TABLE II

OXIDATION PRODUCTS

III	Mp, °C	Form	Formula	C, % Calcd	C, % Found	H, % Calcd	H, % Found	N, % Calcd	N, % Found
a	252–254	a	$C_{14}H_{12}ClNO_6S$	47.00	47.07	3.38	3.46	3.92	3.99
b	226–227[b]	a	$C_{15}H_{14}ClNO_6S$	48.45	48.41	3.80	3.78	3.77	3.71
c	239–241[c]	d	$C_{16}H_{16}ClNO_6S$	49.81	49.97	4.18	4.12	3.63	3.80
d	181–183[c]	d	$C_{15}H_{14}ClNO_6S$	48.45	48.52	3.80	3.70	3.77	3.90
e	228–230	d	$C_{16}H_{16}ClNO_6S$	49.81	49.89	4.18	4.25	3.63	3.71
f	268–270[c]	a	$C_{15}H_{14}ClNO_6S$	48.45	48.63	3.80	3.94	3.77	4.08

[a] Needles. [b] Crystallized from acetonitrile–methanol. [c] Evacuated capillary. [d] Irregular.

Phenanthridizinium Perchlorate (II, R = H).—A solution of 0.8 g of pyrido[2,1-*b*]benzo[*f*]-1,3-thiazepinium perchlorate (I), 1.0 ml of 30% hydrogen peroxide, and 10 ml of glacial acetic acid was heated at 56° for 18 hr, then at 100° for 12 hr. From the cooled solution a buff-colored solid was precipitated by addition of ether. Recrystallization of the solid afforded 0.43 g (63%) of colorless needles, mp 193–195°. A recrystallized sample melted at 197–198° (lit.[6] mp 197°), had the expected composition, and did not depress the melting point of an authentic sample[6] of phenanthridizinium perchlorate.

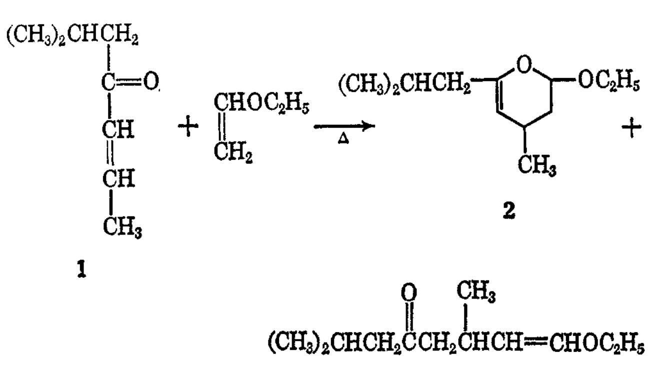
Synthesis of Menthenone and Dihydro Rose Oxide

KENT C. BRANNOCK AND HERMAN E. DAVIS

Research Laboratories, Tennessee Eastman Company, Division of Eastman Kodak Company, Kingsport, Tennessee

Received October 15, 1965

We wish to report a new and convenient synthetic route to menthenone (2-isopropyl-5-methyl-2-cyclohexene-1-one) (7) and dihydro rose oxide (tetrahydro-2-isobutyl-4-methylpyran) (5).[1-4] The condensation of acetaldehyde with methyl isobutyl ketone[5] gave a mixture of the *cis* and *trans* isomers of 6-methyl-2-hepten-4-one (1). The Diels–Alder reaction of 1 with ethyl vinyl ether at elevated temperatures gave a mixture of the *cis* and *trans* isomers of 2-ethoxy-3,4-dihydro-6-isobutyl-4-methyl-2H-pyran (2) along with the lesser amounts of the *cis* and *trans* isomers of 8-ethoxy-2,6-dimethyl-7-octen-4-one (3). The *cis* and *trans* assignments were based on the magnitude of the $-HC{=}CH-$ coupling constants in the nmr spectra.[6]

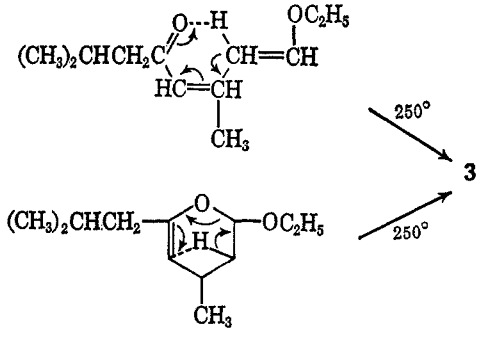


1 2

$$\overset{O}{\underset{}{\|}}\quad (CH_3)_2CHCH_2\overset{O}{\overset{\|}{C}}CH_2\overset{CH_3}{\overset{|}{C}}HCH{=}CHOC_2H_5$$

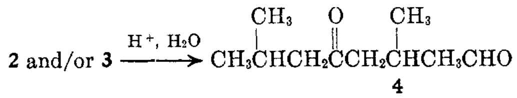
3

As the temperature at which the Diels–Alder reaction was carried out was increased, the relative amount of 3 increased. It is not clear whether 3 was formed directly from the reactants or whether it was derived from 2 by rearrangement. It is possible to explain the formation of 3 by either route as shown. We did show, however, that 2 on heating at 250° was largely converted to 3.



2

Acid-catalyzed hydrolysis of both 2 and 3 gave 3,7-dimethyl-5-oxooctanal (4), which on treatment with base gave methenone (7).



$$2 \text{ and/or } 3 \xrightarrow{H^+,\ H_2O} CH_3\overset{CH_3}{\overset{|}{C}}HCH_2\overset{O}{\overset{\|}{C}}CH_2\overset{CH_3}{\overset{|}{C}}HCH_3CHO$$

4

The hydrogenation of 4 over a supported nickel catalyst gave a mixture of the *cis* and *trans* isomers of dihydro rose oxide (5) as the major product and 3,7-dimethyl-1,5-octanediol (6) as the minor product. The use of a copper chromite catalyst gave the diol as the major product and 5 as the minor product. The diol was readily converted to a mixture of the *cis* and *trans* isomers of 5 by refluxing it in a solvent in the presence of a catalytic amount of an acid.

Experimental Section

6-Methyl-2-hepten-4-one (1).—A mixture of acetaldehyde (132 g, 3 moles) and 4-methyl-2-pentanone (400 g, 4 moles) was cooled in an ice bath and added over a 2-hr period to a solution of potassium hydroxide (11 g) in isopropyl alcohol (300 ml) and 4-methyl-2-pentanone (1200 g, 12 moles). The reaction mixture was stirred and kept at 10–15° during and for 15 min after the addition. Ethyl ether (300 ml) was added, and the solution was washed with water to remove potassium hydroxide.

---

(1) C. F. Seidel and M. Stoll, *Helv. Chim. Acta*, **42**, 1830 (1959).

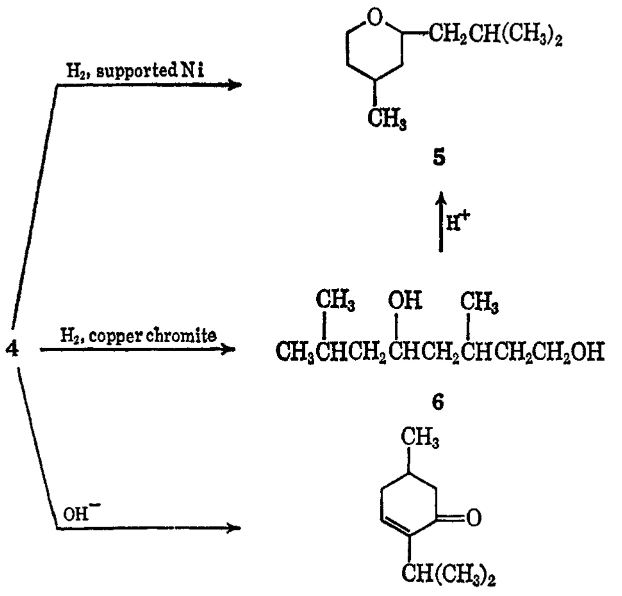
(2) C. F. Seidel, *et al.*, *ibid.*, **44**, 598 (1961).

(3) Y. R. Naves, D. Lamparsky, and P. Ochsner, *Bull. Soc. Chim. France*, 645 (1961).

(4) M. Julia and B. Jacquet, *ibid.*, 1983 (1963).

(5) R. Luft, *Ann. Chim.* (Paris), [13] **4**, 745 (1959); *Chem. Abstr.*, **54**, 8626 (1960).

(6) L. M. Jackson, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press Inc., New York, N. Y., 1959, p 85.



p-Toluenesulfonic acid (0.1 g) was added, and the mixture was distilled to give, after removal of unreacted starting materials, 206 g (55%) of *cis*- and *trans*-6-methyl-2-hepten-4-one, bp 167–168°, $n^{20}\mathrm{D}$ 1.4412 [lit.[5] bp 56–57° (10 mm), $n^{20}\mathrm{D}$ 1.4396].

2-Ethoxy-3,4-dihydro-6-isobutyl-4-methyl-2H-pyran (2).—Ethyl vinyl ether (72 g, 1.0 mole), 6-methyl-2-hepten-4-one (63 g, 0.5 mole), and hydroquinone (0.25 g) were charged into an autoclave and heated at 225° for 5 hr. The mixture was distilled to give, after removal of the excess ethyl vinyl ether, 76 g (77%) of 2, bp 84° (8 mm), $n^{20}\mathrm{D}$ 1.4410. Analysis by glpc and nmr indicated the distillate to be an approximately 50:50 mixture of the *cis* and *trans* isomers of 2; however, the two were not isolated.

Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.7; H, 11.2. Found: C, 72.6; H, 10.9.

8-Ethoxy-2,6-dimethyl-7-octen-4-one (3).—A number of residues from the synthesis of 2 were combined and fractionally distilled at a 9:1 reflux ratio using a 1 × 48 in. vacuum-jacketed column packed with Podbielniak Helipak. Two fractions corresponding to the *cis* and *trans* isomers of 3 were obtained.

The *cis* isomer had a bp of 104–105° (7.7–7.8 mm); $n^{20}\mathrm{D}$ 1.4400; infrared absorptions[7] (smear), 5.88 (s), 6.04 (s), 9.1 (s), and 13.40 (m) μ; nmr spectrum[8] (neat), multiplet at 0.82–1.00 (methyl groups adjacent to >C–H), triplet at 1.19 and quartet at 3.75 (ethoxy), multiplets at 1.8–2.4 (>CH–, –CH₂–) and 3.10 (>CHC=C), a pair of doublets at 4.17 (J = 6.6 and 8.8 cps) (*cis* O–C=CH–), and a doublet at 5.84 ppm, (J = 6.6 cps) (*cis* –OCH=C–). Areas were in the ratio of 9:5:5:1:1:1.

Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.7; H, 11.2. Found: C, 73.3; H, 11.2.

The *trans* isomer had bp 102.5–103° (4.9 mm); $n^{20}\mathrm{D}$ 1.4429; infrared absorptions (smear), 5.85 (s), 6.01 (m), 6.1 (m), 8.5 (s), and 10.72 (m) μ; nmr spectrum (neat), doublets at 0.88 [CH₃–C(CH₃)<] and 0.98 [>C(CH₃)–C=C], triplet at 1.19 and quartet at 3.63 (ethoxy group), multiplet at 1.8–2.7 (>CH, –CH₂–), pair of doublets at 4.63 (J = 12.7 and 7.7 cps) (*trans* –O–C=CH–), and a doublet at 6.24 ppm (J = 12.7 cps, *trans* –OCH=C–). Areas were in the ratio of 6:3:5:6:1:1.

Effect of Heat on 2.—A mixture of the *cis* and *trans* isomers of 2 (92%) and the *cis* and *trans* isomers of 3 (8%) was heated in an autoclave at 250° for 5 hr. By glpc analysis the product was found to consist of 71% 3, 20% 2, and 9% impurities.

3,7-Dimethyl-5-oxooctanal (4) from 2.—A mixture of 2 (79 g, 0.4 mole) and aqueous 1% phosphoric acid (400 ml) was heated and stirred while ethyl alcohol was removed by distillation. When the removal of ethyl alcohol was complete, the organic layer was separated, washed with water to remove the phosphoric acid, and distilled to give 58 g (85%) of 4, bp 69–71° (0.5 mm); $n^{20}\mathrm{D}$ 1.4377; infrared absorptions (smear), 3.9 (w), 5.8 (s), and 5.85 (s) μ; nmr spectrum (neat), doublets at 0.89 (isopropyl methyl groups) and 0.97 (CH₃C<), multiplet at 1.8–2.8 (>CH–, –CH₂–), and triplet at 9.82 ppm (J = 1.5 cps, –CH=O). Areas were in the ratios of 6:3:8:1.

Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.6; H, 10.7. Found: C, 70.5; H, 10.6.

The **mono-2,4-dinitrophenylhydrazone** derivative of 4 melted at 81°.

Anal. Calcd for $C_{16}H_{22}N_4O_5$: C, 54.8; H, 6.3. Found: C, 55.1; H, 6.2.

3,7-Dimethyl-5-oxooctanal (4) from 3.—A mixture of 3 (40 g, 0.2 mole) and aqueous 1% phosphoric acid (200 ml) was stirred and heated while ethyl alcohol was removed selectively by distillation. When the removal of the ethyl alcohol was complete, the organic layer was separated, washed with water to remove the phosphoric acid, and distilled to give 26 g (80%) of 4. Infrared and glpc data were identical with those of the compound obtained from 2.

Menthenone (7).—A mixture of 4 (58 g, 0.338 mole), aqueous 1% sodium hydroxide (400 ml), and isopropyl alcohol (100 ml) was stirred and heated at 80–85° for 3 hr. The organic layer was separated, washed with water, and distilled to give 42 g (82.5%) of 7: bp 81–82° (8 mm); $n^{20}\mathrm{D}$ 1.4716; infrared absorptions (smear), 6.0 (s) and 6.15 (shoulder) μ; nmr spectrum (CCl₄), doublet at 1.05 (methyl groups), multiplets at 2.34 (–CH₂– in ring and –CH) and 3.02 (C=C–CH<), and a doublet at 7.04 ppm (HC=C–). Areas were in the ratio of 9:5:1:1.

Anal. Calcd for $C_{10}H_{16}O$: C, 78.9; H, 10.6. Found: C, 78.9; H, 10.5.

The **semicarbazone** derivative of 7 melted at 155–157° (lit.[9] mp 145–146° and, after solidification, 160–161°).

Anal. Calcd for $C_{11}H_{19}N_3O$: C, 63.1; H, 9.2; N, 20.1. Found: C, 63.1; H, 9.1; N, 20.1.

The **2,4-dinitrophenylhydrazone** derivative of 7 melted at 145–146°.

Anal. Calcd for $C_{16}H_{20}N_4O_4$: C, 57.8; H, 6.1; N, 16.9. Found: C, 57.8; H, 6.1; N, 16.9.

Dihydro Rose Oxide (5) from 4.—Ethyl alcohol (70 ml), 4 (70 g, 0.41 mole), and Girdler G 49A nickel catalyst (7 g) were charged into an autoclave and hydrogenated at 125° and 2000 psi until no further hydrogen was absorbed. The catalyst was removed by filtration, and the mixture was distilled to give, after removal of ethyl alcohol, 43 g (67%) of 5, bp 75–76° (19 mm), $n^{20}\mathrm{D}$ 1.4323, and 12 g of residue which was shown to be mostly 6 by glpc analysis.

Anal. Calcd for $C_{10}H_{20}O$: C, 76.9; H, 12.9. Found: C, 77.0; H, 13.0.

Each isomer of 5 was separated by preparative-scale glpc, and the composition of the mixture as determined by glpc analysis, using the method of Carrol,[10] was 89% *cis* isomer, $n^{20}\mathrm{D}$ 1.4305, lit.[3] $n^{20}\mathrm{D}$ 1.4314, and 11% *trans* isomer, $n^{20}\mathrm{D}$ 1.4379, lit.[3] $n^{20}\mathrm{D}$ 1.4367.

The infrared spectrum of each isomer was in agreement with the data of Naves,[3] except for the absence of a weak absorption at 1716 cm⁻¹ which he reported for the *cis* isomer and which was probably due to a –C=O impurity in his sample. In addition, an authentic sample of 5 prepared by Julia[4] contained two components with retention times identical with ours, although it was predominantly the *trans* isomer.

3,7-Dimethyl-1,5-octanediol (6).—Ethyl alcohol (70 ml), 4 (70 g, 0.41 mole), and copper chromite 1106-P (Harshaw Chemical Co., 7 g) were charged into an autoclave and hydrogenated at 150° and 2500 psi until no further hydrogen was absorbed. The catalyst was removed, and the mixture was distilled to give, after removal of ethyl alcohol and a small amount of 5, 53 g (75%) of 6: bp 124–125° (1.5 mm); $n^{20}\mathrm{D}$ 1.4558; infrared absorptions (smear), 3.0 (s), 7.22 (m), 7.35 (m), and 9.5 (s) μ.

Anal. Calcd for $C_{10}H_{22}O_2$: C, 68.9; H, 12.7. Found: C, 69.5; H, 13.0.

Dihydro Rose Oxide (5) from 6.—Toluene (100 ml), 6 (17.4 g, 0.1 mole), and *p*-toluenesulfonic acid (0.1 g) were heated at reflux temperature while water (1.8 ml) was removed by azeotropic distillation. The crude mixture was washed with water

---

[7] Infrared spectra were recorded on a Baird AB-2 instrument.

[8] Nmr spectra were recorded on a Varian A-60 instrument at 60 Mc. Field position values are referred to tetramethylsilane as an internal standard.

[9] H. E. Eschinazi and H. Pines, *J. Am. Chem. Soc.*, **78**, 1176 (1956).

[10] K. K. Carrol, *Nature*, **191**, 377 (1961).

and then distilled to give, after removal of toluene, 10 g (64%) of a mixture of *cis* (62%) and *trans* (38%) **5**, bp 41° (1 mm), $n^{20}D$ 1.4350. Infrared data and glpc data were in agreement with that of the dihydro rose oxide prepared from **4**.

Acknowledgment.—The authors are grateful to Dr. V. W. Goodlett of these laboratories for interpreting the nmr spectra and to Professor Julia for his kindness in providing the sample of dihydro rose oxide.

Synthesis of β-Substituted Alkylamines *via* Alkylation of N,N-Disubstituted Amides

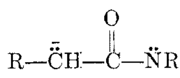
PAUL G. GASSMAN AND B. LAWRENCE FOX[1]

Department of Chemistry, The Ohio State University,
Columbus, Ohio 43210

Received November 15, 1965

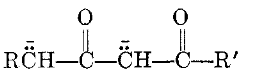
While elucidating the structure of complex rearrangement products from the reaction of N-chloroamines we were confronted with the problem of synthesizing certain 3-substituted 1-methylpyrrolidines. An attractive route to these β-substituted amines appeared to be through lithium aluminum hydride reduction of the corresponding lactams. Lactams of this type were obtainable by base-catalyzed alkylation of the readily available 1-methyl-2-pyrrolidone. While examples of α-C-alkylations of amides in a variety of base-solvent systems can be found in the literature, nearly all such studies have been carried out on α-aryl-substituted amides[2-11] or on amides containing other carbanion-stabilizing substituents on the α-position.[12-16]

Comparison of the anion of an N,N-disubstituted amide (I) and the dianion of a β-diketone (II) shows



$$R{-}\bar{C}H{-}\overset{\overset{O}{\|}}{C}{-}\ddot{N}R_2$$

I

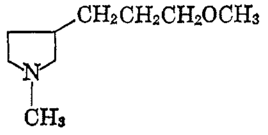


$$R\bar{C}H{-}\overset{\overset{O}{\|}}{C}{-}\bar{C}H{-}\overset{\overset{O}{\|}}{C}{-}R'$$

II

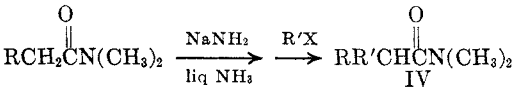
that these ions are isoelectronic. It has been amply demonstrated that dianions of type II may be formed by the reaction of β-diketones with sodium amide in liquid ammonia and that these dianions can be subsequently alkylated.[17] The alkylations of unactivated N,N-disubstituted amides under similar conditions appeared quite feasible.

Addition of 1-methyl-2-pyrrolidone to sodium amide in liquid ammonia caused conversion of the pyrrolidone to a monoanion of type I. Alkylation of this anion with 1-bromo-3-methoxypropane followed by reduction of the resulting lactam with lithium aluminum hydride afforded the expected amine, 1-methyl-3-(3-methoxypropyl)pyrrolidine (III), in 42% over-all yield. In view of these results, it appeared that this procedure would be an efficacious route to a variety of β-alkyl-substituted amines. To delineate the usefulness of this synthetic scheme we carried out the typical reactions compiled in Tables I and II.



III

TABLE I

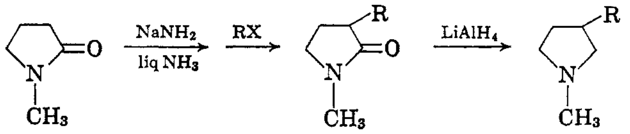


$$RCH_2\overset{\overset{O}{\|}}{C}N(CH_3)_2 \xrightarrow[\text{liq NH}_3]{\text{NaNH}_2} \xrightarrow{R'X} \underset{\text{IV}}{RR'CH\overset{\overset{O}{\|}}{C}N(CH_3)_2}$$

R	R'X	% yield of IV	Bp, °C (mm)	$n^{20}D$
H	CH_3I	68	74 (42)	1.4398[a]
H	CH_3CH_2Br	75	82–83 (37)	1.4421[a]
H	$(CH_3)_2CHBr$	75	72–74 (8)	1.4412
CH_3	CH_3CH_2Br	62	70 (10)	1.4421[b]

[a] Structure was authenticated by comparison with known material. [b] R. Lukěs and J. Langthaler [*Chem. Listy*, **51**, 1869 (1957)] reported bp 76–77° (12 mm), $n^{20}D$ 1.4418.

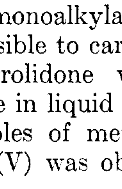
TABLE II



RX	% yield of amine	Bp, °C (mm)	$n^{20}D$	Picrate mp, °C
$CH_3OCH_2CH_2CH_2Br$	42	63–64 (7)	1.4438	127–128
CH_3CH_2Br	41	77 (154)	1.4416	150.5–152.0[a]
$(CH_3CH_2O)_2CHCH_2CH_2Cl$	13	87–88 (1.4)	1.4422	. . .

[a] R. Lukěs, M. Ferles, and O. Strouf [*Collection Czech. Chem. Commun.*, **24**, 212 (1959)] reported bp 123° (740 mm), $n^{20}D$ 1.4303, picrate mp 152.0–152.5°.

In addition to the monoalkylations listed in Tables I and II, it is also possible to carry out a dialkylation. When 1-methyl-2-pyrrolidone was treated with 2 moles of sodium amide in liquid ammonia followed by the addition of 2 moles of methyl iodide, 1,3,3-trimethyl-2-pyrrolidone (V) was obtained in 45% yield.



V

---

(1) Esso Fellow, summer 1964; American Cyanamid Fellow, 1964–1965; Goodyear Foundation Fellow, 1965–1966.

(2) R. B. Meyer and C. R. Hauser, *J. Org. Chem.*, **26**, 3187 (1961).

(3) L. Cheney, W. Wheatly, M. Speeter, W. Byrd, W. Fitzgibbon, W. Minor, and S. Binkley, *ibid.*, **17**, 770 (1952).

(4) P. Janssen, *J. Am. Chem. Soc.*, **78**, 3762 (1956).

(5) T. Hino, *Chem. Pharm. Bull.* (Tokyo), **9**, 979 (1961).

(6) O. Martensson and E. Nilsson, *Acta Chem. Scand.*, **14**, 1129 (1960); **15**, 1026 (1961).

(7) R. B. Moffett and B. D. Aspergren, *J. Am. Chem. Soc.*, **79**, 4462 (1957).

(8) M. Bochmühl and G. Ehrhart, German Patent 731,560 (1943); *Chem. Abstr.*, **38**, 551^2 (1944).

(9) A. E. Brändström, N. S. Hjelte, and O. Martensson, British Patent 771,814 (1957); *Chem. Abstr.*, **52**, 1279*h* (1958).

(10) J. Cusic, U. S. Patent 2,776,282 (1957); *Chem. Abstr.*, **51**, 8813*e* (1957).

(11) O. Martensson, British Patent 796,839 (1958); *Chem. Abstr.*, **53**, 11313*i* (1959).

(12) K. Shimo and S. Wakamatsu, *Kogyo Kagaku Zasshi*, **64**, 299, 303 (1961).

(13) R. Asami, *ibid.*, **60**, 1138 (1957); **61**, 1241 (1958).

(14) K. Shimo, S. Wakamatsu, and T. Inoue, *J. Org. Chem.*, **26**, 4868 (1961).

(15) K. Shimo and R. Asami, *Nippon Kagaku Zasshi*, **78**, 798, 803 (1957).

(16) A. Searles and D. Ressler, *J. Am. Chem. Soc.*, **80**, 3656 (1958).

(17) K. G. Hampton, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, **30**, 61 (1965), and references cited therein.