Effect of β Substituents on the Reactions of Amines with α-Bromo-α,β-Unsaturated Ketones

NORMAN H. CROMWELL AND MARVIN C. MCMASTER[1]

Avery Laboratory, University of Nebraska, Lincoln, Nebraska 68508

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The acyclic α-bromo-α,β-unsaturated ketone, 2-bromo-3,3-diphenylacrylophenone (**2**), and a cyclic analog, 2-bromo-3-phenylindenone-1 (**11**), were studied from the standpoint of the effect of the presence of two β-aryl groups on the reactions with amines. The bromo ketone **2** produced α-amino-α,β-unsaturated ketones with both primary and secondary amines. These acyclic α-amino-α,β-unsaturated ketones undergo a facile acid-catalyzed hydrolysis–cyclization to 1,3-diphenyl-1-hydroxyindan-2-one. The cyclic bromo ketone **11** gave 2-amino-3-phenylindenones with secondary amines but produced a new type of aziridine with primary amines. Thus cyclohexyl amines gave 1-cyclohexyl-6-(cyclohexylimino)-1,1a,6,6a-tetrahydro-1a-phenylindeno[1,2-*b*]azirine.

The reactions of acyclic α,β-dibromo ketones with primary and secondary amines have been discussed in a review article,[2] and in several subsequent papers[3] from this laboratory. It is shown that dehydrobromination of the dibromo ketone to an α-bromo-α,β-unsaturated ketone, as a first step, is followed by 1,4 additions of the amines. The resulting α-bromo-β-amino ketones react further to give either α,β-diamino ketones, α- or β-amino-α,β-unsaturated ketones, or, when primary amines are used, aziridinyl ketones.

Examples of endocyclic α-bromo-α,β-unsaturated ketones were also examined and found to give similar results,[4] but the reactions of amines with dibromo addition products of the exocyclic α,β-unsaturated ketones, 2-benzal-1-tetralones,[5] and 2-benzal-1-indanones,[5b,6] which have no hydrogen α to the carbonyl gave quite different results often leading to elimination–rearrangement–substitution products of the β-ketoallylamine type.[5b,7]

This paper reports the first study of the reactions of amines with bromine derivatives of α,β-unsaturated ketones having no hydrogen β to the carbonyl. We chose for this purpose the known and related 3,3-diphenylacrylophenone[8] and 3-phenylindenone-1 derivatives.[9]

Results and Discussion

Reactions with Amines.—2-Bromo-3,3-diphenylacrylophenone (**2**) reacted with the secondary amines, morpholine, piperidine, and N-methylcyclohexylamine to give good yields of the 3,3-diphenyl-2-(N,N-disubstituted amino)acrylophenones (**3**, **4**, and **5**), respectively. No trace of α,β-diamino ketones was detected in these experiments. Previously the less substituted α-bromochalcone had been found to give mixtures of α-aminochalcones and α,β-diaminodihydrochalcones with these bases.[2] In using this α-bromo-α,β-unsaturated ketone **2** the most interesting result was the formation of 2-cyclohexylamino-3,3-diphenylacrylophenone (**6**) from the reaction with cyclohexylamine. The product **6** appears to be the first example of an acyclic α-monosubstituted amino-α,β-unsaturated ketone. Ordinarily, primary amines give aziridinyl ketones[2,3a] in these reactions. In the present case the presence of the second phenyl group in the β position is expected to add to the resonance stabilization of the α,β-unsaturated carbonyl system. (See Scheme I.)

In a preliminary communication[10] it was reported that 2-bromo-3-phenylindenone (**11**)[6] reacts with piperidine in benzene solution at room temperature to give 2-piperidino-3-phenylindenone (**12**). This cyclic α-bromo-α,β-unsaturated ketone has been found to react in an analogous manner with morpholine to produce the corresponding α-amino-α,β-unsaturated ketone **13**. These same products were obtained in somewhat higher yield, starting with the α,β-dibromo ketone, 2,3-dibromo-3-phenylindanone (**10**, Scheme II).[9]

The reaction of these two bromine derivatives of 3-phenylindenone with primary amines gave interesting aziridine derivatives of a new class. With cyclohexylamine and methylamine the Schiff bases **15** and **16** of the expected ethylenimine ketones resulted. Previously,[11] it was reported that the cyclic α-bromo-α,β-unsaturated ketone, 8-bromoperinaphthenone-7, reacts with cyclohexylamine to give the ethylenimine ketone rather than the Schiff base. Apparently the carbonyl group of the saturated five-membered ring of indanones is very reactive toward amines,[12] but it was found that the α-amino-α,β-unsaturated ketone **13** was unchanged on standing with cyclohexylamine in benzene solution.

Structure Studies with Amino Derivatives.—In previously studied series[2,3,11] acid hydrolysis of α-amino-α,β-unsaturated ketones to known 1,2-diketones has been offered as part of the proof of structure. The 2-amino-3,3-diphenylacrylophenones **3**–**6** were somewhat slow to hydrolyze and color was discharged from the solutions only after prolonged heating with 20% sulfuric acid. The product obtained in good yield in all instances was the known[13] 1,3-diphenyl-1-hydroxy-

(1) Abstracted from the Ph.D. Thesis of M. C. McMaster, University of Nebraska, 1965; presented in part at the 153rd National Meeting of the American Chemical Society, Miami Beach, Fla., April 1967.

(2) N. H. Cromwell, *Chem. Rev.*, **38**, 83 (1946).

(3) (a) For reactions with primary amines, see N. H. Cromwell, R. E. Bambury, and J. L. Adelfang, *J. Am. Chem. Soc.*, **82**, 4241 (1960), and previous papers in the series. (b) For reactions with secondary amines, see N. H. Cromwell and G. D. Mercer *ibid.*, **79**, 3819 (1957); J. D. Sculley and N. H. Cromwell, *J. Org. Chem.*, **16**, 94 (1951); N. H. Cromwell and K.-C. Tsou, *ibid.*, **15**, 1219 (1950).

(4) See N. H. Cromwell and R. D. Campbell, *ibid.*, **22**, 520 (1957), and previous papers in the series.

(5) (a) A. Hassner and N. H. Cromwell, *J. Am. Chem. Soc.*, **80**, 901 (1958); (b) E.-M. Wu, Ph.D. Thesis, University of Nebraska, 1966.

(6) B. D. Pearson, R. P. Ayer, and N. H. Cromwell, *J. Org. Chem.*, **27**, 3038 (1962).

(7) N. H. Cromwell and E.-M. Wu, *Tetrahedron Letters*, 1499 (1966).

(8) R. Barre and E. P. Kohler, *J. Am. Chem. Soc.*, **50**, 2036 (1928).

(9) R. Weisz and S. Luft, *Monatsch.*, **48**, 338 (1927).

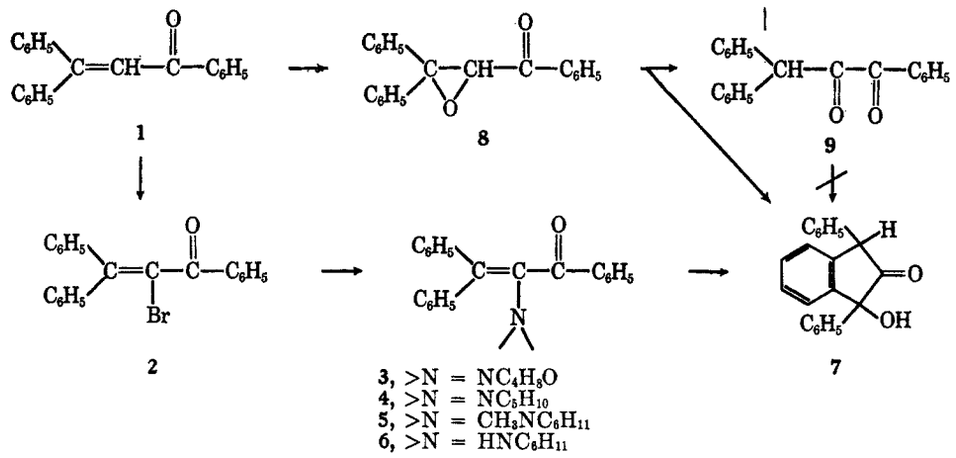
(10) A. E. Pohland, M. C. McMaster, R. D. Badger, and N. H. Cromwell, *J. Am. Chem. Soc.*, **87**, 2510 (1965).

(11) N. H. Cromwell, D. B. Capps, and S. E. Palmer, *ibid.*, **73**, 1226 (1951).

(12) In an unpublished study 3-phenyl-1-indanone has been found to react at room temperature with cyclohexylamine in benzene solution after standing for 5 days to produce a good yield of 3-phenyl-1-cyclohexyliminoindanone, mp 97–98°.

(13) S. Ecary, *Ann. Chim.* (Paris), [12] **3**, 445 (1948).

SCHEME I



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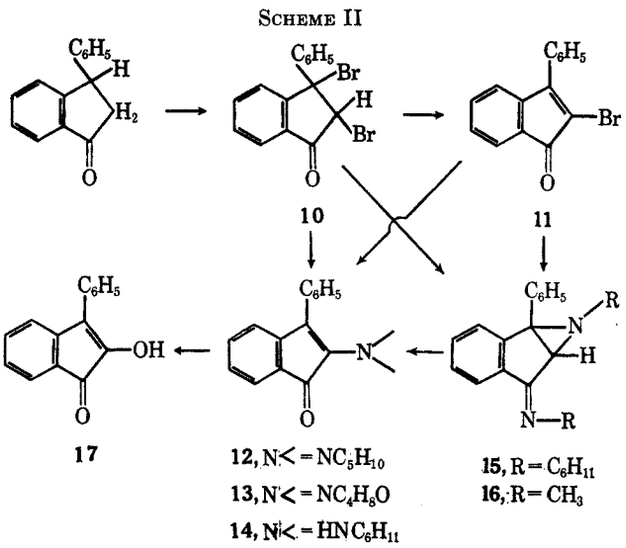


indanone-2 (**7**). Although it seemed reasonable that the known 1,2-diketone, 1,3,3-triphenylpropane-1,2-dione (**9**)[14] was an intermediate product in the hydrolysis this was shown not to be the case. Refluxing **9** with 20% sulfuric acid for 12 hr left the diketone relatively unchanged. Somewhat related cyclizations of this acyclic chain have been reported by Kohler and Weiner[14b] who obtained 1-chloro-1,3-diphenylindanone-2 on reaction of 3,3-diphenyl-2,3-epoxypropiophenone (**8**) with hydrogen chloride in glacial acetic acid at −10°. Barre and Kohler[8] found that bromination of **1** in chloroform at room temperature, rather than at reflux temperature, gave a mixture of the expected monobromo ketone **2** along with some 1,2-dibromo-1,3-diphenylindene, which was also obtained on refluxing **2** with acetic acid saturated with hydrogen bromide.

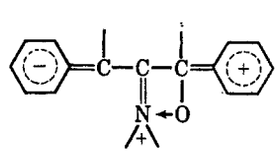
The rearrangement of 1,3-diphenyl-2,3-epoxyacrylophenone (**8**) by alkoxide produces mainly the 1,2-diketone **9**,[14b] but we have now found that a small amount (~7%) of the cyclized product **7** is also formed on making the basic reaction mixture acidic with sulfuric acid. The mechanism of these cyclizations, which would seem to involve protonation of the carbonyl group to produce a carbonium ion (C+OH), is being explored in further work.

(14) (a) H. O. House and D. J. Reif, *J. Am. Chem. Soc.*, **77**, 6525 (1955); (b) E. P. Kohler and N. Weiner, *ibid.*, **56**, 434 (1934).

The acid-catalyzed hydrolysis of the 2-amino-3-phenylindanones **12–14** gave the known[15] 3-phenylindan-1,2-dione **17**, as did the indenoazirines **15** and **16**. The partial hydrolysis of **15** to **14** in low yield has been accomplished using a solution of potassium acetate in acetic acid and will be reported elsewhere.[16]

The infrared and ultraviolet spectra of the new α-amino-α,β-unsaturated ketones **1–6** and **12–14** further justified the assignment of the structures. The carbonyl infrared bands between 1656 and 1665 cm^{-1} for **1–6** may be compared with those reported earlier[17] for α-aminochalcones between 1664 and 1672 cm^{-1}. This same band was found at 1712 cm^{-1} for the 2-amino-3-phenylindenones, **12** and **13**, and at 1720 cm^{-1} for the cyclohexylamino ketone **14**,[10] as expected for the indenone ring system.[18] The two indenoazirines, **15** and **16**, exhibited medium-intensity imino absorption peaks at 1658 and 1667 cm^{-1}, respectively.

Both the 3,3-diphenylacrylophenones and 3-phenylindenones showed the ultraviolet absorption normally associated with conjugated ketones: benzoyl $\pi \rightarrow \pi^*$, cinnamoyl, and, in some cases, small acrylophenone resonance bands. The α-amino-α,β-unsaturated ketones also showed the long wavelength band previously ascribed as characteristic for the delocalization (**17**)



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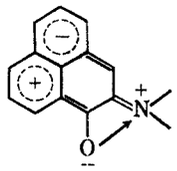
possible in such systems.[19] In both of the new series of compounds this latter band appears at longer wavelengths, and, in some cases, with a stronger extinction coefficient than the similar band for α-aminochalcones,[19] implying increased resonance stabilization and increased probability of attaining the ionic excited state. The visible purple color of the 2-amino-3-phenylindenones **12–14** was reminiscent of the 8-aminoperinaphthenone-7

(15) C. F. Koelsch, *ibid.*, **58**, 1321 (1936).
(16) D. K. Wall, A. E. Pohland, J.-L. Imbach, R. C. Badger, M. C. McMaster, and N. H. Cromwell, unpublished work.
(17) N. H. Cromwell, F. A. Miller, A. R. Johnson, R. L. Frank, and D. J. Wallace, *J. Am. Chem. Soc.*, **71**, 3337 (1949).
(18) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc, New York, N. Y., 1958, pp 132–157.
(19) N. H. Cromwell and W. R. Watson, *J. Org. Chem.*, **14**, 411 (1949).

derivatives which also are red or purple in color.[11,20] These two cyclic series have related opportunities for extensive electron delocalization, **18** and **19**.



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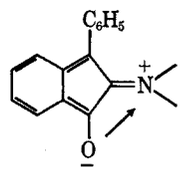

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Proton magnetic resonance spectra of the azirines **15** and **16** were useful in showing the presence of the three-ring proton in the 2 position at τ 6.8.

Experimental Section[21]

3,3-Diphenyl-2-morpholinoacrylophenone (3).—A 2-g (0.0055 mole) sample of 2-bromo-3,3-diphenylacrylophenone (**2**)[8] in 50 ml of morpholine was refluxed for 22 hr. The red solution was cooled and diluted with anhydrous ether precipitating 97.3% of morpholine hydrobromide. Evaporation of the filtrate gave a red oil. Chromatography of the oil on Fluorisil, eluting with dichloromethane–hexane (1:3), and crystallization of the crude product from hexane gave red needles of **3**: 1.18 g (58%); mp 119–121°; infrared bands at 1659 cm^{-1} (C=O); ultraviolet λ_{max} 250 mμ (ε 11,940), sh 310 (7300), and 421 (3400).

Anal. Calcd for $C_{25}H_{23}NO_2$: C, 81.26; H, 6.28; N, 3.79. Found: C, 80.91; H, 6.27; N, 4.24.

3,3-Diphenyl-2-piperidinoacrylophenone (4).—In a similar manner, 1 g (0.00275 mole) of **2** was heated for 21.5 hr at 85° in 15 ml of piperidine to yield a dark orange solution from which precipitated 80% of the amine hydrobromide on dilution with ether. Evaporation of the filtrate left a solid residue which was recrystallized from petroleum ether (bp 30–70°) to yield **4** as large, orange crystals: 0.72 g (71.3%); mp 129–130.5°; infrared band at 1662 cm^{-1} (C=O); ultraviolet λ_{max} 246 mμ (ε 17,800), sh 309 (7300), and 425 (2900).

Anal. Calcd for $C_{26}H_{25}NO$: C, 84.94; H, 6.86; N, 3.81. Found: C, 84.44; H, 6.60; N, 3.91.

3,3-Diphenyl-2-(N-methylcyclohexylamino)acrylophenone (5).—Refluxing 2 g (0.0055 mole) of **2** in 35 ml of N-methylcyclohexylamine under nitrogen for 8.5 hr gave a red solution which precipitated 89% of N-methylcyclohexylamine hydrobromide on dilution with ether. The oil from evaporation of the filtrate was chromatographed on alumina, eluting with benzene–petroleum ether (bp 60–70°) (3:7). Recrystallization from methanol gave bright red needles of **5**: 1.33 g (61%); mp 118–120°; infrared band at 1656 cm^{-1} (C=O); ultraviolet λ_{max} 247 mμ (ε 20,300), sh 313 (9000), and 440 (4800).

Anal. Calcd for $C_{28}H_{29}NO$: C, 85.02; H, 7.39; N, 3.54. Found: C, 84.73; H, 7.60; N, 3.42.

2-Cyclohexylamino-3,3-diphenylacrylophenone (6).—A mixture of 3 g (0.0083 mole) of **2** and 50 ml of cyclohexylamine was refluxed under nitrogen for 6 hr. The solution was cooled and diluted with ether to give a quantitative precipitate of cyclohexylamine hydrobromide. Evaporation of the filtrate yielded a red oil. Suction chromatography on alumina, eluting with benzene–petroleum ether (bp 60–70°) (1:4), yielded red-orange crystals of IV: 0.69 g (22%); mp 95–97°; infrared band at 1665 cm^{-1} (C=O); ultraviolet λ_{max} 246 mμ (ε 20,800), sh 278 (10,800), and 410 (3000). This compound decomposed to a thick gum on standing in solution.

Anal. Calcd for $C_{27}H_{27}NO$: C, 85.00; H, 7.13; N, 3.67. Found: C, 84.92; H, 6.88; N, 3.62.

Hydrolysis of 2-Amino-3,3-diphenylacrylophenones.—A suspension of a 0.48-g (0.0013 mole) sample of **3** was refluxed for 5 hr in a 20% aqueous sulfuric acid solution. A white solid weighing 0.35 g (89.6%), mp 183–193°, was filtered from the reaction mixture. Recrystallization from 80% aqueous acetic acid gave 1,3-diphenyl-1-hydroxyindan-2-one (**7**), mp 198–202°. This compound gave an undepressed mixture melting point and an infrared spectrum superimposable with that of an authentic sample.[13]

In a similar manner **7** was obtained from **4** in 88.4% yield, from **5** in 83.4% yield, and from **6** in 79.8% yield. All products gave undepressed mixture melting points with an authentic sample of **7**.[13]

Rearrangement of 1,3-Diphenyl-2,3-epoxyacrylophenone (8).—Following the method of Kohler and Weiner[14b] 2.0 g (0.0067 mole) of the epoxy ketone **8** was refluxed for 2 min with 0.725 g (0.0134 mole) of sodium methoxide in 25 ml of ethanol. The deep red solution was cooled, neutralized with dilute sulfuric acid, and poured onto crushed ice. From the yellow oily product was obtained a 60% yield of the 1,2-diketone **9** and a 7% yield of 1,3-diphenyl-1-hydroxyindan-2-one (**7**). Treating the impure oily **9** with *o*-phenylenediamine produced 2-phenyl-3-benzhydrylquinoxaline,[14b] mp 195–198°, in 56% yield.

Stability of 1,3,3-Triphenylpropane-1,2-dione (9) to Acid.—A 1-g sample of the impure oil **9** was refluxed for 12 hr in 20% sulfuric acid under the conditions used to hydrolyze 2-amino-3,3-diphenylacrylophenones. On cooling, the yellow residue was extracted with ether and the solvent was evaporated. The infrared spectra of this residue and of the yellow starting material were superimposable.

2-Morpholino-3-phenylindenone (13).—A benzene solution of 5 g (0.013 mole) of 2,3-dibromo 3-phenylindanone (**10**)[9] and 5.65 ml (0.065 mole) of morpholine stood for 4 days at room temperature. On diluting with 100 ml of ether, the solution precipitated 4.35 g (99.8%), mp 229–231°, of morpholine hydrobromide. Evaporation of the filtrate and crystallization of the dark residue from ethanol gave 3.16 g (84.4%) of **13** as black crystals: mp 107–108°; ultraviolet λ_{max} 268 mμ (ε 35,700) and 525 mμ (ε 1855); infrared band at 1712 cm^{-1} (C=O).

Anal. Calcd for $C_{19}H_{17}NO_2$: C, 78.33; H, 5.88; N, 4.81. Found: C, 78.33; H, 6.01; N, 4.97.

Compound **13** was also prepared from 2-bromo-3-phenylindenone (**11**)[9,22] in 63% yield by reaction with 4 molar equiv of morpholine in benzene.

2-Piperidino-3-phenylindenone (12).—A 2-g (0.0055-mole) sample of **10** and 2.45 ml (0.025 mole) of piperidine reacted exothermically in 20 ml of benzene to produce a purple solution. After standing for 3 days at room temperature, the purple reaction mixture precipitated 1.70 g (85.5%) of piperidine hydrobromide, mp 229–233°, on dilution with ether. The filtrate was evaporated and the residue was redissolved in ether and washed with water to give a solution from which was recovered 1.26 g (82%) of lustrous, black crystals of **12**: mp 80.5–81.5° (ethanol); ultraviolet λ_{max} 272 mμ (ε 29,900) and 540 mμ (ε 1950); infrared band at 1712 cm^{-1} (C=O).

Anal. Calcd for $C_{20}H_{19}NO$: C, 83.01; H, 6.62; N, 4.84. Found: C, 83.45; H, 6.74; N, 4.79.

Compound **12** was obtained in 32.7% yield by treating **11** with 4 molar equiv of piperidine in benzene.

1-Cyclohexyl-6-(cyclohexylimino)-1,1a,6,6a-tetrahydro-1a-phenylindeno[1,2-*b*]azirine (15).—A mixture of 16.7 ml (0.138 mole) of cyclohexylamine and 10 g (0.028 mole) of **10** in 40 ml of benzene in a foil-wrapped flask was allowed to react at room temperature. After 4 days, diluting with ether precipitated 9.74 g (98%) of cyclohexylamine hydrobromide, mp 202–203°. A yellow solid was recovered from the filtrate. Recrystallization from petroleum ether (bp 60–70°) (charcoal) gave 8.48 g (81.1%) of **15** as a white solid: mp 159–160°; ultraviolet λ_{max} 252 mμ (ε 17,950); infrared band at 1658 cm^{-1} (C=N); pmr signals at τ 8.0–9.0 (24 H), 6.8 (1 H), and 2.1–2.9 (9 H).

Anal. Calcd for $C_{32}H_{27}N_2$: C, 84.33; H, 8.39; N, 7.29. Found: C, 84.10; H, 8.46; N, 7.16.

In a similar manner **15** was prepared in 73% yield from **11** on standing for 4 days at room temperature with 4 molar equiv of cyclohexylamine in benzene solution.

(20) N. H. Cromwell and R. D. Campbell, *J. Am. Chem. Soc.*, **79**, 3456 (1957).

(21) Melting points were determined on a Kofler micro hot stage or in a capillary in a stirred oil bath. Infrared spectra were determined in carbon tetrachloride, except where indicated, with either a Perkin-Elmer Model 21 or Model 327 spectrophotometer. Ultraviolet spectra were measured with a Cary 11-ms spectrophotometer in 2,2,4-trimethylpentane. Proton magnetic resonance spectra were measured on a Varian A-60 spectrometer using carbon tetrachloride containing tetramethylsilane as an internal reference. Elemental analyses were performed by Microtech Laboratory, Skokie, Ill. and by Alfred Bernhardt, Mikroanalytisches Laboratorium, Mülheim, Germany.

(22) An alternate preparation of 2-bromo-3-phenylindenone (**11**) consists of dehydrohalogenation of **10** by reaction with 4 molar equiv of N-methylpiperidine in benzene. After ether precipitation of the amine hydrobromide, **11** can be crystallized from methanol as orange plates (70.4%), mp 113–114°.

1-Methyl-6-(methylimino)-1,1a,6,6a-tetrahydro-1a-phenylindeno[1,2-*b*]azirine (16).—A solution of 5 g (0.014 mole) of the dibromo ketone **10** in 300 ml of anhydrous ether was saturated with methylamine. The closed flask was allowed to stand at room temperature for 24 hr. Isolation of the product and recrystallization from petroleum ether (bp 60–70°) gave colorless, light-sensitive crystals: mp 99–100°; yield 70%; $\gamma_{C=N}^{CCl_4}$ 1667 cm^{-1}; λ_{max} 247 mμ (ε 14,600); nmr τ 7.94 (three-ring CH_3), 6.81 (three-ring H), 6.58 (=NCH_3), 2.20–2.87 (nine aromatic H's).

Anal. Calcd for $C_{17}H_{16}N_2$: C, 82.22; H, 6.50; N, 11.28. Found: C, 81.93; H, 6.49; N, 11.09.

The azirine **16** was also prepared in 77% yield from the reaction of the monobromo ketone **11** with methylamine in ether solution on standing for 4 days at room temperature.

2-Hydroxy-3-phenylindenone (17).—A magenta solution of 1 g (0.0034 mole) of **12** dissolved in 10 ml of cold, concentrated sulfuric acid was poured with vigorous stirring into 800 ml of water (70°). On cooling, 0.65 g (85.3%) of a red-brown solid, mp 140–144°, was obtained. A mixture melting point with an authentic sample of **17**[15] was undepressed and infrared spectra were superimposable; infrared (CCl_4) bands were at 3500 (OH) and 1724 cm^{-1} (C=O); ultraviolet showed λ_{max} (MeOH) 252 mμ (ε 31,000) and 480 mμ (ε 1360).

In a similar manner, **17** was produced in 88.4% yield from **14**, in 72.4% from **15**, and in 81.3% from **16**.

Registry No.—**3**, 13118-12-2; **4**, 13118-13-3; **5**, 13118-14-4; **6**, 13135-39-2; **12**, 1713-38-8; **13**, 13118-15-5; **15**, 1981-53-9; **16**, 13118-16-6; **17**, 1713-37-7.

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The Stereochemistry of Some Diphenylbicyclo[3.3.1] Ketones

HENRY M. HELLMAN, ROBERT A. JERUSSI,

Department of Chemistry, New York University, New York, New York 10453

AND JOHN LANCASTER

Central Research Division, American Cyanamid Company, Stamford, Connecticut

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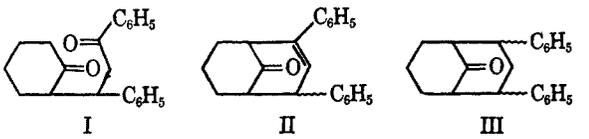
Spectral and chemical methods have been used to determine the configurations of the two epimers of 2,4-diphenylbicyclo[3.3.1]non-2-en-9-one and of the three possible stereoisomers of 2,4-diphenylbicyclo[3.3.1]nonan-9-one. Three compounds corresponding to these formulas have been reported previously, but they were not characterized stereochemically. Details of the isolation of these five compounds are described.

In 1933, Allen and Sallans[1] prepared 2-(α-phenyl-β-benzoylethyl)cyclohexanone (I) by the Michael addition of cyclohexanone to benzalacetophenone, and treated it with concentrated sulfuric acid in ethanol to give 55% of 2,4-diphenylbicyclo[3.3.1]non-2-en-9-one (II), mp 143°. Cyclization at a lower temperature gave about 1% of an isomeric ketone, mp 151°.

Structure II has also been prepared in 70–88% yields by heating I with acetic acid–hydrochloric acid,[2] or more simply with acetic acid–*p*-toluenesulfonic acid.[3] None of these investigations involved stereochemical identifications, but Cope, Fawcett, and Munn[2] showed from spectral data that II has the double bond in the 2 position rather than at 1 (bridgehead) as formulated by Allen and Sallans.

Hydrogenation of II gave 2,4-diphenylbicyclo[3.3.1]-nonan-9-one (III), mp 143–143.8°, not further identified.[2]

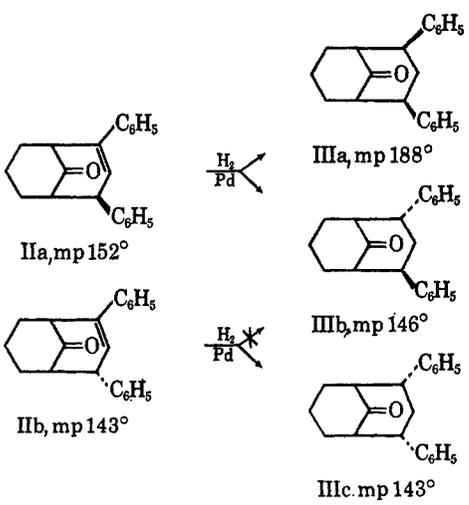


I II III

Results and Discussion

We have been able to prepare II in the yields reported,[2] but usually cyclization of I in acetic acid–hydrochloric acid gave a product having a wide melting range. This was identified as a mixture of the isomeric ketones originally described by Allen and Sallans[1] by isolation of both ketones, mp 152 and 143°, from one cyclization reaction. That these are the epimeric ketones IIa and IIb (Scheme I) is suggested by their mode of formation, by the fact that the 143° isomer could be isomerized to the 152° isomer with base, and by their nmr spectra. The infrared spectra of the two isomers were different and they gave different 2,4-dinitrophenylhydrazone and oxime derivatives. Each absorbed 1 mole of hydrogen, and the 143° compound reduced potassium permanganate in 95% ethanol[2] while the 152° one did not.

SCHEME I



Direct evidence concerning the stereochemistry at the C-4 position was obtained by inspection of the proton magnetic resonance spectra of the two unsaturated isomers shown in Figures 1 and 2. The spectrum of the 152° isomer (Figure 1) has singlets at τ 7.35 and

(1) C. F. H. Allen and H. R. Sallans, *Can. J. Res.*, **9**, 574 (1933).
(2) A. C. Cope, F. S. Fawcett, and G. Munn, *J. Am. Chem. Soc.*, **72**, 3399 (1950).
(3) S. Julia and D. Varech, *Bull Soc. Chim. France*, 1127 (1959).