Reaction of 2-Acyl-1,3-indandiones with 1,8-Naphthalenediamine. A New Route to 2-Substituted Perimidines

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A number of 2-acyl-1,3-indandiones reacted with 1,8-naphthalenediamine to give 2-substituted perimidines and 1,3-indandione. Under essentially the same conditions 2-diphenylacetyl-1,3-indandione gave 2-methylperimidine, 2,2′-*o*-phenylenediperimidine, and diphenylmethane. Mechanisms for these different reactions are presented. A number of new perimidines are described.

The reactions of 2-acyl-1,3-indandiones with diamines have been shown to give noncyclic or cyclic condensation products, depending upon the structure of the acyl group and the reaction conditions.[1-4] Among the cyclic compounds, indenopyrazolones and diazepinones have been reported from this laboratory.[2,4]

The specific reaction of 2-acyl-1,3-indandiones (**1**) with 1,8-naphthalenediamine (**2**) has now been investigated as a possible route to eight-membered heterocyclic compounds. We have found, however, that this reaction proceeds similarly to that reported by Sachs[5] between β-keto esters and 1,8-naphthalenediamine. In fact, 2-substituted perimidines[6a] (**5a–j**, Scheme I) and 1,3-indandione were obtained, instead of the expected 8-substituted benzo[3,4]cyclopenta[2,1-*f*]naphtho[1,8-*b*,*c*][1,5]diazocin-9(14*H*)-one[6b] (**3**).

The mechanism proposed for this reaction is shown in Scheme II and contains a series of nonisolable intermediates.

The absence of even small amounts of a noncyclized condensation compound among the reaction products indicates that ring closure of **6** occurs rapidly. The cleavage of **7** can be considered formally analogous to the cleavage of β diketones in the presence of bases.[7] The carbanion resulting from cleavage of a β diketone is stabilized through resonance with the remaining carbonyl group. In structure **7** the cleavage is even more favorable due to the presence of two carbonyl groups, either of which could stabilize the pair of electrons remaining with the indandione molecule.

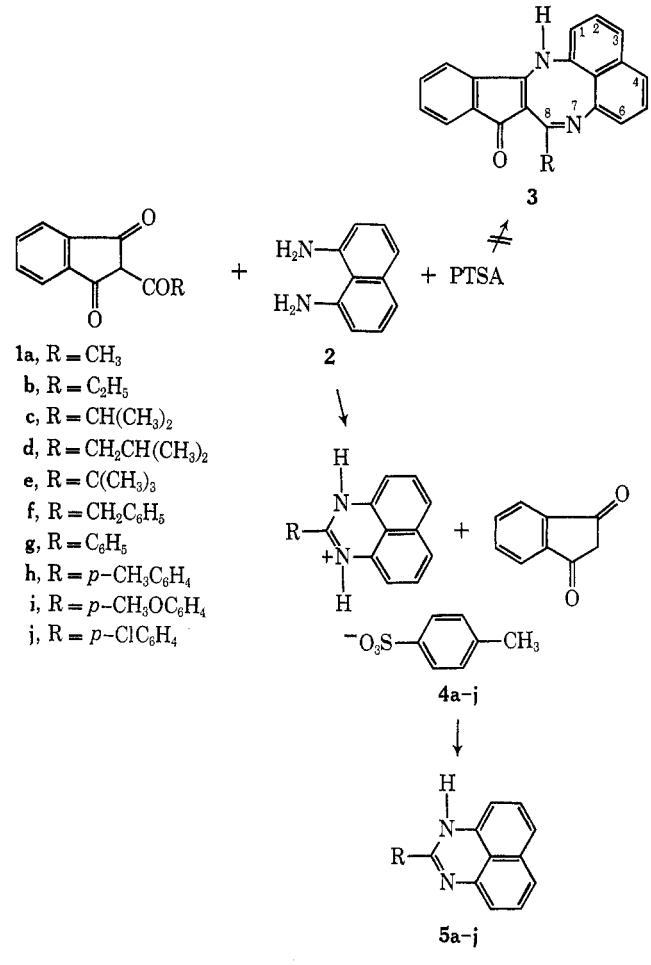
The condensation of the 2-acyl-1,3-indandiones **1a–j** with diamine **2** was run in ethanol, using a stoichiometric amount of *p*-toluenesulfonic acid as the catalyst. The perimidines were separated as the *p*-toluenesulfonic acid salts (**4a–j**) in yields of 50% or better. The other product of the reaction, 1,3-indandione, was isolated through column chromatography of the reaction residue and identified by comparison with an authentic sample.

The perimidine salts bearing an alkyl group in the 2 position are green, whereas those with an aryl group in this position are yellow-orange. The elemental analyses of these salts were found to agree with their molecular formulas.

Salts **4a–j** were converted to the free bases (**5a–j**) by neutralization with dilute ammonium hydroxide. Several of these perimidines had previously been synthesized and in these cases the melting points were in agreement with those reported in the literature.

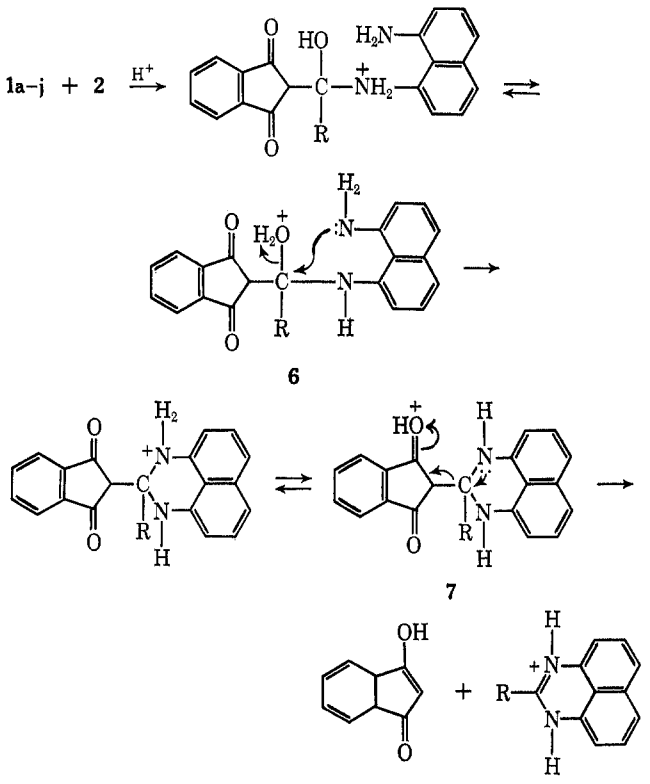
Unlike the acylindandiones **1a–j**, 2-diphenylacetyl-1,3-indandione reacts with diamine **2** to give 2-methylperimidine (**5a**), 2,2′-*o*-phenylenediperimidine (**11**), and diphenylmethane. This different behavior is not completely unexpected, considering that 2-diphenylacetyl-1,3-indandione was found to be the only 2-acyl-1,3-indandione investigated to give with hydrazine a derivative with the hydrazono group in the indan ring.[1] A reasonable mechanism for the formation of compounds **11** and **5a** is shown in Scheme III.

SCHEME I

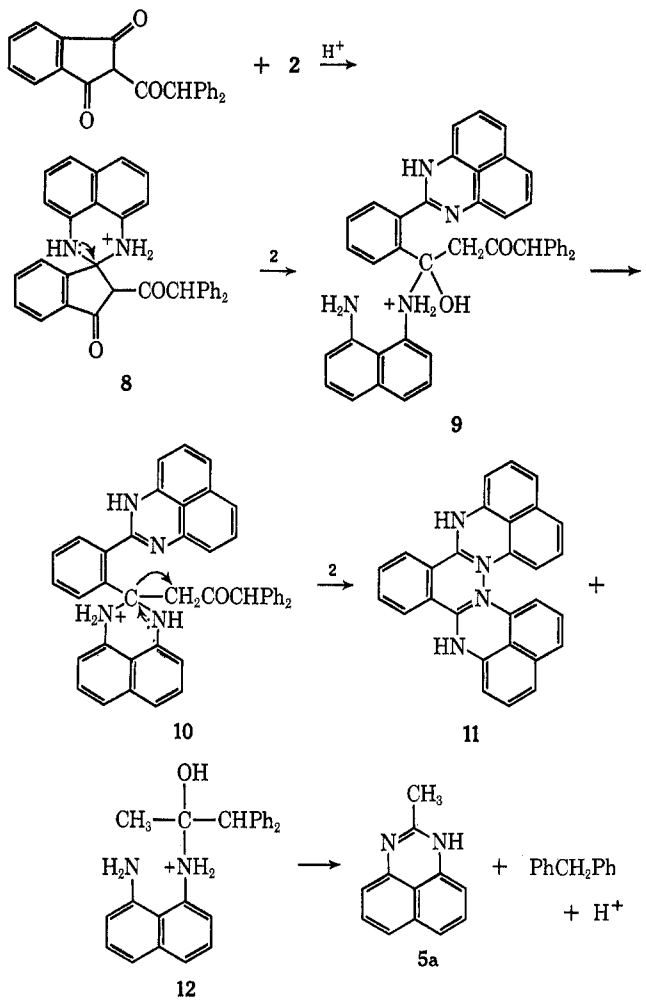


(1) R. A. Braun and W. A. Mosher, *J. Amer. Chem. Soc.*, **80**, 2749 (1958).
(2) R. A. Braun and W. A. Mosher, *J. Org. Chem.*, **24**, 648 (1959).
(3) W. A. Mosher and S. Piesch, *ibid.*, **35**, 1026 (1970).
(4) W. A. Mosher and S. Piesch, *ibid.*, **35**, 2109 (1970).
(5) F. Sachs, *Justus Liebigs Ann. Chem.*, **365**, 72, 156 (1909).
(6) (a) The possibility of the formation of 2-substituted perimidines from 1,8-naphthalenediamine and the acid-cleaved products (esters) of 2-acyl-1,3-indandiones, as suggested by the referee, is eliminated by the fact that 2-acyl-1,3-indandiones are not cleaved by acids. (b) The referee has suggested that the use of a weak acid and a nonalcoholic solvent in the reaction of 2-acyl-1,3-indandiones and 1,8-naphthalenediamine would favor the formation of the diazocinone **3**. Unpublished work by W. A. Mosher and S. Piesch showed that the diazocinone **3** was not formed when this reaction was run in ethanol or in chlorobenzene in the presence of acetic acid as the catalyst.
(7) E. Gould, "Mechanism and Structure in Organic Chemistry," Holt, Reinhart and Winston, New York, N. Y., 1959, pp 337–339.

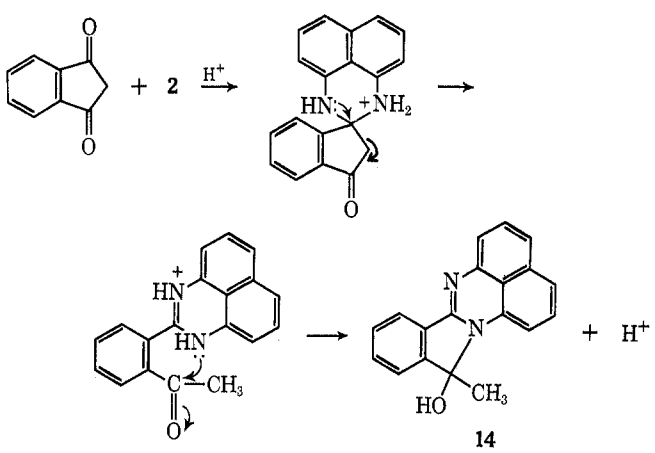
SCHEME II



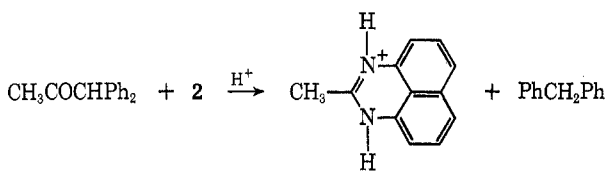
SCHEME III



The assumption that diamine **2** attacks the indan carbonyl with subsequent ring opening (step **8** to **9**) is supported by the results of a separate experiment where 1,3-indandione was allowed to react with **2**. The only product isolated was 10-methyl-10-phthaloperinol (**14**) indicating that ring opening must have occurred along the following path.



Once the ring opening has taken place, it is apparent that two subsequent cleavage reactions would account for the presence of 2-methylperimidine. The first of these cleavages (step **10** to **11**) is formally analogous to that shown by β diketones and previously mentioned. That the second cleavage (step **12** to **5a**) occurred is supported by the results of a separate experiment where



2-methylperimidine and diphenylmethane were obtained from the reaction of 1,1-diphenylacetone and diamine **2** in the presence of *p*-toluenesulfonic acid.

The identity of **5a**, **11**, and diphenylmethane was established by comparing the properties of these compounds with those of authentic samples prepared by independent routes.

In the condensation of 2-acyl-1,3-indandiones with diamines, such as hydrazines and *o*-phenylenediamines, to form noncyclic 1,1 adducts, several tests have been used thus far to indicate which of the available carbonyl groups participate in the reaction.[1,4,8] The results of this investigation show that formation of 1,3-indandione from the reaction of 2-acyl-1,3-indandiones with 1,8-naphthalenediamine may be used as another, more reliable, test to indicate that the side chain carbonyl is the reacting group.

Experimental Section[9]

2-Substituted Perimidine *p*-Toluenesulfonates (4a–j).—To a refluxing solution of diamine **2** (0.013 mol) and *p*-toluenesulfonic

(8) W. A. Mosher and I. S. Bechara, *J. Heterocycl. Chem.*, **7**, 843 (1970).

(9) Melting points were taken on a Fisher-Johns melting point apparatus between circular cover plates and are uncorrected. The infrared spectra were determined in potassium bromide pellets with a Perkin–Elmer Model 137 spectrophotometer. The ultraviolet spectra were taken on a Perkin-Elmer spectrophotometer, Model 202. The nuclear magnetic resonance spectra were obtained on a Varian Associates spectrometer, Model A-60A. Elemental analyses were performed by Dr. A. Bernhardt, Mikroanalytisches Laboratorium, Max Planck Institute fur Kohlenforschung, Mülheim (Ruhr), West Germany; by the Micro Analysis, Inc., Marshallton, Del.; and by the M-H-W Laboratories, Garden City, Mich.

TABLE I

2-SUBSTITUTED PERIMIDINE *p*-TOLUENESULFONATES (4a–j)

Compd	R	Mp, °C[a]	Yield, %	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
4a	CH_3	285–287	72	$C_{19}H_{18}N_2O_3S$	64.39	5.12	7.91	64.70	5.36	7.77
4b	C_2H_5	281–283	63	$C_{20}H_{20}N_2O_3S$	65.19	5.47	7.60	65.20	5.33	7.68
4c	$CH(CH_3)_2$	280–282	50	$C_{21}H_{22}N_2O_3S$	65.94	5.80	7.33	65.78	5.60	7.25
4d	$CH_2CH(CH_3)_2$	258–260	55	$C_{22}H_{24}N_2O_3S$	66.64	6.10	7.07	66.51	5.93	6.93
4e	$C(CH_3)_3$	257–259	54	$C_{22}H_{24}N_2O_3S$	66.64	6.10	7.07	66.83	6.26	6.93
4f	$CH_2C_6H_5$	255–256	54	$C_{25}H_{22}N_2O_3S$	69.74	5.15	6.51	69.60	5.30	6.32
4g	C_6H_5	245–246	70	$C_{24}H_{20}N_2O_3S$	69.21	4.84	6.72	69.68	5.00	7.03
4h	*p*-$CH_3C_6H_4$	246–247	56	$C_{25}H_{22}N_2O_3S$	69.74	5.15	6.51	69.52	5.00	6.55
4i	*p*-$CH_3OC_6H_4$	287–288	50	$C_{25}H_{22}N_2O_4S$	67.24	4.97	6.27	67.06	5.18	6.39
4j	*p*-ClC_6H_4	310–312	62	$C_{24}H_{19}N_2O_3SCl$	63.92	4.25	6.21	63.79	4.34	6.05

[a] All compounds decompose at the melting point.

TABLE II

2-SUBSTITUTED PERIMIDINES (5a–j)

Compd	R	Mp, °C Found	Mp, °C Lit.	Infrared spectrum, cm^{-1} NH	Infrared spectrum, cm^{-1} C=N and C=C	Chemical shift, NH, δ (broad)[a]
5a	CH_3	210 dec	210[b]	3140	1645, 1610–1595[c]	9.41
5b	C_2H_5	182 dec	161[b]	3145	1645, 1605–1590[c]	7.00
5c	$CH(CH_3)_2$	146–147	143[d]	3150	1640, 1600	7.00
5d	$CH_2CH(CH_3)_2$	169–170		3160	1645, 1605–1595[c]	6.83
5e	$C(CH_3)_3$	162		3200	1640, 1595	7.00
5f	$CH_2C_6H_5$	197–198 dec	194[b]	3140	1645, 1605–1595[c]	7.00
5g	C_6H_5	188	187[b]	3150	1640, 1600	7.66
5h	*p*-$CH_3C_6H_4$	141–142		3160	1645, 1601	7.16
5i	*p*-$CH_3OC_6H_4$	210–211 dec	212[d]	3140	1640, 1595	7.00
5j	*p*-ClC_6H_4	172–173		3200	1640, 1600	7.16

[a] The NH proton in each case exchanged on addition of deuterium oxide and integrated after exchange for one proton. [b] See ref 5. [c] Doublet. [d] N. Buu-Hoi, P. Jacquignon, and M. Marty, *Bull. Soc. Chim. Fr.*, 461 (1960).

acid monohydrate (0.011 mol) in anhydrous ethanol (200–250 ml) was added dropwise over a 0.5–1-hr period a solution of the appropriate 2-acyl-1,3-indandione[10,11] (0.010 mol) in 65 ml of ethanol (except in **4j** where the ethanolic solution of **1j** was added in one portion). The mixture was refluxed for an additional 24 hr, concentrated to half-volume under reduced pressure, and cooled. The precipitate was collected by filtration, washed with ether, dried, and recrystallized from ethanol to give **4a–j**, as green or yellow-orange crystals. Partial evaporation of the filtrate gave an additional amount of product. (The mother liquor A was saved and chromatographed as described below.) Yields, melting points, and analyses of compounds **4a–j** are listed in Table I. These compounds show ir absorption bands in the 2700–2800-cm^{-1} region (N^+H_2), at 1650 (C=N or C=C) and 1150–1200 cm^{-1} (asymmetric SO_2), and doublets at 1010–1050 cm^{-1} (symmetric SO_2).

In the special case of compound **4a**, the above quantities of reactants were changed to acylindandione **1a** (0.026 mol), diamine **2** (0.036 mol), *p*-toluenesulfonic acid (0.027 mol), and ethanol (450 ml). For compound **4j**, 600 ml of ethanol was used.

The mother liquor A was evaporated to dryness and the residue dissolved in chloroform (4 ml) and chromatographed on activated alumina (elution with chloroform). The compounds isolated from the column in order of elution were diamine **2**, 1,3-indandione, and unreacted 2-acyl-1,3-indandione.

Most of the 1,3-indandione dimerized on the alumina, as indicated by the appearance of a bright purple band at the head of the column, which did not elute with chloroform. This band was removed from the alumina by extraction with water. The resulting purple solution was acidified with 6 *N* hydrochloric acid and the precipitate was crystallized from dioxane to give bright yellow crystals of [$\Delta^{1,2'}$-biindan]-1′,3,3′-trione (bindone), mp 210–211° (lit.[12,13] 208–211°). Mixture melting point showed no depression. An authentic sample of 1,3-indandione chromatographed and extracted following the above procedure gave an identical product (mixture melting point showed no depression).

2-Substituted Perimidines (5a–j).—The general procedure used to prepare these compounds is illustrated by the preparation of **5g**. To a stirred slurry of finely pulverized **4g** (1 g, 0.0024 mol) in water (100 ml) was added concentrated ammonium hydroxide (4 ml). After standing for 4 hr, the precipitate was collected by filtration, washed with water until the washings were neutral, and dried at 60° *in vacuo* to yield 0.59 g (100%) of **5g**. The melting points, ir absorption frequencies, and NH chemical shifts of perimidines **5a–j** are listed in Table II.

Reaction of 2-Diphenylacetyl-1,3-indandione with Diamine 2.—A solution of 2-diphenylacetyl-1,3-indandione (17 g, 0.05 mol) in ethanol (1000 ml) was added in one portion to a refluxing solution of compound **2** (10 g, 0.065 mol) and *p*-toluenesulfonic acid monohydrate (10 g, 0.053 mol) in ethanol (500 ml), and the mixture refluxed as described in the method for preparing compounds **4**. Upon cooling in ice unreacted 2-diphenylacetyl-1,3-indandione (13.2 g) was recovered by filtration. Successive evaporation and cooling of the filtrate gave a precipitate, which through fractional crystallization from ethanol yielded 1.9 g (27% based on diamine **2** available) of **4a** as green platelets, mp 285–287° (this salt neutralized with ammonium hydroxide gave **5a** as shown by mixture melting point with an authentic sample prepared from 2-acetyl-1,3-indandione as described above), and 2.5 g (20% based on diamine **2** available) of the *p*-toluenesulfonic acid salt of 2,2′-*o*-phenylenediperimidine as bright yellow needles, mp >300°.

Anal. Calcd for $C_{42}H_{34}N_4O_6S_2$: C, 66.83; H, 4.54; N, 7.42. Found: C, 66.77; H, 4.62; N, 7.31.

The above salt, neutralized with ammonium hydroxide, gave a product which was found identical (ir and nmr spectra) with an authentic sample of **11** prepared by a different route (see below).

The mother liquor, after separation of **4a** and of the *p*-toluenesulfonic acid salt of **11**, was taken up in chloroform, concentrated to approximately 20 ml, and chromatographed on activated alumina (elution with chloroform). Evaporation of the first fraction gave 0.25 g of diphenylmethane, identified by spectral comparison with an authentic sample.

2,2′-*o*-Phenylenediperimidine (11).—A solution of 2-(2-perimidyl)benzoic acid[14] (2 g, 0.007 mol) and *p*-toluenesulfonic

(10) L. B. Kilgore, J. H. Ford, and W. C. Wolfe, *Ind. Eng. Chem.*, **34**, 494 (1942).

(11) R. L. Horton and K. C. Murdock, *J. Org. Chem.*, **25**, 938 (1960).

(12) W. Wislicenus and A. Kötzle, *Justus Liebigs Ann. Chem.*, **252**, 72 (1889).

(13) K. C. Murdock, *J. Org. Chem.*, **24**, 845 (1959).

(14) F. Sachs, *Justus Liebigs Ann. Chem.*, **365**, 60 (1909).

acid (1.32 g, 0.007 mol) in ethanol (250 ml) was added dropwise over a 1-hr period to a refluxing solution of compound **2** (2.2 g, 0.014 mol) and *p*-toluenesulfonic acid (1.32 g, 0.007 mol) in ethanol (100 ml). The mixture was refluxed for 24 hr and cooled in ice. A small amount of the *p*-toluenesulfonic acid of **2** was separated by filtration and the filtrate was concentrated *in vacuo* to approximately 150 ml and cooled in ice. The precipitate was collected by filtration and washed with ether until all the formed 10-phthaloperinone was removed. Recrystallization of the residue from ethanol yielded 1.6 g (30%) of the *p*-toluenesulfonic acid salt of **11** as bright yellow needles, mp >300°. This salt was neutralized with ammonium hydroxide. Chromatography on alumina of the resulting red solid and recrystallization from dimethylformamide–water gave **11**, mp >300°.

Anal. Calcd for $C_{28}H_{18}N_4$: C, 81.93; H, 4.42; N, 13.65. Found: C, 81.84; H, 4.88; N, 13.47.

Reaction of 1,3-Indandione with Diamine 2. 10-Methyl-10-phthaloperinol (14).—To a refluxing solution of **2** (1.58 g, 0.01 mol) and *p*-toluenesulfonic acid monohydrate (1.9 g, 0.01 mol) in ethanol (100 ml) was added dropwise over 0.5 hr a solution of 1,3-indandione (1.46 g, 0.01 mol) in ethanol (100 ml). The mixture was refluxed for an additional 24 hr, concentrated to *ca.* 50 ml under reduced pressure, and cooled in ice to give 2.7 g (54%) of the *p*-toluenesulfonic acid salt of **14** with ethanol of crystallization as bright red-orange needles, mp 114–124°, with softening and evolution of ethanol. Removal of the ethanol of crystallization was carried out by refluxing a mixture of the above salt (2.7 g) with acetone (250 ml) for 24 hr, collecting the solid by filtration, and washing with acetone. A 62% yield was obtained.

To a slurry of the above *p*-toluenesulfonic acid salt (1.6 g, 0.0035 mol) in water (50 ml) was added concentrated ammonium hydroxide (2 ml); the mixture was allowed to stand for 4 hr. The yellow precipitate collected by filtration, washed with water until free of ammonia, and dried at 60° *in vacuo* gave 1.0 g (100%) of a product which was found identical (mixture melting point, ir, and nmr) with an authentic sample of **14**, prepared from phthalic acid and diamine **2** following the method of Sachs.[15]

Reaction of 1,1-Diphenylacetone with Diamine 2.—A solution of 1,1-diphenylacetone (4.2 g, 0.02 mol) in ethanol (75 ml) was treated with a solution of diamine **2** (3.2 g, 0.02 mol) and *p*-toluenesulfonic acid monohydrate (3.8 g, 0.02 mol) in ethanol (200 ml), following the procedure described above for compound **14**. Upon cooling, 5.7 g (80%) of green platelets was separated and identified as **4a**. The filtrate was evaporated and the dark gummy residue taken up in chloroform and chromatographed on alumina gave diphenylmethane, identified by spectral comparison with an authentic sample.

Registry No.—**2**, 479-27-6; **4a**, 28478-03-7; **4b**, 28478-04-8; **4c**, 28478-05-9; **4d**, 28478-06-0; **4e**, 28478-07-1; **4f**, 2847-08-2; **4g**, 28478-09-3; **4h**, 28537-42-0; **4i**, 28478-10-6; **4j**, 28478-11-7; **5a**, 5157-10-8; **5b**, 28478-13-9; **5c**, 28478-14-0; **5d**, 28478-15-1; **5e**, 28478-16-2; **5f**, 28537-43-1; **5g**, 15666-84-9; **5h**, 25110-47-8; **5i**, 25110-46-7; **5j**, 28478-19-5; **11**, 28478-20-8; **11** *p*-toluenesulfonic acid salt, 28478-21-9.

Acknowledgment.—We gratefully acknowledge the valuable assistance of Dr. Mario F. Sartori in connection with this research.

(15) F. Sachs, *Justus Liebigs Ann. Chem.*, **365**, 117, 120 (1909).

Tetrahydroindan Derivatives. Products from the Diels–Alder Condensation of 1-Vinylcyclopentene and *trans*-*o*-Methyl-β-nitrostyrene

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Three isomeric 5-*o*-tolyl-4-nitro- and 4-*o*-tolyl-5-nitro-3a,4,5,6-tetrahydroindans (compounds **1**, **2**, and **3**) were obtained from the Diels–Alder condensation of 1-vinylcyclopentene and *trans*-*o*-methyl-β-nitrostyrene. The presence of the fourth isomer was not detected. Structure assignment was done by nmr.

Vapor phase chromatography (vpc) of the product of the Diels–Alder condensation of *trans*-*o*-methyl-β-nitrostyrene and 1-vinylcyclopentene indicated three components which were designated **1**, **2**, and **3** according to the order of emergence from a QF-1 column. The integrated peaks were in the approximate ratio of 2:1:1, respectively. The products were separated by descending dry column chromatography[2] on silica gel. The presence of the fourth isomer was not detected. The isolated isomers were characterized by nmr to be *trans*-4-nitro-*cis*-5-*o*-tolyl-3a,4,5,6-tetrahydroindan (**1**), *cis*-4-*o*-tolyl-*trans*-5-nitro-3a,4,5,6-tetrahydroindan (**2**), and *cis*-4-nitro-*trans*-5-*o*-tolyl-3a,4,5,6-tetrahydroindan (**3**).[3] Compound **1** was isomerized to **5** when chromatographed on acid-washed alumina or by treating with base. Compounds **2**, **3**, and **5** were desired as possible intermediates for the preparation of certain cyclopentanohexahydrophenanthridines.

Characterization by nmr was done from the signals of the hydrogens at C-4 and C-5, which are isolated from those of the other alicyclic hydrogens. The signal of the hydrogen on the nitro-bearing carbon is readily recognized because of the large deshielding resulting from the electronegativity and magnetic anisotropy of the nitro group.[4] The signal of the hydrogen on the *o*-tolyl-bearing carbon is also recognizable from other signals, as shown for *trans*-4-nitro-5-*o*-tolycyclohexene-3,3,6,6-d_4 (**6**)[5] (see Table I for chemical shift data). The positions of the substituents, C-4 *vs.* C-5, are readily determined from the multiplicity of the signals. H-4 is adjacent to only two hydrogens and its signal will be either a triplet or a quartet (doublet of doublets), while the signals of H-5 will be more complex because of spin–spin splitting by three adjacent hydrogens. Thus, structures **1** and **3** can be differentiated from their positional isomers **2** and **4**. Differentiation between diastereomers is readily done from the widths of the signals of H-4 and H-5; for example, in isomer **3**, in its most probably conformation, H-4 is axial and coupled with axial H-5 and pseudoaxial H-4a, while in the diastereo-

(1) (a) Public Health Service Predoctoral Fellow 5-F01-GM-34,830; (b) abstracted in part from the Ph.D. dissertation of B. D. Whelton, University of Washington, 1970.

(2) B. Loev and M. M. Goodman, *Chem. Ind. (London)*, 2026 (1967).

(3) In the nomenclature adopted the configuration of the substituents (cis or trans) is related to the axial bridgehead hydrogen on C-3a.

(4) (a) A. C. Huitric and W. F. Trager, *J. Org. Chem.*, **27**, 1926 (1962); (b) W. F. Trager, F. F. Vincenzi, and A. C. Huitric, *ibid.*, **27**, 3006 (1962); (c) D. B. Roll, B. J. Nist, and A. C. Huitric, *Tetrahedron*, **20**, 2851 (1964).

(5) A. C. Huitric, J. B. Carr, W. F. Trager, and B. J. Nist, *ibid.*, **19**, 2145 (1963).