

perature. Samples of the hydrocarbon layer were then examined for perchlorate content by the colorimetric method described below.

The LiClO_4 served only as a source of HClO_4 and could be replaced by any inorganic perchlorate which would dissolve sufficiently in H_2SO_4 to liberate the required perchloric acid. Alternatively 70% HClO_4 could be added directly to 96% H_2SO_4 . If a large amount of perchloric acid was used, it was necessary to add oleum to compensate for the water in the 70% HClO_4 . The hexane could be replaced with a variety of other substances providing they did not react with H_2SO_4 and the alkyl perchlorate was soluble in them.

Due to the explosive nature of the compounds prepared, the reaction vessel was shielded and isolation of the perchlorate esters was avoided. As long as solvent was present the esters were apparently quite stable. However, if a drop of the hydrocarbon solution was placed on a hot plate, a bright flash was observed after the evaporation of the solvent, illustrating the highly explosive nature of these compounds.

Determination of Perchlorate Esters.—The amount of perchlorate ester present in the hydrocarbon phase of the reaction was estimated by a colorimetric method similar to that described by Bodenheimer and Weiler.³ A standard solution of the copper nitrate-pyridine complex was prepared by combining 4.8 g of $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$, 50 ml of H_2O , and 11 ml of pyridine and diluting to 1 l. with ethanol. Reference standards were prepared from a titrated solution of 70% HClO_4 in EtOH, EtOH, hexane, and the standard solution such that the final solutions contained 5.0 ml of standard, 1.0 ml of EtOH, and 2.0 ml of hexane. The amount of perchlorate formed in a reaction was determined by combining 5.0 ml of standard, 1.0 ml of EtOH, and varying quantities of the hexane layer from the reaction. Additional hexane was added such that the total amount of hexane was 2.0 ml and the tubes were allowed to stand for 1 hr. After centrifuging, the color was compared to the reference tubes. The amount of perchlorate found was then extrapolated to the entire hexane layer. By making 4–6 determinations using different quantities of the hexane layer, an accuracy of $\pm 3\%$ was achieved.

Determination of Nmr Spectra of Alkyl Perchlorates.—The nmr spectra were determined on either a Varian A-60 or T-60 spectrometer. For this purpose the alkyl perchlorates were prepared as described above with the exception that chlorobenzene or hexafluorobenzene was substituted for the hexane layer. The concentration of the perchlorates was 10–20% in the solvent and TMS was used as an internal standard.

On several occasions the nmr was used to estimate the yield of alkyl perchlorate. A weighed portion of toluene was used as the internal standard and combined with a portion of the chlorobenzene layer containing the alkyl perchlorate. The amount of perchlorate was then extrapolated to the entire chlorobenzene layer. This analysis was in very close agreement ($\pm 2\%$) with the one obtained by the colorimetric method.

Registry No.—Perchloric acid, 7601-90-3.

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Reactions of 2,6-Cycloheptadienone and 2,7-Cyclooctadienone with Primary and Secondary Amines. Synthesis of Tropinones and Pseudopelletierines

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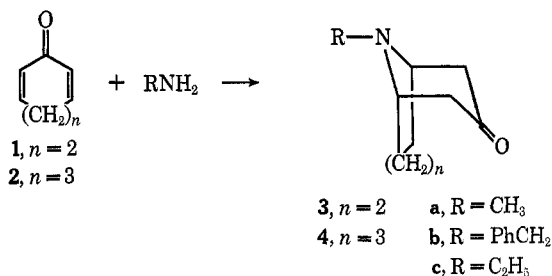
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In his paper describing the synthesis of tropinone (3a) by condensation of methylamine with succindi-

aldehyde and acetonedicarboxylic acid, Robinson¹ also noted "that tropinone might result... by the addition of methylamine to a cycloheptadienone..." Nearly 10 years ago, Horák² reported the characterization by paper chromatography of tropinone prepared from a large excess of methylamine and 20 mg of a mixture of cycloheptadienones, which had been prepared by treatment of a tropinonium salt with base.³ In 1965, Garbisch⁴ described the preparation of 2,6-cycloheptadienone (1), 2,7-cyclooctadienone (2), and other cycloalkadienones from their corresponding cycloalkanones. Although four steps are required in Garbisch's synthesis, they are described thoroughly and the overall yields are good. The reasonable accessibility of 1 and 2 made it possible for us to check and extend the alternative synthetic route suggested by Robinson, and we describe here an easily accomplished synthesis of tropinone (3a), pseudopelletierine (4a), and several of their N-substituted homologs.⁵

Addition of 1 equiv of 2,6-cycloheptadienone⁴ (1) to a 2 M solution of methanolic methylamine at room temperature resulted in a mildly exothermic reaction that could be followed conveniently by examination of the vinyl region in the nmr spectrum. Within 30 min, >95% of the dienone had reacted, and evaporation of the solvent left crude tropinone (3a). Use of 2,7-cyclooctadienone⁴ (2) in place of 1 resulted in a more rapid reaction leading to pseudopelletierine (4a).⁶ We have also used this method to prepare N-benzyl- and N-ethyltropinone (3b and 3c) and N-benzylpseudopelletierine (4b).



In addition, we have found that the cycloalkadienones 1 and 2 react rapidly (10 and 1 min, respectively) with equivalent amounts of dimethylamine hydrochloride (2 M in methanol) in the presence of dimethylamine (ca. 0.1 M) to give the methochlorides of 3a and 4a (5 and 6) directly.⁸

Yields of purified products and their melting or boiling points are summarized in Table I.

Preparation of tropinone, pseudopelletierine, and their N-substituted homologs by condensation of a

(1) R. Robinson, *J. Chem. Soc.*, **111**, 762 (1917).

(2) V. Horák and P. Zuman, *Tetrahedron Lett.*, 746 (1961); V. Horák, *Collect. Czech. Chem. Commun.*, **28**, 1614 (1963).

(3) J. Meinwald, S. L. Emerman, N. C. Yang, and G. Büchi, *J. Amer. Chem. Soc.*, **77**, 4401 (1955).

(4) E. W. Garbisch, Jr., *J. Org. Chem.*, **30**, 2109 (1965). *Caution!* 1 and 2 are skin irritants.

(5) A related condensation has been described by C. Grundmann and G. Ottman [*Justus Liebigs Ann. Chem.*, **605**, 24 (1957)], who prepared anhydroecgonine by condensing methylamine at 125° with the isomeric cycloheptatriene-carboxylic acids obtained by the Buchner reaction.

(6) The cyclooctadienone obtained by oxidation of 1,5-cyclooctadiene⁷ might also be suitable for this and related preparations.

(7) W. J. Farrissey, Jr., U. S. Patent 3,287,427 (Nov 22, 1966); *Chem. Abstr.*, **66**, P115361y (1967).

(8) For other examples of formation of a bicyclic system by Michael-type addition of a tertiary amine, see L. A. Paquette and L. D. Wise, *J. Amer. Chem. Soc.*, **87**, 1561 (1965).

TABLE I

PRODUCTS FROM CONDENSATIONS OF 2,6-CYCLOHEPTADIENONE
OR 2,7-CYCLOOCTADIENONE WITH PRIMARY AMINES
AND DIMETHYLAMINE HYDROCHLORIDE

Compd	Yield, % (wt, g) ^a	Mp or bp (mm), °C
3a	64 (0.89)	42.5–44 (dist), ^b 97 (12)
3b	59 (3.2)	23–24 (dist), 123–124 (0.18) ^c
3c	56 (1.7)	48 (0.1) ^d
4a	53 (0.65)	62–64 (subl) ^e
4b	62 (1.70)	72–73 (MeOH–H ₂ O) ^f
5	64 (1.2)	213 dec (MeOH–Et ₂ O) ^g
6	78 (0.79)	268 dec (MeOH–Et ₂ O) ^h

^a Results tabulated here were from the first effort. Purified products were also characterized by means of their ir and nmr spectra. ^b Mmp 42.5–44°. ^c n_{D}^{25} 1.5540 [lit.^{11a} bp 134–137° (0.4 mm), n_{D}^{25} 1.5526]. Dipiperonylidene derivative, mp 194–195° (C₂H₅OAc) (lit.^{11b} mp 194–195°). ^d n_{D}^{24} 1.4892 [lit.^{11c} bp 41–42° (0.08 mm), n_{D}^{20} 1.4885]. Picrate, mp 190–191° (H₂O) (lit.^{11c} mp 189°). ^e Lit.^{10b} mp 62–64°. ^f Lit.^{11d} mp 70–73° (employing petroleum ether). ^g Anal. Calcd for C₉H₁₆NOCl: C, 56.98; H, 8.45; N, 7.38. Found: C, 57.00; H, 8.45; N, 7.35. ^h Anal. Calcd for C₁₀H₁₈NOCl: C, 58.96; H, 8.90; N, 6.87. Found: C, 58.88; H, 8.94; N, 6.61.

primary amine with the appropriate cycloalkadienone appears to be the most attractive alternative⁹ to the versatile and well-tested Robinson–Schöpf synthesis.^{1,10,11}

Registry No.—1, 1192-93-4; 2, 1073-76-3; 3a, 532-24-1; 3b, 28957-72-4; 3c, 3423-30-1; 4a, 28861-13-4; 4b, 28861-14-5; 5, 28861-15-6; 6, 28957-73-5.

Acknowledgment.—We wish to thank Professor E. C. Friedrich for a generous sample of 2.

(9) For other alternatives, see P. Karrer and H. Alagil, *Helv. Chim. Acta*, **30**, 1776 (1947); B. F. Putney and T. O. Soine, *J. Amer. Pharm. Ass.*, **44**, 17 (1955); W. Parker, R. A. Raphael, and D. I. Wilkinson, *J. Chem. Soc.*, 2433 (1959); N. J. Turro and S. S. Edelson, *J. Amer. Chem. Soc.*, **90**, 4499 (1968).

(10) (a) C. Schöpf and G. Lehmann, *Justus Liebig's Ann. Chem.*, **518**, 1 (1935); (b) A. C. Cope, H. L. Dryden, Jr., and C. F. Howell, "Organic Syntheses," Collect. Vol. IV, Wiley, New York, N. Y., 1963, p 816.

(11) Papers in which applications of the Robinson–Schöpf synthesis are described include (a) S. Archer, U. S. Patent 2,845,427 (July 29, 1958) [*Chem. Abstr.*, **53**, 430 (1959)]; (b) L. C. Keagle and W. H. Hartung, *J. Amer. Chem. Soc.*, **68**, 1608 (1946); (c) K. Nador, Gy. Hajdu, B. Szecso, and F. Zima, *Arzneim.-Forsch.*, **12**, 305 (1962); (d) C. F. Boehringer and Soehne GmbH, Netherland Appl. 284,570 (Jan 25, 1965); *Chem. Abstr.*, **63**, 4354 (1965).

Geometrical Isomers of Ortho-Substituted Acetophenone *N,N*-Dimethylhydrazones

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Our previous paper² described the preparation of aldehyde and ketone *N,N*-dimethylhydrazones and their facile conversion to the corresponding azine-free unsubstituted hydrazones. We now wish to report the presence of *E* and *Z* ortho-substituted acetophenone *N,N*-

dimethylhydrazones³ and the isolation of their methiodides. During the course of this work, 16 meta- and para-substituted acetophenone *N,N*-dimethylhydrazones were prepared² and in each case existed as a single stereoisomer, which was presumed to have the *E* configuration through the analysis of the nmr spectral data. The CCH₃ chemical shifts varied randomly from 2.24 to 2.35 ppm downfield from TMS, whereas the NCH₃ chemical shifts changed from 2.49 to 2.62 ppm correlating rather well to the Hammett $\sigma_{m,p}$ parameters,⁴ albeit the chemical shift differences are quite small. Similar preponderance of a single isomer has been reported for ketone *N*-methyl imines⁵ and aldehyde *N,N*-dimethylhydrazones.⁶

The nmr spectra of the ortho-substituted acetophenone *N,N*-dimethylhydrazones (1a–d)² no longer appeared as two characteristic methyl singlets but rather indicated a mixture of two geometric isomers or conceivably restricted rotational isomers. The observed resonances have been attributed to mixtures of *E* and *Z* isomers, since the latter was eliminated by absence of any simplification of the nmr spectra at elevated temperatures.⁷ The glc analysis⁸ of 1a showed a 60:40 ratio of the isomeric dimethylhydrazones; attempted preparative glc collection of each isomer in our hands resulted in the isolation of fractions which isomerized to mixtures identical with the starting material as attested to by both nmr and glc analysis. Similar results were obtained with 1 irrespective of the ortho substituent (Table I). The rapid syn–anti isomerization of 1a–d

TABLE I
PMR CHEMICAL SHIFTS^a FOR METHYL PROTONS

Compd	R	<i>E</i> isomer		Isomer ratio, <i>E</i> : <i>Z</i>	<i>Z</i> isomer	
		C–CH ₃	N–CH ₃		C–CH ₃	N–CH ₃
1a	OCH ₃	2.25	2.51	60:40	2.10	2.28
1b	CH ₃	2.31	2.50	53:47	2.08	2.28
1c	Br	2.24	2.52	57:43 ^b	2.15	2.31
1d	Cl	2.28	2.51	68:32 ^b	2.15	2.25
1e	H	2.26	2.52	100:0		

^a Chemical shifts are parts per million downfield from internal TMS; CCl₄ solvent, concentration 7%. ^b Estimated by nmr data.

can occur *via* either the in-the-plane inversion mechanism or out-of-plane rotation mechanism; the inversion mechanism seems to have been conclusively verified in

(3) J. E. Blackwood, C. L. Gladys, K. L. Loening, A. E. Petrarca, and J. E. Rush, *J. Amer. Chem. Soc.*, **90**, 509 (1968); reviewed by E. L. Eliel, *J. Chem. Educ.*, **48**, 163 (1971).

(4) J. Hine, "Physical Organic Chemistry," 2nd ed, McGraw-Hill, New York, N. Y., 1962, pp 85–93.

(5) J. B. Lambert, W. L. Oliver, and J. D. Roberts, *J. Amer. Chem. Soc.*, **87**, 5085 (1965).

(6) (a) G. J. Karabatsos, R. A. Taller, and F. M. Vane, *Tetrahedron Lett.*, 1081 (1964); (b) G. J. Karabatsos and R. S. Taller, *Tetrahedron*, **24**, 3923 (1968).

(7) Samples were subjected to temperatures of as high as 180°; the nmr spectra were essentially unaltered over the range –80 to 180°. The distribution ratio at both 30 and 180° corresponded well to the glc ratio of isomers.

(8) A 0.5 in × 9 ft stainless steel column packed with 20% SE-30 on 60–80 Chromosorb W at 150° was employed in conjunction with a Varian Aerograph Model 90-P. All samples were trapped at –80° and immediately subjected to nmr analysis.

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(2) G. R. Newkome and D. L. Fishel, *J. Org. Chem.*, **31**, 677 (1966); *Org. Syn.*, **50**, 102 (1970).