[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, POLYTECHNIC INSTITUTE OF BROOKLYN]

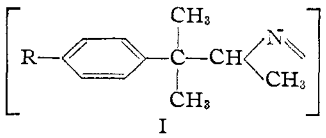
Azo Compounds. XXII. Synthesis of Neophyl-type Azo Compounds[1]

BY C. G. OVERBERGER AND HAROLD GAINER[2]

RECEIVED FEBRUARY 5, 1958

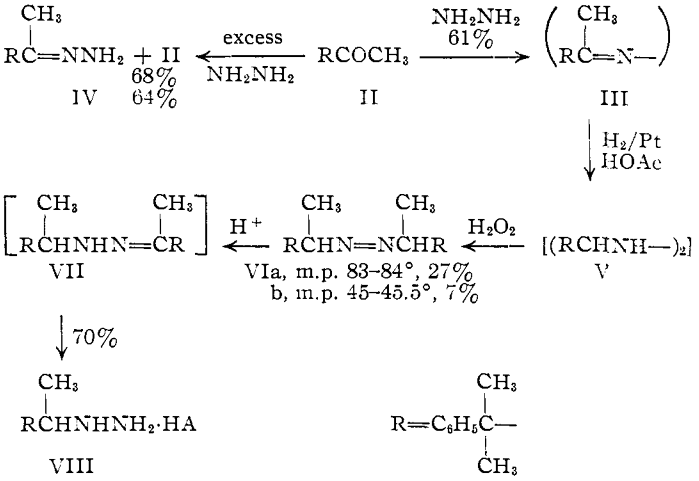
Four neophyl-type azo compounds of the general formula $[p\text{-R-C}_6\text{H}_4\text{-C(CH}_3)_2\text{CH(CH}_3)\text{-N=}]_2$ where R = H (two diastereoisomers), OCH_3 and $NHCOCH_3$ have been prepared and characterized. New synthetic procedures for many intermediates are described.

Neophyl-type radicals have been shown to rearrange with the aromatic group moving in a 1–2 manner.[3–6] In all the cited examples the neophyl radical has been generated by a secondary process so that the rate of neophyl radical formation has not been measurable. When azo compounds are thermally decomposed in solution, free radicals are often formed in a primary process which usually approximates a unimolecular first-order decomposition.[7,8] With neophyl-type azo compounds, there is a possibility of phenyl participation in the rate-determining step, the dissociation of the carbon–nitrogen bond. The influence of *p*-substituents on the rate of formation of the neophyl radical would disclose whether participation of this type (see succeeding paper) was occurring. It was desirable to synthesize a number of such neophyl azo compounds of the type I, R = H (two diastereoisomers), CH_3O and $NHCOCH_3$, and study their rates and products of decomposition. In this paper, the synthetic procedures are described; in a following paper, the products, rates of decomposition and interpretation are reported.



I

DIAGRAM A, 2-AZO-BIS-3-METHYL-3-PHENYLBUTANE



The ketone II was obtained from the Friedel–Crafts reaction of 3-bromo-3-methyl-2-butanone and benzene.[9] A synthesis of this ketone II has also been reported by direct methylation of phenylacetone.[10]

The azine III then was prepared by reaction with hydrazine.[9,11] An alternative synthesis of ketazine III was reaction of the ketone II with an excess of hydrazine to yield the substituted hydrazone IV which could be treated with another mole of ketone to yield the desired ketazine III. There was no advantage to the latter synthesis since the over-all yield from ketone II in two steps was 44%.

The azine III was reduced readily to the corresponding hydrazine V with hydrogen and Adams catalyst in glacial acetic acid. No serious attempt was made to isolate the intermediate hydrazine V which was unstable in air. The azo compound VI was formed by direct oxidation of V with 30% hydrogen peroxide in buffered media.[12] Dilute mineral acid readily isomerized the azo compounds VIa and b to the unisolated hydrazone VII with subsequent hydrolysis to the corresponding hydrazine VIII isolated as its hydrochloride (70%) and oxalate (50%) salts. The hydrazine hydrochlorides obtained from both diastereoisomers were identical.

Since the symmetrical 2-azo-bis-3-methyl-3-phenylbutane has two asymmetric carbon atoms, one *dl*-pair and one *meso* form are possible.[13] Both were obtained by fractional crystallization of the crude product. One form, obtained in 27% yield, melted at 83–84° ($\epsilon_{\max}$ 29.4, $\lambda_{\max}$ 366 mμ in methanol) and the other diastereoisomer was obtained in 7% yield and melted at 45–45.5° ($\epsilon_{\max}$ 24.2, $\lambda_{\max}$ 364 mμ in methanol). The infrared absorption spectra for both compounds were virtually identical.

---

[1] This is the 22nd in a series of papers concerned with the preparation and decomposition of azo compounds. For the previous paper in this series see C. G. Overberger, J. G. Lombardino and R. G. Hiskey, THIS JOURNAL, **80**, 3009 (1958).

[2] This paper comprises a portion of a Dissertation presented by Harold Gainer in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Graduate School of the Polytechnic Institute of Brooklyn.

(3) W. H. Urry and M. S. Kharasch, THIS JOURNAL, **66**, 1438 (1944).

(4) S. Winstein and F. H. Seubold, Jr., *ibid.*, **69**, 2916 (1947).

(5) W. H. Urry and N. Nicolaides, *ibid.*, **74**, 5163 (1952).

(6) D. Y. Curtin and M. J. Hurwitz, *ibid.*, **74**, 5381 (1952).

(7) C. G. Overberger, M. T. O'Shaughnessy and H. Shalit, *ibid.*, **71**, 2661 (1949).

(8) S. G. Cohen and C. H. Wang, *ibid.*, **77**, 2457 (1955).

(9) J. M. Hoyt, Ph. D. Dissertation, Polytechnic Institute of Brooklyn, June, 1951, Part II.

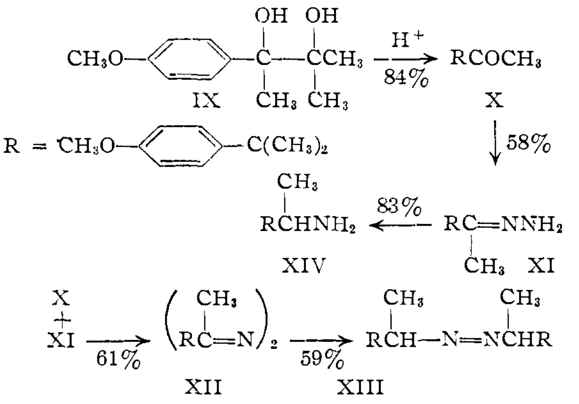
(10) A. Jönsson, *Acta Chem. Scand.*, **8**, 1206 (1954). This methylation is a one-step method whereas the procedure described in reference 15 proceeds by two successive steps.

(11) We are indebted to Dr. John Hoyt for these procedures.

(12) S. G. Cohen, S. J. Groszos and D. B. Sparrow, THIS JOURNAL, **72**, 3947 (1950).

(13) C. G. Overberger and M. B. Berenbaum, *ibid.*, **73**, 2618 (1951).

DIAGRAM B, 2-AZO-BIS-3-(p-METHOXYPHENYL)-3-METHYLBUTANE



The corresponding p-methoxyphenyl substituted azo compound could not be prepared in an analogous fashion. This was due to the failure of anisole and 3-bromo-3-methyl-2-butanone to give the desired intermediate ketone X under a variety of Friedel–Crafts conditions. Subsequently two syntheses of the ketone X were developed.

p-Methoxyphenylacetone, prepared from acetone according to Winstein, *et al.*,[14] was methylated in two steps employing the method of Suter and Weston for the alkylation of phenylacetone.[15] Another synthesis of the ketone X was reported by Jönsson[10]; p-methoxyphenylacetone was dimethylated in one step by a modification of the Suter and Weston method. Because of the low yield of p-methoxyphenylacetone (32%) and the difficulty of obtaining X free of p-methoxyphenylacetone and the monomethylated intermediate due to their similar boiling points, the following synthesis of V was preferable:

Ethyl p-methoxyphenylglyoxylate[16] was treated with methylmagnesium iodide to yield predominantly 3-hydroxy-3-(p-methoxyphenyl)-2-butanone (77%) along with 9% of the glycol IX. The ketol did not react normally with common hydroxyl and ketone group reagents such as phenyl isocyanate and hydroxylamine. The infrared absorption spectrum indicated an α-hydroxy group (3.87 μ, medium) and an unconjugated carbonyl (5.8 μ, strong). Subsequent reaction of the ketol with an excess of methylmagnesium iodide gave the glycol. Methyllithium gave consistently better yields (62%) of the desired glycol IX. The pinacol rearrangement of this glycol with 60% sulfuric acid resulted in the ketone X which was characterized by comparison of the oxime with the corresponding derivative of the ketone prepared by the previously described method of methylation. The fact that the same ketone was obtained by two methods constitutes evidence of its structure.

Reaction of the ketone X with hydrazine to obtain the azine, as in the case of the unsubstituted ketone, gave very poor results. Instead, the ketone was treated with an excess of hydrazine to give the hydrazone XI which was then allowed to react equimolecularly with the corresponding ketone X affording the azine (XII) in good yield. Reduction of the hydrazone XI with Adams catalyst in glacial acetic acid gave the amine XIV. The same amine was obtained by reduction of the oxime of X with 10% palladium-on-charcoal in methanol. Hydrogenation of the azine to the corresponding intermediate hydrazine was effected using Adams catalyst in glacial acetic acid in the presence of ethyl acetate to moderate the reduction. The reaction conditions are very specific. The intermediate hydrazine was not isolated but was oxidized directly to the azo compound XIII. Preparation of one of the diastereoisomers was effected by careful fractional crystallization from n-butyl alcohol. The ultraviolet absorption spectrum of a material of melting point 90–95° (ϵ_{max} 31.4, λ_{max} 363 mμ in methanol) did not differ appreciably from that of the pure isomer, m.p. 97–99° (ϵ_{max} 30.9; λ_{max} 363 mμ in methanol).

2-Azo-bis-3-(p-acetamidophenyl)-3-methylbutane.—The necessary intermediate 3-methyl-3-(p-nitrophenyl)-2-butanone azine could be obtained by direct nitration of 3-methyl-3-phenyl-2-butanone azine. However, the product was very difficult to purify and it was therefore synthesized more satisfactorily in the following manner.

Nitration of 3-methyl-3-phenyl-2-butanone at −20° gave the p-nitrophenyl derivative (50%). That the aromatic ring was substituted in the p-position by the nitro group was demonstrated by oxidation of the compound to p-nitrobenzoic acid and by an independent synthesis of the ketone from p-nitrophenylisobutyryl chloride and dimethylcadmium. Reaction of the nitroketone with a large excess of hydrazine gave its hydrazone (74%) which was then allowed to react equimolecularly with the original nitroketone to yield the symmetrical azine (83%).

The nitroazine then was hydrogenated in tetrahydrofuran over 10% palladium-on-charcoal as catalyst to the unisolated intermediate diaminoazine. In one experiment under these conditions much more than the theoretical amount of hydrogen was absorbed. Attempts to isolate this intermediate led only to a small yield of compound which was probably 3-methyl-3-(p-aminophenyl)-2-butanone. Instead, the intermediate diaminoazine was acetylated directly with acetic anhydride to give 3-(p-acetamidophenyl)-3-methyl-2-butanone azine. Reduction of the acetamido azine in glacial acetic acid with Adams catalyst yielded the corresponding hydrazine which was not isolated but was oxidized directly to the azo compound with yellow mercuric oxide in chloroform. Hydrogen peroxide was not used as an oxidant in the presence of chloroform since reaction with the solvent occurred. The ultraviolet absorption spectrum of the acetamido azo compound in chloroform showed the symmetrical peak characteristic of azo compounds at 365 mμ and an extinction coefficient of 43.2, somewhat larger than the unsubstituted or p-methoxy azo compounds.

Experimental

All melting points are uncorrected. Analyses are by Dr. A. Steyermark, Hoffman-La Roche, Inc., Nutley, N. J.;

---

[14] S. Winstein, M. Brown, K. C. Schreiber and A. H. Schlessinger, THIS JOURNAL, **74**, 1140 (1952).

[15] C. M. Suter and A. W. Weston, *ibid.*, **64**, 533 (1942).

[16] K. Kindler, W. Metzendorf and Dschi-yin-kwok. *Ber.*, **76**, 308 (1943).

Dr. K. Ritter, Basel, Switzerland; and Dr. F. Schwarzkopf, New York, N. Y.

3-Methyl-3-phenyl-2-butanone (II).[9]—3-Bromo-3-methyl-2-butanone was prepared in 80% yield according to the procedure of Favorskii.[17] The crude distillate could be used without further purification, b.p. 84–90° (139 mm.), n^{26}D 1.4571 (b.p. 83–84° (150 mm.), n^{16}D 1.4590 prepared by bromination of 3-methyl-2-butanone in the presence of aqueous potassium chlorate).[18]

To a gently refluxing and stirred mixture of 329 g. (2.48 moles) of anhydrous aluminum chloride and 910 ml. of benzene was added 185 g. (1.12 moles) of 3-bromo-3-methylbutanone in 1.75 hours. Refluxing was continued for 3.25 hours and the reaction mixture was poured onto a mixture of 200 ml. of concentrated hydrochloric acid and 1.5 kg. of crushed ice. The organic layer was separated and washed successively with water, 5% aqueous sodium bicarbonate and water. After drying over anhydrous magnesium sulfate the product was distilled, b.p. 95.5–97° (11 mm.), 93.3 g. (51%), n^{25}D 1.5093 (b.p. 76–77° (2 mm.), n^{25}D 1.5074, prepared from α-phenylisobutyronitrile and methylmagnesium iodide[19] and b.p. 99–99.5° (12 mm.), n^{29}D 1.5083, by alkylation of phenylacetone with methyl iodide[15]).

The semicarbazone was prepared in the usual way,[20] m.p. 185.5–188.5° (185.5–186.5°).[15]

3-Methyl-3-phenyl-2-butanone Hydrazone (IV).—A solution of 10 g. (0.06 mole) of 3-methyl-3-phenyl-2-butanone, 30 ml. (0.5 mole) of 85% hydrazine hydrate and 30 ml. of absolute alcohol was refluxed for 70 hours. The solvent was removed by warming under vacuum and the resultant oil dissolved in 10 ml. of warm Skellysolve C (b.p. 90–100°). The product crystallized upon cooling at Dry Ice temperatures. The product was removed by filtration and washed with very cold Skellysolve C, 7.44 g. (68%). A sample was recrystallized for analysis from Skellysolve C, m.p. 40–41°.

Anal. Calcd. for $C_{11}H_{16}N_2$: C, 74.95; H, 9.15; N, 15.90. Found: C, 74.79; H, 8.95; N, 16.09.

3-Methyl-3-phenyl-2-butanone Azine (III). **Method A.**[9]—This azine was prepared according to a general method described by Szmant and McGinnis.[21] A solution of 140 g. (0.86 mole) of 3-methyl-3-phenyl-2-butanone, 860 ml. of absolute alcohol, 5 drops of concentrated sulfuric acid and 29.4 g. (0.5 mole) of 85% hydrazine hydrate was refluxed in a Soxhlet apparatus containing 48.5 g. (0.87 mole) of calcium oxide in the extraction thimble. The extraction thimble must be suitably protected against bursting due to expansion of the hydrated calcium oxide. After extracting for 48 hours the calcium oxide was replenished and the extraction continued for another 48 hours. A small amount of decolorizing charcoal was added and the solvent was removed from the filtered solution by warming under vacuum. The residue was recrystallized from methanol, m.p. 83–84°, 84.2 g. (61%). The infrared absorption spectrum showed a medium band at 6.11 μ (azomethine).

Anal. Calcd. for $C_{22}H_{28}N_2$: C, 82.46; H, 8.80. Found: C, 82.20; H, 8.72.

Method B.—The azine also was prepared by refluxing a solution of 7.44 g. (0.042 mole) of 3-methyl-3-phenyl-2-butanone hydrazone, 6.9 g. (0.042 mole) of 3-methyl-3-phenyl-2-butanone and 0.03 g. (0.2 mmole of *p*-toluenesulfonic acid in 25 ml. of xylene for 97 hours. In later preparations the use of a Dean–Stark trap reduced the time considerably. After washing with dilute aqueous sodium hydroxide and water, and drying with anhydrous magnesium sulfate, the solvent was removed by warming under vacuum. A crystalline residue was obtained which was recrystallized from methanol, m.p. 83–84°, 8.6 g. (64%). A mixed melting point with a sample, m.p. 83–84° prepared by method A, showed no depression, m.p. 83–84°.

2-Azo-bis-3-methyl-3-phenylbutane (VIa), **High Melting Isomer.**—Thirty-five grams (0.11 mole) of 3-methyl-3-phenyl-2-butanone azine was reduced under 3.5 atmospheres hydrogen in a prereduced mixture of 150 ml. of glacial acetic acid and 0.5 g. of Adams catalyst. The uptake was approximately 100% when the reaction ceased after one hour. The mixture was filtered rapidly and the solvent removed under reduced pressure and nitrogen with a little warming. The oily residue was made alkaline with 2 *N* sodium hydroxide and extracted with 150 ml. of ether. A mixture of the ethereal extract, 200 ml. of water, 25 g. of sodium bicarbonate and 30 ml. of 30% hydrogen peroxide was stirred vigorously for two hours. The ethereal layer was separated, dried over anhydrous magnesium sulfate and the solvent removed under vacuum with a little warming. The oily residue was dissolved in 40 ml. of absolute ethyl alcohol and cooled overnight to precipitate the slowly crystallizing azo compound. The crude azo compound was repeatedly recrystallized from methanol and from isopropyl alcohol or absolute ethyl alcohol, m.p. 83–84°, 9.5 g. (27%), ϵ_{max} 29.4, λ_{max} 366 mμ in methanol.

Anal. Calcd. for $C_{22}H_{30}N_2$: C, 81.93; H, 9.38; N, 8.69. Found: C, 81.80; H, 9.24; N, 8.94.

2-Azo-bis-3-methyl-3-phenylbutane (VIb). **Low Melting Isomer.**—The combined mother liquors from the recrystallizations of the crude azo compound obtained as in the preparation of VIa in several preparations were allowed to evaporate. The resultant oily precipitate was pressed on a porous plate and the crystalline residue was repeatedly fractionally crystallized from methanol. It was usually necessary to filter the higher melting isomer as a first crop while the solution was cooling, and then cooling at Dry Ice temperature to obtain the more soluble low melting isomer, m.p. 45–45.5°, 6.8%, ϵ_{max} 24.2, λ_{max} 364 mμ in methanol.

Anal. Calcd. for $C_{22}H_{30}N_2$: C, 81.93; H, 9.38; N, 8.69. Found: C, 81.84; H, 9.11; N, 8.88.

Salts of (1,2-Dimethyl-2-phenylpropyl)-hydrazine (VIII). A. Oxalate.—A solution of 940 mg. (2.9 mmoles) of 2-azo-bis-3-methyl-3-phenylbutane, m.p. 83–84°, 1.2 g. (9.5 mmoles) of oxalic acid dihydrate and 10.7 ml. of water was allowed to stand overnight at room temperature and was then refluxed for 2 hours. The addition of 2 volumes of ether precipitated a crude product, 393 mg. (50%), m.p. 148–150° eff., which was removed by filtration. Recrystallization of a sample for analysis several times from absolute ethyl alcohol gave a m.p. 152° eff.

Anal. Calcd. for $C_{13}H_{20}N_2O_4$: C, 58.19; H, 7.51; N, 10.44. Found: C, 58.42; H, 7.63; N, 10.74.

B. Hydrochloride.—A solution of 100.3 mg. (0.31 mmoles) of 2-azo-bis-3-methyl-3-phenylbutane in 1.0 ml. of absolute ethyl alcohol and 3 ml. of dry ether was treated with 0.15 ml. of concentrated hydrochloric acid. After standing overnight at room temperature and adding of 2 ml. more of dry ether the hydrochloride crystallized. The solid was filtered and washed with ether, m.p. 161–162°, 45.1 mg. (68%).

The ethereal filtrate on treatment with 0.25 *M* 2,4-dinitrophenylhydrazine[22] gave the 2,4-dinitrophenylhydrazone of 3-methyl-3-phenyl-2-butanone, m.p. 148–149° A mixed melting point with an authentic sample, m.p. 148–149°, melted at 148–149°.

A similar experiment was repeated as above with 100.0 mg. of the diastereoisomeric azo compound, m.p. 44–45.5°. The hydrochloride obtained in 87% yield, m.p. 161–162°, did not depress the melting point of the hydrochloride obtained above when mixed, m.p. 161–162°.

Ethyl Chloroglyoxalate.—The potassium salt of ethyl hydrogen oxalate was prepared in 73% yield according to the method of Southwick and Seivard.[23] Stirring was necessary to prevent bumping which occurred as the product precipitated in the boiling reaction mixture. The melting point of the product, 228° with effervesence, depended on the rate of heating (m.p. 222–225°).[23] This ester was converted to the acid chloride of the half-ester according to the method of Southwick and Seivard[23] except that an inert diluent was used as the reaction medium. To 222.8 g. (1.43 moles) of potassium ethyl oxalate suspended in 360 ml. of petroleum ether (b.p. 30–60°) was added 103 ml. (1.43 moles) of thionyl chloride. After refluxing on the

---

(17) A. Favorskii, *J. prakt. Chem.*, [2] **88**, 641 (1913).

(18) J. R. Catch, D. H. Hey, E. R. H. Jones and W. Wilson, *J. Chem. Soc.*, 276 (1948).

(19) W. D. Kumler, L. A. Strait and E. L. Alpen, THIS JOURNAL, **72**, 1463 (1950).

(20) R. L. Shriner and R. C. Fuson, "Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 3rd Ed., 1948, p. 170.

(21) H. H. Szmant and C. McGinnis, THIS JOURNAL, **72**, 2890 (1950).

(22) L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed., D. C. Heath and Co., Boston, Mass., 1955, p. 316.

(23) P. L. Southwick and L. L. Seivard, THIS JOURNAL, **71**, 2532 (1949).

steam-bath for four hours the precipitated potassium chloride was removed by filtration and the filtrate was distilled to give 130 g. (67%), b.p. 123–132° (760 mm.) (b.p. 133–135° (760 mm.)[23]). Ethyl chloroglyoxylate was then converted to ethyl (*p*-methoxyphenyl)-glyoxylate with anisole in 74% yield.[16]

3-Hydroxy-3-(*p*-methoxyphenyl)-2-butanone and 1-(*p*-Methoxyphenyl)-1,2,2-trimethylethylene Glycol (IX).—To a Grignard reagent prepared from 218 g. (9 g. atoms) of magnesium and 1.28 kg. (9 moles) of methyl iodide in 4 liters of anhydrous ether was added, in 20 minutes, a solution of 627.5 g. (3.0 moles) of ethyl (*p*-methoxyphenyl)-glyoxylate with stirring and sufficient Dry Ice cooling to control the reaction. The mixture was refluxed for 1.25 hours and then treated with a solution of 5 liters of 20% ammonium chloride. The ethereal layer was separated, dried over anhydrous magnesium sulfate and distilled in vacuum. The fraction boiling at 119–129° (2 mm.), 448 g. (77%), was collected as the ketol; a second fraction boiled at 134–140° (3 mm.). Redistillation of a sample of the first fraction for elemental analysis, gave material boiling at 117–118° (2 mm.), $n^{25.5}\text{D}$ 1.5228, d^{25}_{4} 1.1130. The infrared absorption spectrum showed a strong band at 5.8 μ (unconjugated carbonyl) and a medium band at 2.87 μ (α-hydroxyl).

Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 68.02; H, 7.65.

The fraction which boiled at 134–140° (3 mm.) crystallized slowly. The solid was dissolved in a minimum of warm benzene, and Skellysolve C (b.p. 90–100°) was added to crystallize the glycol. The product was recrystallized from a solution of benzene and Skellysolve C, m.p. 87–88°, 58 g. (9%).

Anal. Calcd. for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63. Found: C, 68.60; H, 8.41.

1-(*p*-Methoxyphenyl)-1,2,3-trimethylethyleneglycol (IX). Method A.—To 48.0 g. (6.9 g. atoms) of lithium sand[24] washed twice with 500-ml. portions of anhydrous ether by removing the solvent under reduced pressure through a loosely plugged glass tube, was added 1.5 liters of anhydrous ether and then 490 g. (3.45 moles) of methyl iodide. The addition was carried out with stirring for two hours while keeping the temperature at 25° with very efficient cooling. Since the reaction has an induction period and is strongly exothermic, no more than 25 ml. of methyl iodide was added before reaction was observed and the initial reaction was carefully controlled with Dry Ice cooling. The mixture was stirred an additional 0.25 hour at room temperature until essentially all the lithium had dissolved. Titration of an aliquot with 0.1 *N* hydrochloric acid indicated a 67% yield (2.3 moles) of methyllithium. To the well-stirred solution of methyllithium was added, in 20 minutes, a solution of 190.5 g. (0.98 mole) of 3-hydroxy-3-(*p*-methoxyphenyl)-2-butanone in 200 ml. of anhydrous ether. The temperature was kept at 10° during the addition. The mixture was refluxed overnight, then cooled, treated with 50 ml. of methanol and then with one liter of water. The ethereal layer was separated, dried over magnesium sulfate and, after filtration, the solvent was removed by warming under reduced pressure. The crystalline residue was taken up in about 300 ml. of Skellysolve C (b.p. 90–100°), filtered and recrystallized from a solution of 150 ml. of benzene and 350 ml. of Skellysolve A (b.p. 30–40°), m.p. 87–88°, 129 g. (63%). A mixed melting point with the glycol obtained in the previous preparation, m.p. 87–88°, showed no depression, m.p. 87–88°.

Method B.—To a solution of methylmagnesium iodide prepared from 43.7 g. (0.3 mole) of methyl iodide, 7.2 g. (0.3 g. atom) of magnesium and 200 ml. of anhydrous ether was added, in 20 minutes, a solution of 27.3 g. (0.14 mole) of 3-hydroxy-3-(*p*-methoxyphenyl)-2-butanone and 75 ml. of ether. The mixture was refluxed for four hours and then decomposed with a solution of 250 ml. of 15% aqueous ammonium chloride. The mixture was separated and extracted further with a little ether to which had been added a few milliliters of concentrated hydrochloric acid to break the emulsion. After drying with anhydrous magnesium sulfate and filtration, the ethereal extract was distilled. The fraction collected, 25 g., b.p. 122–128° (3 mm.), crystallized and was pressed on a porous plate and then recrystallized from a solution of benzene and petroleum ether, b.p. 30–60°. Reworking of the mother liquors gave a total yield of 11.7 g., m.p. 87–88° (40%). A mixed melting point with a sample prepared according to method A, m.p. 87–88°, melted at 87–88°.

3-(*p*-Methoxyphenyl)-3-methyl-2-butanone (X). Method A.—A mixture of 129 g. (0.62 mole) of 1-(*p*-methoxyphenyl)-1,2,2-trimethylethylene glycol, 360 ml. of concentrated sulfuric acid and 840 ml. of water was refluxed and stirred for five hours. The resultant oil was separated with the aid of a little ether, washed with water, saturated sodium bicarbonate, dried over anhydrous magnesium sulfate, and the residue distilled, b.p. 109–114° (2.5 mm.), 99.4 g. (84%). For the analysis a sample was redistilled; b.p. 89° (2 mm.), $n^{29}\text{D}$ 1.5322, d^{25}_{4} 1.0283 (b.p. 138–141° (10 mm.)[10]).

Anal. Calcd. for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.10; H, 8.52.

Method B.—To a solution of 110 ml. of *t*-butyl alcohol and 15 ml. of toluene was added 12.27 g. (0.31 g. atom) of potassium. The mixture was stirred and refluxed one hour until the metal had dissolved. While the mixture was maintained near the boiling point, 46.8 g. (0.29 mole) of 3-(*p*-methoxyphenyl)-2-butanone was added, followed by dropwise addition of 55 g. (0.39 mole) of methyl iodide to the hot solution during 45 minutes. The mixture was then refluxed 0.5 hour. The cooled mixture was treated with 50 ml. of water and the excess solvent removed under vacuum with a little heating. The residue was then extracted with ether and the ethereal layer, after drying with anhydrous magnesium sulfate, was fractionally distilled twice, b.p. 72–80° (1.5 mm.), 21.5 g. (42%), $n^{25}\text{D}$ 1.5300.

A high boiling fraction was obtained, b.p. 182–186° (1 mm.), 6.0 g. (12%) which had an acceptable analysis for a Claisen condensation product involving two molecules of 3-(*p*-methoxyphenyl)-2-butanone.

Anal. Calcd. for $C_{22}H_{26}O_3$: C, 78.07; H, 7.74. Found: C, 78.16; H, 7.81.

The oxime of 3-(*p*-methoxyphenyl)-3-methyl-2-butanone was prepared[25] and recrystallized from ethanol, m.p. 164–167°. A mixed melting point with material prepared by method A melted at 165–168°.

Anal. Calcd. for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.60; H, 8.15; N, 6.90.

3-(*p*-Methoxyphenyl)-3-methyl-2-butanone Hydrazone (XI).—A solution of 85.5 g. (0.45 mole) of 3-(*p*-methoxyphenyl)-3-methyl-2-butanone in 200 ml. (3.4 moles) of 85% hydrazine hydrate was refluxed for 39 hours. The solvent was removed by evaporation under vacuum to yield a crystalline mass. Several recrystallizations from Skellysolve C (b.p. 90–100°) gave 53.3 g., m.p. 74–75° (58%).

Anal. Calcd. for $C_{12}H_{18}N_2O$: C, 69.87; H, 8.80; N, 13.58. Found: C, 69.97; H, 8.58; N, 13.82.

2-Amino-3-(*p*-methoxyphenyl)-3-methylbutane Acetate (XIV). Method A.—A mixture of 380 mg. (1.84 mmoles) of 3-(*p*-methoxyphenyl)-3-methyl-2-butanone hydrazone, 10 ml. of glacial acetic acid and 50 mg. of platinum oxide absorbed two moles (100 ml.) of hydrogen in one hour at atmospheric pressure and room temperature. After filtration and evaporation of the solvent under vacuum, the product was crystallized with ether and finally recrystallized from Skellysolve C (b.p. 90–100°) or benzene, m.p. 117–118°, 340 mg. (73%).

Anal. Calcd. for $C_{14}H_{23}NO_3$: C, 66.37; H, 9.15; N, 5.53. Found: C, 66.47; H, 9.27; N, 5.52.

Method B.—For comparative purposes, the amine was prepared by low pressure catalytic hydrogenation of 3-(*p*-methoxyphenyl)-3-methyl-2-butanone oxime in methanol with 10% palladium-on-charcoal at 60°, b.p. 105° (2 mm.), $n^{27}\text{D}$ 1.5246.

Anal. Calcd. for $C_{12}H_{19}NO$: C, 74.57; H, 9.91; N, 7.25. Found: C, 74.74; H, 9.55; N, 7.00.

A small sample of the amine was converted to the acetate, m.p. 117–118°. A mixed melting point of the acetate from methods A and B melted at 117–118°.

3-(*p*-Methoxyphenyl)-3-methyl-2-butanone Azine (XII).—A solution of 42.3 g. (0.22 mole) of 3-(*p*-methoxyphenyl)-3-methyl-2-butanone, 45.5 g. (0.22 mole) of 3-(*p*-methoxy-

---

[24] T. D. Perrine and H. Rapoport, *Anal. Chem.*, **20**, 635 (1948).

[25] R. L. Shriner, R. S. Fuson and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th ed., John Wiley and Sons, Inc., New York, N. Y., p. 255.

phenyl)-3-methyl-2-butanone hydrazone and 0.2 g. (1.2 mmoles) of *p*-toluenesulfonic acid in 500 ml. of xylene was refluxed overnight. The water which was separated was collected in a Dean–Stark trap, the theoretical amount of water being collected in 4.5 hours. Decolorizing carbon was added, the mixture was filtered, and the solvent removed under vacuum with gentle heating. The crystalline residue was recrystallized twice from methanol, m.p. 87–87.5°, 51 g. (61%). The infrared absorption spectrum showed a medium band at 6.12 μ (azomethine).

Anal. Calcd. for $C_{24}H_{32}N_2O_2$: C, 75.75; H, 8.48; N, 7.36. Found: C, 75.85; H, 8.32; N, 7.30.

2-Azo-bis-3-(*p*-methoxyphenyl)-3-methylbutane (XIII).—A solution containing 1.52 g. (4 mmoles) of 3-(*p*-methoxyphenyl)-3-methyl-2-butanone azine in 10 ml. of ethyl acetate, and 33 ml. of glacial acetic acid was hydrogenated at room temperature and atmospheric pressure with 150 mg. of Adams catalyst. After one hour the reaction ceased, the catalyst was removed by filtration and the solvent removed under vacuum with a little warming. The liquid residue was made alkaline with 25 ml. of 1 *N* sodium hydroxide and extracted with ether. The ethereal layer was separated and stirred vigorously for 7.5 hours with 0.8 g. of sodium bicarbonate, 4 ml. of water and 6 ml. of 30% hydrogen peroxide. The ethereal layer was then separated, dried over anhydrous magnesium sulfate, filtered, and the solvent removed under vacuum to yield a crystalline product. On recrystallization from the same solvent, a material was obtained for analysis, m.p. 90–95°, $\epsilon_{\max}$ 31.4, $\lambda_{\max}$ 363 mμ in methanol.

Anal. Calcd. for $C_{24}H_{34}N_2O_2$: C, 75.35; H, 8.96; N, 7.32. Found: C, 75.79; H, 8.77; N, 7.55.

A few recrystallizations of the "crude" azo compound (m.p. 90–95°) from Skellysolve C (b.p. 90–100°) though entailing large losses, raised the melting point; m.p. 97–99°, $\epsilon_{\max}$ 30.9, $\lambda_{\max}$ 363 mμ in methanol. The ultraviolet infrared spectra of both the "crude," m.p. 90–95°, and purified, m.p. 97–99°, azo compounds were virtually identical. It is probable that the crude sample was a mixture of diastereoisomers.

Anal. Calcd. for $C_{24}H_{34}N_2O_2$: C, 75.35; H, 8.96; N, 7.32. Found: C, 75.23; H, 9.03; N, 7.29.

3-(*p*-Methoxyphenyl)-2-butanone was prepared utilizing the method of Suter and Weston[15] who methylated phenylacetone. To a solution of 16.4 g. (0.71 g. atom) of sodium in 500 ml. of dry isopropyl alcohol heated on the steam-bath was added a solution of 112.4 g. (0.69 mole) of *p*-anisylacetone prepared according to Winstein, *et al.*,[14] in 100 ml. of dry isopropyl alcohol. Since sodium isopropoxide readily precipitated under these concentrations, the mixture was kept fairly hot. While heating and stirring were continued, 108 g. (0.76 mole) of methyl iodide was added slowly during one hour. The mixture was stirred and heated an additional hour, then cooled and treated with a small amount of water to dissolve the precipitated salts. Some excess solvent was removed with heating under reduced pressure and the resultant mixture was extracted with ether. After drying over magnesium sulfate, the ether was removed under vacuum and the residual oil distilled, b.p. 131–136° (11 mm.), 47.2 g. (39%), n^{24}D 1.5243 (b.p. 267° (760 mm.) n^{20}D 1.5287, prepared by oxidation of the corresponding alcohol with chromic acid[23]).

The oxime was prepared by the usual method,[25] m.p. 121.5–123.0° (m.p. 122–123°).[26]

3-Methyl-3-(*p*-nitrophenyl)-2-butanone. Method A.—To a well-stirred mixture of 300 ml. of concentrated sulfuric acid and 300 ml. of concentrated nitric acid, at about −20°, was added dropwise 150 g. (0.93 mole) of 3-methyl-3-phenyl-2-butanone with careful control of the temperature. The mixture was stirred vigorously for an additional 70 minutes at −20° and then poured onto 2 kg. of finely crushed ice. The resultant semi-solid was extracted portionwise with two liters of ether and the ethereal extract was washed with water, sodium bicarbonate solution and dried over magnesium sulfate. After filtration and removal of the solvent under vacuum, the crystalline residue was recrystallized from 250 ml. of methanol, m.p. 89–90°, 96.3 g. (50%).

Anal. Calcd. for $C_{11}H_{13}NO_3$: C, 63.75; H, 6.32; N, 6.76. Found: C, 63.58; H, 6.38; N, 6.76.

α-Phenylisobutyric Acid.—A mixture of 86 g. (0.53 mole) of 3-methyl-3-phenyl-2-butanone and sodium hypochlorite prepared from 211 g. of chlorine, 285 g. of sodium hydroxide and 1800 ml. of water was stirred at 55° for 3 hours. A small amount of insoluble oil was removed by extracting with ether and 140 ml. of concentrated hydrochloric acid was added to the aqueous portions. The precipitated acid was filtered, washed thoroughly with water and recrystallized from Skellysolve C (b.p. 90–100°), m.p. 79–80°, 65.2 g. (75%) (m.p.78–79°, from the same ketone by oxidation with alkali and bromine[27]).

α-(*p*-Nitrophenyl)-isobutyric Acid.—To a mixture of 130 ml. of concentrated nitric acid and 130 ml. of concentrated sulfuric acid was added 65.2 g. (0.40 mole) of α-phenylisobutyric acid at 10° in one hour. After stirring for an additional 80 minutes the mixture was poured onto 1.5 kg. of crushed ice and the precipitate was extracted with 250 ml. of chloroform. The acid was extracted from the chloroform layer with 200 ml. of 2 *N* sodium hydroxide and then reprecipitated with 200 ml. of 2 *N* hydrochloric acid. After several recrystallizations from toluene, the yield was 37.7 g. (45%), m.p. 132–133° (m.p. 128–129° prepared by hydrolysis of α-(*p*-nitrophenyl)-isobutyronitrile[10]).

3-Methyl-3-(*p*-nitrophenyl)-2-butanone. Method B.—To a solution of methylmagnesium bromide prepared from 10 g. (0.105 mole) of methyl bromide, 200 ml. of ether and 2.35 g. (0.097 g. atom) of magnesium was added 8.97 g. (0.049 mole) of anhydrous cadmium chloride. There was a vigorous reaction and the mixture was then refluxed 15 minutes. The ether was distilled off and to the residue was added a solution of 10 g. (0.044 mole) of α-(*p*-nitrophenyl)-isobutyryl chloride, m.p. 55–58°, prepared in 97% yield according to Jönsson,[10] (m.p. 55–56°),[10] in 100 ml. of benzene. After refluxing for 1.5 hours, the mixture was treated with 100 ml. of 1 *N* hydrochloric acid and the benzene layer was dried over magnesium sulfate and distilled, b.p. 118–140° (1.5 mm.). The product solidified and was recrystallized from Skellysolve C (b.p. 90–100°), m.p. 89–90°, 1 g. (11%). A mixed melting point with material, m.p. 89–90°, prepared from method A melted at 89–90°.

The oxime[25] of the nitroketone was prepared, m.p. 162–163°.

Anal. Calcd. for $C_{11}H_{14}N_2O_3$: C, 59.45; H, 6.35; N, 12.60. Found: C, 59.71; H, 6.29; N, 12.92.

Oxidation of 3-Methyl-3-(*p*-nitrophenyl)-2-butanone.—To an ice-cold solution of 0.2 g. (0.97 mmole) of 3-methyl-3-(*p*-nitrophenyl)-2-butanone in 3 ml. of concentrated sulfuric acid was added 0.84 g. (8.4 mmoles) of chromic acid. After a few minutes a vigorous exothermic reaction occurred which was moderated with cooling. The mixture was then poured into water, any solid removed by filtration, and after standing a few days crystals deposited from the filtrate. The solid was purified by dissolving in alkali and reprecipitating with acid. The material was identified as *p*-nitrobenzoic acid by a mixed melting point with an authentic sample, m.p. 238–239°, mixed m.p. 238–239°.

3-Methyl-3-(*p*-nitrophenyl)-2-butanone Hydrazone.—A solution of 55 g. (0.27 mole) of 3-methyl-3-(*p*-nitrophenyl)-2-butanone, 130 ml. (2.2 moles) of 85% hydrazine hydrate and 400 ml. of absolute ethyl alcohol was refluxed for 53 hours. Addition of 500 ml. of water precipitated the hydrazone which was removed by filtration and washed with 50% aqueous alcohol, m.p. 94–95°, 43.5 g. (74%). On recrystallization of a sample from absolute alcohol the melting point remained unchanged.

Anal. Calcd. for $C_{11}H_{15}N_3O_2$: C, 59.71; H, 6.83; N, 18.99. Found: C, 60.08; H, 6.57; N, 18.71.

3-Methyl-3-(*p*-nitrophenyl)-2-butanone Azine. Method A.—A solution of 29 g. (0.14 mole) of 3-methyl-3-(*p*-nitrophenyl)-2-butanone, 31 g. (0.14 mole) of 3-methyl-3-(*p*-nitrophenyl)-2-butanone hydrazone, 0.3 g. (1.7 mmoles) of *p*-toluenesulfonic acid and 400 ml. of xylene was refluxed overnight with a Dean–Stark trap. The solution was decanted from a small amount of resin and the product crystallized with cooling. After filtration, the product was washed with xylene, Skellysolve A (b.p. 30–40°) and recrystallized from 150 ml. of *n*-butyl alcohol, m.p. 159–160°, 47.5 g. (83%). The infrared absorption spectrum showed a medium band at 6.11 μ (azomethine).

---

(26) A. Sosa, *Ann. chim.*, **14**, 100 (1940).

(27) A. Favorskii, T. W. Zalesskaya, D. I. Rosanov and G. V. Chelintzev, *J. Gen. Chem.* (*U.S.S.R.*), **5**, 1728 (1935); *Bull. soc. chim.*, [5] 3, 239 (1936).

Anal. Calcd. for $C_{22}H_{26}N_4O_4$: C, 64.37; H, 6.39; N, 13.65. Found: C, 64.43; H, 6.49; N, 13.64.

Method B.—To a solution of 20 ml. of concentrated nitric acid and 20 ml. of concentrated sulfuric acid kept at 0 to −5° was added, with stirring, 10 g. (0.03 mole) of 3-methyl-3-phenyl-2-butanone azine in 10 minutes. The mixture was stirred at 0 to −5° for 1.25 hours, then added to crushed ice and the oil was washed by decanting with water. The product crystallized upon the addition of 50 ml. of methanol. Successive recrystallizations from glacial acetic acid, xylene, and isopropyl alcohol raised the melting point to 157–158°, 1.66 g. (13%). A mixed melting point with material, m.p. 159–160°, prepared from method A melted at 158–160°.

3-(*p*-Acetamidophenyl)-3-methyl-2-butanone Azine.—A solution of 14.16 g. (0.035 mole) of 3-methyl-3-(*p*-nitrophenyl)-2-butanone azine in 150 ml. of dry tetrahydrofuran was reduced under 3.5 atmospheres of hydrogen with 1.2 g. of 10% palladium-on-charcoal. The reduction was highly exothermic and was controlled with cooling and intermittent shaking of the autoclave. The theoretical amount of hydrogen was absorbed and the reaction ceased in about 30 minutes of total shaking time. The catalyst was removed by filtration and the solution was concentrated to about 35 ml. by warming under vacuum. Upon the addition of 50 ml. of acetic anhydride crystallization occurred and the mixture was cooled, treated with an equal volume of Skellysolve A (b.p. 30–40°) and the product was removed by filtration. Recrystallization from 430 ml. of *n*-butyl alcohol gave 10 g., m.p. 276–276.5° (67%). The infrared absorption spectrum showed a medium band at 6.12 μ (azomethine), a strong band at 6.0 μ (amide carbonyl) and a medium band at 3.04 μ (imide).

Anal. Calcd. for $C_{26}H_{34}N_4O_2$: C, 71.86; H, 7.89; N, 12.89. Found: C, 72.01; H, 7.92; N, 12.74.

2-Azo-bis-3-(*p*-acetamidophenyl)-3-methylbutane.—Four hundred and thirty milligrams (1.0 mmole) of 3-methyl-3-(*p*-acetamidophenyl)-2-butanone azine was reduced over 75 mg. of prereduced Adams catalyst and 10 ml. of glacial acetic acid with hydrogen at atmospheric pressure. The reaction ceased in an hour when the theoretical amount of hydrogen was absorbed. The catalyst then was removed by filtration and the solvent removed by warming under vacuum. The remaining acetic acid was neutralized with a saturated sodium bicarbonate solution and the mixture extracted with 25 ml. of chloroform. The organic layer was then separated, dried over anhydrous magnesium sulfate, and after removal of the drying agent by filtration was stirred overnight with 1 g. of yellow mercuric oxide. After filtration and evaporation of the solvent the resultant residue was recrystallized rapidly from 1.5 ml. of *n*-butyl alcohol. The solid was dissolved in a minimum of chloroform, any insoluble material was removed by filtration and finally precipitated with Skellysolve A (b.p. 30–40°), m.p. 214.5–216.5°, 46 mg. (10.5%), ϵ_{max} 43.2, λ_{max} 365 mμ in chloroform.

Anal. Calcd. for $C_{26}H_{36}N_4O_2$: C, 71.52; H, 8.31; N, 12.83. Found: C, 71.67; H, 8.43; N, 13.16.

Acknowledgment.—The authors gratefully acknowledge numerous helpful discussions with Dr. Richard G. Hiskey during the investigation.

BROOKLYN 1, N. Y.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, POLYTECHNIC INSTITUTE OF BROOKLYN]

Neophyl-type Azo Compounds[1]; Their Decomposition and Rearrangement of the Neophyl-type Free Radical

BY C. G. OVERBERGER AND HAROLD GAINER[2]

RECEIVED FEBRUARY 5, 1958

Neophyl radicals were generated by thermal decomposition in solution of azo compounds of the type $[p\text{-}RC_6H_4C(CH_3)_2\text{-}CH(CH_3)\text{-}N{=}]_2$ where R = H, CH_3O or CH_3CONH. The rates of decomposition of the three compounds did not differ from each other by more than 31%, from which it was concluded that the phenyl group did not participate appreciably in the dissociation of the carbon–nitrogen bond (the rate-determining step). The products isolated from the decomposition of the azo compound R = H indicated that at least 23% rearrangement of the neophyl radical had occurred.

Of the several known methods for the generation of neophyl free radicals in solution, none involves the formation of the radical in a primary step.[3–6] This lack of a primary process thus complicates any study of the kinetics of the reaction. When aliphatic azo compounds are thermally decomposed in solution, free radicals usually are formed by an essentially unequivocally first-order unimolecular decomposition.[7] With a free radical of the type derived from VIII there is a great likelihood of rearrangement of the phenyl group.[3–6] A question arises as to whether there is phenyl participation in the rate-determining step, the dissociation of the carbon–nitrogen bond. Substituents in the *p*-position of the phenyl ring might be expected to have some effect, small though measurable, due to resonance interaction of intermediate of type VIa and b on the rate of dissociation of the carbon–nitrogen bond if the phenyl group is participating.

The thermal decomposition in solution of four neophyl-type azo compounds were studied; two diastereoisomers of 2-azo-bis-3-methyl-3-phenylbutane, VIIIa and b, and the *p*-substituted analogs, VIIIc and d. Further, it was of interest to isolate the products of the decomposition of 2-azo-bis-3-methyl-3-phenylbutane to test whether rearrangement of the neophyl radical occurred. An unsuccessful attempt also was made to trap the unrearranged neophyl radical by decomposition of the neophyl azo compound (VIIIa in 1-dodecanethiol).

Decomposition Products. A. Results.—The products which were identified in the decomposition of 2-azo-bis-3-methyl-3-phenylbutane in diphenyl ether as solvent at 255° are indicated

---

(1) This is the 23rd in a series of papers concerned with the preparation and decomposition of azo compounds. For the previous paper in this series, see C. G. Overberger and H. Gainer, THIS JOURNAL, **80**, 4556 (1958).

(2) This paper comprises a portion of a Dissertation presented by Harold Gainer in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Graduate School of the Polytechnic Institute of Brooklyn.

(3) W. H. Urry and M. S. Kharasch, THIS JOURNAL, **66**, 1438 (1944).

(4) S. Winstein and F. H. Seubold, Jr., *ibid.*, **69**, 2916 (1947).

(5) W. H. Urry and N. Nicolaides, *ibid.*, **74**, 5163 (1952).

(6) D. Y. Curtin and M. J. Hurwitz, *ibid.*, **74**, 5381 (1952).

(7) J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1956, p. 422.