mc. with a Varian Model A-60 n.m.r. spectrometer. The mass spectra were obtained with a CEC Model 21-130 mass spectrometer. The microanalyses were performed by Dr. S. M. Nagy and his associates and by the Scandinavian Microanalytical Laboratory.

(6) E. Feltenstein, *Ann. Chim.* (Paris), [13] **2**, 587 (1957).

(7) F. von Konek and E. Pascu, *Ber.*, **51**, 855 (1918).

(8) Determined in chloroform solution.

(9) Determined in 95% ethanol solution.

(10) Determined in deuteriochloroform.

(11) A thin layer chromatography plate coated with silica gel was employed for this analysis.

alumina to remove colored impurities and the fractions (65.2 g.) eluted with benzene were redissolved in 500 ml. benzene and treated with *ca.* 1 ml. of concentrated sulfuric acid. This solution was refluxed for 45 min. and then washed with aqueous sodium bicarbonate, dried, and concentrated to separate 41.49 g. (56.3%) of the crude olefin **18**, m.p. 84–91°. Further heating of the mother liquors with sulfuric acid followed by the same isolation procedure yielded an additional 7.83 g. (total yield, 49.32 g. or 66.9%) of the olefin **18**, m.p. 86–90°. Recrystallization from ether–benzene mixtures separated the pure olefin as pale yellow rectangular platelets, m.p. 89.8–90.6°, with infrared absorption[8] at 1515 and 1350 cm.$^{-1}$ (NO_2), at 1609 cm.$^{-1}$ (conj. C=C) and 968 cm.$^{-1}$ (*trans* CH=CH) and no absorption in the 3- or 6-μ regions attributable to a hydroxyl or carbonyl function. The product has an ultraviolet maximum[9] at 265 mμ (ϵ 26,600); its n.m.r. spectrum[10] has a singlet at 6.20 τ (3H, CH_3O), a doublet (J = 6 c.p.s.) at 6.39 τ (2H, CH_2), and a complex series of peaks in the region 1.6–3.9 τ (10H, vinyl and aryl C—H). Although we have formulated this olefin as **18** our data do not exclude rigorously the possibility that this product has the isomeric structure, 3-(4-methoxyphenyl)-1-(4-nitrophenyl)-*trans*-1-propene.[12] Since either of these isomeric olefins could be used in our synthesis, the question was not pursued further.

Anal. Calcd. for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.36; H, 5.48; N, 5.07.

1-(4-Methoxyphenyl)-3-(4-nitrophenyl)-2-propanone (15).—To a cold (15°) solution of 26.18 g. (0.0971 mole) of the olefin **18** in 100 ml. of acetic acid was added dropwise and with stirring over a 16-min. period, 38 g. of a solution containing 0.2 mole of peracetic acid in acetic acid. The resulting solution was stirred at 15–25° for 4 hr. and then poured into 500 ml. of aqueous sodium bisulfite and extracted with ether. After the ethereal extract had been washed successively with water and aqueous sodium bicarbonate, it was dried and concentrated to leave 27.53 g. (82%) of the crude hydroxy acetate **19** with infrared absorption[8] at 3500–3600 cm.$^{-1}$ (O—H) and at 1745 cm.$^{-1}$ (ester C=O). A solution of this material in 250 ml. of ethanol containing 40 ml. of water and 40 ml. of concentrated sulfuric acid[13] was refluxed for 5 hr. and then decanted from a small amount of insoluble material and allowed to cool whereupon the crude ketone **15** (14.11 g. or 51% based on **18**, m.p. 93–94.3°) separated. Recrystallization from an ether–benzene mixture gave the pure ketone **15** as white needles, m.p. 94–94.5°, with infrared absorption[8] at 1717 cm.$^{-1}$ (C=O), an ultraviolet maximum[9] at 275 mμ (ϵ 7,190) with a point of inflection at 220 mμ (ϵ 11,500), and a series of n.m.r. peaks[10] in the region 1.6–3.3 τ (8H, aryl CH) as well as a singlet at 6.27 τ (2H, CH_2) and two partially resolved peaks (presumably singlets) at 6.18 and 6.19 τ (5H, CH_2 and CH_3O).

Anal. Calcd. for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.32; H, 5.39; N, 4.96.

Preparation of the Oximes and Oxime Tosylates 1 and 2.—A solution of 26.09 g. (0.0915 mole) of the ketone **15**, 27.80 g. (0.40 mole) of hydroxylamine hydrochloride and 78.52 g. (0.80 mole) of anhydrous potassium acetate in 915 ml. of ethanol was refluxed for 1 hr. and then concentrated under reduced pressure. After the residue had been dissolved in a mixture of 750 ml. of water and 325 ml. of benzene, the organic layer was washed successively with water and aqueous sodium bicarbonate, dried, and concentrated. The residual crude oxime mixture (23.88 g. or 87%) was fractionally crystallized from an ether–1,2-dimethoxyethane mixture (approx. 1:3 by volume) to separate 8.90 g. (32%) of the crude oxime **1a**, m.p. 136.5–143.5°, and 5.14 g. (19%) of the crude oxime **2a**, m.p. 127–132.5°. Recrystallization from an ether–1,2-dimethoxyethane mixture afforded the pure oxime **1a** as white rectangular prisms, m.p. 141.3–143.2°, with infrared absorption[8] at 3580 and 3240 cm.$^{-1}$ (OH) and ultraviolet maxima[9] at 225 mμ (ϵ 13,900) and 277 mμ (ϵ 9880).

Anal. Calcd. for $C_{16}H_{16}N_2O_4$: C, 63.99; H, 5.37; N, 9.33. Found: C, 63.90; H, 5.44; N, 9.31.

A comparable recrystallization gave the pure oxime **2a** as white needles, m.p. 133–134.2°, with infrared absorption[8] at 3580 and 3260 (OH) and an ultraviolet maximum[9] at 275 mμ (ϵ 11,000) with a point of inflection at 220 mμ (ϵ 14,500). The infrared spectra of oximes **1a** and **2a** differ in only minor respects in the fingerprint region.

Anal. Calcd. for $C_{16}H_{16}N_2O_4$: C, 63.99; H, 5.37; N, 9.33. Found: C, 64.02; H, 5.46; N, 9.44.

To a solution of 450.5 mg. (1.50 mmoles) of the oxime **1a** in 25 ml. of ether was added, portionwise with stirring, 624.8 mg. (3.0 mmoles) of phosphorus pentachloride.[14] After the mixture had been stirred for 45 min. at room temperature, 5 ml. of water was added and stirring was continued for an additional 4.5 hr. The ether was removed and the residue was partitioned between aqueous sodium bicarbonate and chloroform. Concentration of the organic solution followed by fractional crystallization from ether–1,2-dimethoxyethane mixtures separated 54.8 mg. (12%) of the crude amide **3**, m.p. 176–180°, and 120.2 mg. (49%) of crude *p*-nitrophenylacetonitrile, m.p. 105–113°. Recrystallization of this nitrile afforded a pure sample, m.p. 114–115.1°, identified with an authentic sample by a mixture melting point determination and comparison of infrared spectra. Recrystallization afforded the pure amide **3** as white prisms, m.p. 181.2–183.1°, with infrared absorption[15] at 3260 cm.$^{-1}$ (N-H), 1640 cm.$^{-1}$ (amide C=O), and 1545 cm.$^{-1}$ (N—H bending) as well as ultraviolet maxima[9] at 222 mμ (ϵ 15,600), 275 mμ (ϵ 11,700), and 282 mμ (ϵ 10,400).

Anal. Calcd. for $C_{16}H_{16}N_2O_4$: C, 63.99; H, 5.37; N, 9.33. Found: C, 64.14; H, 5.45; N, 9.45.

A 108.4-mg. sample of the amide **3** was allowed to react with refluxing 20% aqueous hydrochloric acid for 7.75 hr. After the resulting mixture had been subjected to the usual isolation procedure, the crude acidic fraction (30.3 mg., m.p. 131–140°) was recrystallized from a hexane–ether mixture to separate 8.6 mg. (16.5% based on unrecovered amide) of pure *p*-nitrophenylacetic acid, m.p. 150.8–152.6°, identified by an authentic sample by a mixture melting point determination and comparison of infrared spectra. Thin layer chromatography[11] demonstrated the absence of *p*-methoxyphenylacetic acid in the crude acid fraction.

The same rearrangement procedure with 450.5 mg. (1.50 mmoles) of the oxime **2a**, 624.8 mg. (3.0 mmoles) of phosphorus trichloride, and 40 ml. of ether yielded 160 mg. (35.6%) of the crude amide **4**, m.p. 137–139°. Recrystallization from an ether–hexane–1,2-dimethoxyethane mixture gave the pure amide **4** as pale yellow needles, m.p. 142–143°, with infrared absorption[15] at 3260 cm.$^{-1}$ (OH), at 1645 cm.$^{-1}$ (amide C=O), and at 1550 cm.$^{-1}$ (N—H bending) with ultraviolet maxima[9] at 220 mμ (ϵ 13,900), 275 mμ (ϵ 11,800), and 283 mμ (ϵ 10,100).

Anal. Calcd. for $C_{16}H_{16}N_2O_4$: C, 63.99; H, 5.37; N, 9.33. Found: C, 63.73; H, 5.34; N, 9.48.

Hydrolysis of a 300.3-mg. sample of the amide **4** as previously described yielded 76.6 mg. (50.9% based on unrecovered amide) of *p*-methoxyphenylacetic acid, m.p. 84.8–86°, identified with an authentic sample by a mixture melting point determination and comparison of infrared spectra.

Powdered *p*-toluenesulfonyl chloride (5.910 g. or 0.031 mole) was added in small portions to a cold (0°), stirred solution of 9.010 g. (0.030 mole) of the oxime **1a** in 30 ml. of dry pyridine. The resulting mixture was stirred for 1 hr. at 0° and an additional hour at room temperature and then poured into 400 ml. of cold water. The oil which separated and subsequently solidified was washed with water and taken up in a benzene–hexane mixture. Upon cooling, 8.10 g. (59.5%) of the crude oxime tosylate **1b**, m.p. 62° dec., separated. Recrystallization of this material from an ether–hexane–1,2-dimethoxyethane mixture gave the pure oxime tosylate as either needles or rectangular prisms, m.p. 62° dec. (dependent upon time of heating). The infrared spectra[8] of the two crystalline forms were identical with no bands present in the 3- or 6-μ regions attributable to O—H, N—H, or C=O functions and peaks at 1180, 1195, and 1250 cm.$^{-1}$ (SO_2).

Anal. Calcd. for $C_{23}H_{22}N_2O_6S$: C, 60.79; H, 4.88; N, 6.16; S, 7.04. Found: C, 60.95; H, 5.02; N, 5.49; S, 6.92.

(12) The ultraviolet spectrum [λ_{max} 265 mμ (ϵ 26,600)] observed for our product does not appear to be consistent with the presence of a *p*-nitrostyrene chromophore which is reported [M. J. Kamlet and D. J. Glover, *J. Am. Chem. Soc.*, **77**, 5696 (1955)] to absorb at 300 mμ (ϵ 13,900). However, the spectrum is consistent with the presence of a *p*-methoxystyrene chromophore (as in **18**): *p*-methoxystyrene is reported [J. R. Joy and M. Orchin, *ibid.*, **81**, 305 (1959)] to exhibit a maximum at 260 mμ (ϵ 14,800) with a shoulder in the region 290–294 mμ (ϵ 2000).

(13) The procedure of C. H. DePuy and R. E. Leary, *ibid.*, **79**, 3705 (1957).

(14) This procedure was described by L. G. Donaruma and W. Z. Heldt, *Org. Reactions*, **11**, 1 (1960).

(15) Determined as a suspension in a potassium bromide pellet.

A solution of 1.1363 g. (2.5 mmoles) of this oxime tosylate **1b** and 1 ml. of water in 100 ml. of acetic acid[14] was stirred at room temperature for 38 hr. and then concentrated under reduced pressure. After a chloroform solution of the residue had been washed with aqueous sodium bicarbonate, dried, and concentrated, fractional crystallization of the residue from an ether–1,2-dimethoxyethane mixture separated 55.8 mg. (13.8%) of *p*-nitrophenylacetonitrile, m.p. 110–115° (m.p. 114–115° after recrystallization), and 114.4 mg. (15.2%) of the amide **3**, m.p. 178–181.5° (m.p. 180.5–181.5° after recrystallization). Both products were identified with previously described samples by mixture melting point determinations and comparison of infrared spectra.

A comparable preparation employing 4.0034 g. (0.021 mole) of *p*-toluenesulfonyl chloride, 6.0064 g. (0.020 mole) of the oxime **2a**, and 25 ml. of pyridine yielded 6.563 g. (72.2%) of the crude oxime tosylate **2b**, m.p. 109–110° dec. Recrystallization from an ether–hexane–1,2-dimethoxyethane mixture gave the pure oxime tosylate as white rectangular plates, m.p. 114.8–115.5° dec., with infrared absorption[8] which differed from the spectrum of the isomer **1b** only the relative intensities of certain bands in the fingerprint region.

Anal. Calcd. for $C_{23}H_{22}N_2O_4S$: C, 60.79; H, 4.88; N, 6.16; S, 7.04. Found: C, 61.11; H, 4.95; N, 6.50; S, 6.90.

Solvolysis of a 1.363-g. (2.50 mmoles) sample of this oxime tosylate **2b** in 100 ml. of acetic acid containing 1 ml. of water as previously described produced 354.1 mg. (47%) of the amide **4**, m.p. 140.8–141.5°. A recrystallized sample, m.p. 142–143°, was identified with the previously described sample by a mixture melting point determination and comparison of infrared spectra.

Neber Rearrangement of the Oxime Tosylate 1b.—To a cold (−5°), stirred suspension of 2.2726 g. (5.0 mmoles) of the tosylate **1b** in 8 ml. of ethanol was added 8.7 ml. of an ethanolic solution containing 6 mmoles of potassium ethoxide. The solution, which immediately turned a deep purple color, was stirred at −5 to 0° for 15 hr. and then filtered, and the residue was washed with ethanol. The combined alcohol filtrates were acidified with a solution of 4.756 g. (25 mmoles) of *p*-toluenesulfonic acid in 45 ml. of ether and 20 ml. of benzene, and the resulting mixture was stirred at room temperature for 30 min. and then extracted with aqueous hydrochloric acid. Concentration of the organic phase followed by appropriate manipulations separated 10.3 mg. (0.7%) of the crude amide **3**, m.p. 177.5–178.5°. Gas chromatographic analysis[16] of the residual neutral material employing ethyl *p*-tolylacetate as an internal standard indicated the presence of ethyl *p*-nitrophenylacetate (**13**, calculated yield, 14.3%) and ethyl *p*-methoxyphenyl acetate (**14**, calculated yield, 1%). Samples of each ester were collected and identified with authentic samples by comparison of infrared spectra and retention times.

The aqueous hydrochloric acid extract was concentrated under reduced pressure and the residual amine hydrochloride was acetylated by reaction with a solution of 7.94 g. (0.075 mole) of acetic anhydride in 7.91 g. (0.10 mole) of pyridine for 1 hr. at room temperature. The usual isolation procedure afforded 1.0304 g. of a crude acetamido ketone mixture, m.p. 137–143.5°. Recrystallization from benzene and subsequent chromatography of the mother liquors on silica gel separated 727 mg. (42.5%) of the acetamido ketone **5b**, m.p. 150–152°, and 87.2 mg. (5%) of the enol acetate **5c**, m.p. 154.6–157.5°. Thin layer chromatographic analysis[11] of the various intermediate fractions (total wt. 40 mg.) from column chromatography indicated the presence of **5b**, **5c**, and as mall amount of another component of similar R_f value, possibly the isomeric acetamido ketone **6b**. However, we were unable to isolate any of this third, minor component in pure form. Recrystallization from an ether–benzene mixture gave the pure acetamido ketone **5b** as white needles, m.p. 152.8–153.5°, with infrared absorption[8] at 3400 cm.$^{-1}$ (N—H), at 1730 cm.$^{-1}$ (C=O with an adjacent electronegative group), and at 1675 cm.$^{-1}$ (amide C=O) as well as an ultraviolet maximum[9] at 268 mμ (ε 10,900) with a point of inflection at 220 mμ (ε 13,200). The sample has a series of n.m.r. peaks[10] in the region 1.6–3.3 τ (9H, aryl C—H and N—H) as well as a doublet (J = 6 c.p.s.) at 4.30 τ (1H, CO—CH(Ar)NH—) and singlets at 6.22 τ (3H, CH_3O), at 6.39 τ (2H, CH_2), and at 8.02 τ (3H, CH_3CO).

Anal. Calcd. for $C_{18}H_{18}N_2O_5$: C, 63.15; H, 5.30; N, 8.18. Found: C, 63.12; H, 5.39; N, 8.29.

Recrystallization from a benzene–ether mixture gave the pure enol acetate **5c** as either white prisms, m.p. 164.5–166.5°, or white needles which melted at 148–148.5°. The two crystalline forms have identical infrared spectra[8] with peaks at 3400 cm.$^{-1}$ (N—H), at 1755 cm.$^{-1}$ (enol ester C=O), and at 1690 cm.$^{-1}$ (vinyl amide C=O). The material has ultraviolet maxima[9] at 227 mμ (ε 20,000) and 300 mμ (ε 10,200) (*cf.* ref. 12) with a series of n.m.r. peaks[10] in the region 1.6–3.3 τ (9H, aryl C—H and N—H) as well as a partially resolved multiplet at *ca.* 6.2 τ (CH_2) and singlets at 6.15 τ (CH_3O), at 7.93 τ (3H, CH_3CO), and at 8.10 τ (3H, CH_3CO).

Anal. Calcd. for $C_{20}H_{20}N_2O_6$: C, 62.49; H, 5.24; N, 7.29. Found: C, 62.32; H, 5.34; N, 7.44.

A solution of 11.8 mg. of the enol acetate **5c** in 2 ml. of methanol containing 5 drops of concentrated aqueous hydrochloric acid was heated on a steam bath for 5 min., then diluted with water, and extracted with chloroform. The chloroform extract was washed with aqueous sodium bicarbonate, dried, and concentrated to leave 9.5 mg. of the crude amide **5b**. Recrystallization from a benzene–ether mixture gave 4.4 mg. (42%) of the pure keto amide **5b**, m.p. 153–153.5°, which was identified with the previously described sample by a mixture melting point determination, comparison of infrared spectra, and comparison of R_f values on thin layer chromatography.

After a mixture of 342.3 mg. (1.0 mmole) of the acetamido ketone **5b** and 20 ml. of 20% aqueous hydrochloric acid had been refluxed with stirring for 3.3 hr., the resulting solution was cooled in an ice bath to precipitate 200.1 mg. (59.7%) of the crude hydrochloride of the amino ketone **5a**, m.p. 185–192°. The sample has infrared absorption[15] at 1725 cm.$^{-1}$ (C=O). A mixture of 204.5 mg. (0.608 mmole) of this amino ketone hydrochloride, 389.3 mg. (1.82 mmoles) of sodium metaperiodate, and 5 ml. of saturated aqueous sodium bicarbonate in 10 ml. of ethanol and 15 ml. of water was stirred under nitrogen and at room temperature for 77.5 hr. The resulting mixture was acidified with excess aqueous hydrochloric acid and then extracted with chloroform. After the chloroform solution had been extracted with aqueous sodium bicarbonate, the bicarbonate extract was acidified and extracted with ether. This ethereal solution was dried and concentrated and the resulting residue was crystallized from hexane to separate 45.8 mg. (45.4%) of crude *p*-methoxyphenylacetic acid, m.p. 78–82°. Recrystallization raised the melting point of this acid to 83–86°; the material was identified with an authentic sample by a mixture melting point determination and comparison of infrared spectra. Thin layer chromatography[11] indicated the absence of *p*-nitrophenylacetic acid in the mother liquors from these recrystallizations.

From a comparable cleavage employing 83.5 mg. (0.248 mmole) of the hydrochloride of the amino ketone **5a** and 160.4 mg. (0.75 mmole) of sodium metaperiodate, the chloroform solution of the organic products was extracted successively with aqueous sodium bicarbonate and saturated aqueous sodium bisulfite. After the bisulfite extract had been made basic with excess sodium carbonate and then extracted with chloroform, this chloroform extract was dried and concentrated. Thin layer chromatography[11] of the residual liquid indicated the presence of *p*-nitrobenzaldehyde, but not *p*-methoxybenzaldehyde. Reaction of this material with 2,4-dinitrophenylhydrazine yielded 4.3 mg. (5.5%) of the 2,4-dinitrophenylhydrazone of *p*-nitrobenzaldehyde, m.p. 325° dec., identified with an authentic sample by comparison of infrared spectra.

Neber Rearrangement of the Oxime Tosylate 2b.—The previously described procedure was applied to a mixture of 2.2726 g. (5.0 mmoles) of the oxime tosylate **2b** in 16.7 ml. of ethanol containing 6 mmoles of potassium ethoxide, the dark green reaction mixture being stirred for 15 hr. at −5 to 0°. Analysis of the neutral fraction by gas chromatography[16] with ethyl *p*-tolylacetate as an internal standard indicated the presence of ethyl *p*-methoxyphenylacetate (**14**, calculated yield, 1.8%) and the absence of ethyl *p*-nitrophenylacetate (**13**). A collected[16] sample of the ester **14** was identified with an authentic sample by comparison of retention times and infrared spectra.

The basic product from the reaction was acetylated with 7.94 g. (0.075 mole) of acetic anhydride and 7.91 g. (0.10 mole) of pyridine as previously described. Recrystallization of the crude product (1.0804 g.) from benzene separated 866 mg. (50.6%) of the acetamido ketone **5b**, m.p. 151–153°, identified with the previously described sample by a mixture melting point determination and comparison of infrared spectra. Chromatography of

(16) A column packed Silicone Gum, no. SE-30, suspended on ground firebrick was employed.

the combined mother liquors on silica gel separated an additional 92.5 mg. (total yield, 958.5 mg. or 56%) of the acetamido ketone **5b**, m.p. 148–152°, as well as small quantities (total 56 mg.) of fractions whose thin layer chromatographs[11] indicated the presence of **5b, 5c**, and a third component, possibly **6b**. The R_f value of this third minor component corresponded to the R_f value for the minor unidentified component present in the reaction mixture from the oxime tosylate **1b**. However, as in the previous case, we were unable to obtain a pure sample of this minor component.

Butyllithium-Induced Rearrangement of Methylnaphthyl Phenyl Sulfones[1,2]

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A series of new isomeric sulfones, namely 2-methyl-1-naphthyl phenyl, 1-methyl-2-naphthyl phenyl, 8-methyl-1-naphthyl phenyl, and 3-methyl-2-naphthyl phenyl sulfones, has been synthesized. On treatment with *n*-butyllithium, three of these sulfones rearranged to the corresponding benzylnaphthalenesulfinic acids. The 2,3-substituted sulfone, on similar treatment, gave a low yield of an unstable product.

It has been shown[3a-c] that *o*-methyldiphenyl sulfones, when treated in ether solution with *n*-butyllithium, rearrange to *o*-benzylbenzenesulfinic acids. This study was successfully extended to substituted-phenyl mesityl sulfones and qualitative effects of different substituents on the migrating phenyl ring were noted.[4] The subsequent transformations of the sulfinic acids to sulfonic acids, diarylmethanes, and chloromercuridiarylmethanes also have been demonstrated.[3a,b,4]

This investigation concerns extension of the reaction to naphthyl phenyl sulfones. Unpublished results indicated difficulties when the naphthyl group is the migrating entity in such *n*-butyllithium–induced rearrangements.[5] In view of this, it was of interest to know whether the rearrangement would occur if the methyl group involved was a substituent on the naphthalene ring. Rearrangement studies were carried out on 2-methyl-1-naphthyl phenyl, 1-methyl-2-naphthyl phenyl, 3-methyl-2-naphthyl phenyl, and 8-methyl-1-naphthyl phenyl sulfones. The sulfones were prepared from the corresponding sulfides by hydrogen peroxide oxidation and characterized by physical constants such as melting point and infrared spectrum. 2-Methyl-1-naphthyl phenyl and 8-methyl-1-naphthyl phenyl sulfides were obtained from cuprous benzenethiolate and the suitably substituted aromatic bromide by the method of Adams, Reifschneider, and Nair.[6] In our hands, this method provided significantly increased yields over those obtained from reaction of benzenesulfenyl chloride with naphthyllithium or naphthylmagnesium bromide reagents.[3b,7] The condensation of benzenethiol and the appropriate naphthol in the presence of *p*-toluenesulfonic acid, according to the procedure of Furman and co-workers,[8] provided the sulfide precursors of the other sulfones investigated.

The Experimental section describes the technique for the rearrangement studies and the methods used to obtain derivatives of the sulfinic acids. The propensity to rearrange (see Table I) was estimated from the yields of crude acids[9] and the time required to attain these yields. On this basis, the following qualitative order was observed: 2-methyl-1-naphthyl phenyl > 1-methyl-2-naphthyl phenyl > 8-methyl-1-naphthyl phenyl > 3-methyl-2-naphthyl phenyl sulfone. McClement and Smiles have reported that the base-induced rearrangements of 3-chloro-2-hydroxy-5,6-dimethyl-2′-nitrodiphenyl sulfones and 2-hydroxy-1-naphthyl 2-nitrophenyl sulfone are unusually facile.[10] A similar effect was observed in the analogous *n*-butyllithium-induced rearrangements of aryl sulfones which possess two *o*-methyl groups in the same ring, that is, dimesityl, mesityl phenyl, and phenyl 2,6-xylyl sulfones.[3a,b] The ease with which 2-methyl-1-naphthyl phenyl sulfone rearranges is consistent with the steric acceleration effect proposed by Bunnett and Zahler[11] and supported by Bunnett and Okamoto.[12] There is evidence that the *peri*-hydrogen of naphthalene would provide less steric acceleration for the rearrangement than would an *o*-methyl grouping[13]; this may account in part for the less than quantitative yield of sulfinic acid from this sulfone.

The resistance of 3-methyl-2-naphthyl phenyl sulfone to rearrange may be related to a diminished stabilization of the metalated intermediate by the arylsulfonyl group. This would result in slower metalation of the side chain; hence, nuclear metalation of either ring might predominate under these circumstances.[14]

Similarly, in 8-methyl-1-naphthyl phenyl sulfone, stabilization of the organolithium intermediate may be lowered because the phenylsulfonyl group is more distal; experiments using this isomer produced only a small amount of rearrangement. In addition, the steric requirements for rearrangement should be different in the 1,8-substituted sulfone as compared to those present in other *o*-methyldiaryl sulfones studied, because re-

(1) Abstracted from the Ph.D. thesis of D. C. Hampton.

(2) Paper V in the series "Rearrangements of Aryl Sulfones."

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(9) The sulfinic acids formed were somewhat unstable; it was necessary to avoid heating or exposing these compounds to air for any period of time.

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