Reactions of 2-Acyl-1,3-indandiones with Aliphatic Diamines

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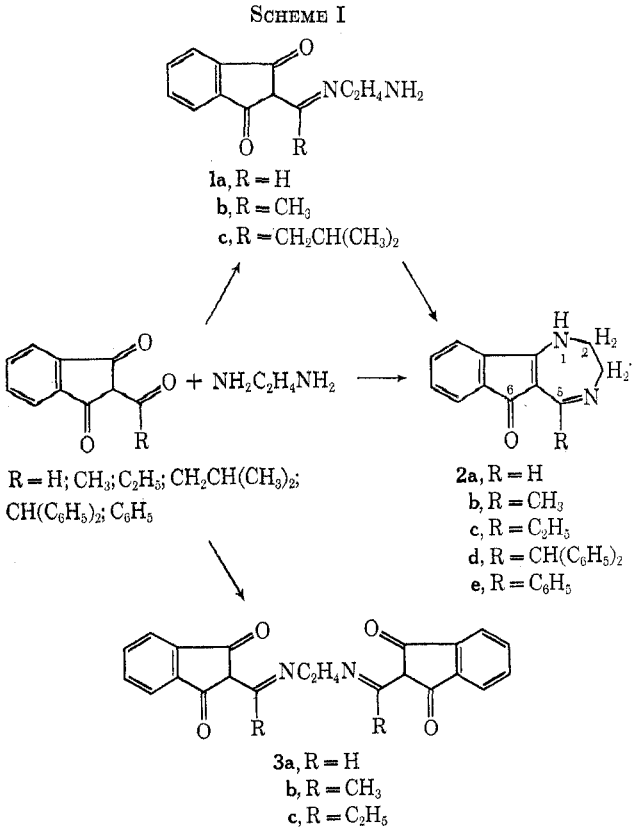
Depending upon the conditions, reaction of 2-acyl-1,3-indandiones with ethylenediamine gave 2[1-(2-aminoethylimino)alkyl]-1,3-indandiones (**1**), 2,3-dihydro-6H-indeno[1,2-*e*][1,4]diazepin-6-ones (**2**), or 2,2′-[ethylenebis(nitriloalkylidyne)]di-1,3-indandiones (**3**). The condensation with methylenediamine was unsuccessful.

Previous papers from this laboratory have reported the reactions of 2-acyl-1,3-indandiones with hydrazines to give monohydrazones[1] and indeno[1,2-*c*]pyrazol-4(1H)-ones.[2] We now report the reactions of 2-acyl-1,3-indandiones with aliphatic diamines.

The condensation of ethylenediamine with open-chain β diketones has been reported to give (a) noncyclized compounds, such as 4,4′-ethylenediiminodipentanone, with acetylacetone,[3] or (b) 2,3-dihydro-1,4-diazepines,[4] depending upon the molar ratio of the reactants.

We have found that treatment of 2-acyl-1,3-indandiones with ethylenediamine yielded three types of products depending upon the nature of the substituents in the side chain of the indandiones and the molar ratio of the reactants (Scheme I).

SCHEME I



Addition of 2-acyl-1,3-indandiones (1 mol) to a refluxing ethanolic solution of ethylenediamine (1.5 mol, except in the case of compound **1a**, where *ca.* 4 mol were used), in the presence of formic acid gave 2-[1-(2-aminoethylimino)alkyl]-1,3-indandiones (**1a–1c**) when R is hydrogen, methyl, or isobutyl, and 5-substituted 2,3-dihydro-6H-indeno[1,2-*e*][1,4]diazepin-6-ones (**2c–2e**), when R is ethyl, diphenylmethyl, or phenyl. The diazepinones **2a** (R = H) and **2b** (R = CH_3) were obtained by heating the corresponding indandiones (**1a** or **1b**), the former in the presence of formic acid and *n*-propanol, the latter in the dry state. Indandione **1c** could not be ring closed to the corresponding diazepinone.

Reverse addition of the reactants and change in molar ratio of ethylenediamine (1.2 mol) to 2-acyl-1,3-indandiones (2 mol) gave 2,2′-[ethylenebis(nitriloalkylidyne)]di-1,3-indandiones (**3a–3c**).

The structures of these compounds are based upon analyses and are consistent with the infrared spectra.

All attempts to react methylenediamine with various 2-acyl-1,3-indandiones in order to prepare 4-substituted 1,2-dihydro-5H-indeno[1,2-*d*]pyrimidin-5-ones failed. In all cases only a compound of empirical formula $(C_{10}H_7NO)_x$ was isolated. No attempts have been made to determine the structure of this compound.

Experimental Section[5]

2-Formyl-1,3-indandione.—A modification of the procedure described in the literature[6] was used. A mixture of triethyl orthoformate (35 ml, 240 mmol) and acetic anhydride (70 ml, 720 mmol) was added to 1,3-indandione (25 g, 170 mmol) with stirring at room temperature. The mixture was heated slowly for *ca.* 45 min to 80° and kept at this temperature for 1 hr. The obtained red solution was filtered hot and immediately cooled to 10° in an ice bath. Cold water (130 ml), previously boiled to remove most of the oxygen, was added at 10° with stirring and the mixture was allowed to crystallize in a refrigerator for 15 hr. The deep red crystals were collected and immediately added to refluxing absolute ethanol (400 ml) with stirring. The mixture was refluxed for 5 min and then filtered rapidly through a preheated sintered-glass funnel. The green-red filtrate, containing *ca.* 20 g of 2-formyl-1,3-indandione, was used directly in the condensation with ethylenediamine. The ethanolic solution of this indandione should not be stored for a long period of time.

All the other 2-acyl-1,3-indandiones were prepared according to known methods[7,8] from dimethylphthalate and the appropriate methyl ketones in the presence of sodium amide.[9]

2[1-(2-Aminoethylimino)alkyl]-1,3-indandiones (1a–1c). Method A.—The general procedure (method A) used to prepare these compounds is illustrated by the synthesis of 2[1-(2-aminoethylimino)ethyl]-1,3-indandione (**1b**). A solution of 2-acetyl-1,3-indandione (50 mmol) in ethanol (200 ml) was added dropwise over a 2-hr period to a refluxing mixture of formic acid (1 ml),

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TABLE I

2-[1-(2-AMINOETHYLIMINO)ALKYL]-1,3-INDANDIONES (1a–1c)

Compd	R	Reaction time[a]	Yield, %	Mp, °C	Empirical formula	Calcd, %	Found, %
1a	H	2 hr	59	90–100 dec	$C_{12}H_{12}N_2O_2$	C, 66.65	C, 66.85
						H, 5.59	H, 5.64
1b	CH_3[b]	2 days	80	224–225	$C_{13}H_{14}N_2O_2$	C, 67.81	C, 68.34
						H, 6.13	H, 6.01
						N, 12.17	N, 12.21
1c	$CH_2CH(CH_3)_2$	3 days	75	96–98	$C_{16}H_{20}N_2O_2$	C, 70.56	C, 69.62
						H, 7.40	H, 7.39

[a] Prepared as in method A (see Experimental Section). [b] Forms a yellow perchlorate, mp 240–242°.

TABLE II

2,3-DIHYDRO-6H-INDENO[1,2-*e*][1,4]DIAZEPIN-6-ONES (2a–2e)

Compd	R	Reaction time	Yield, %	Mp, °C	Empirical formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
2a	H[a]	...	59	104–106	$C_{12}H_{10}N_2O \cdot H_2O$	66.65	5.59	12.96	66.67	5.75	12.28
2b	CH_3[b]	...	50	220–221 dec	$C_{13}H_{12}N_2O$	73.56	5.70	13.20	73.22	6.08	13.01
2c	C_2H_5[b]	2 days[c]	70	194	$C_{14}H_{14}N_2O$	74.31	6.24	12.38	74.20	6.35	12.29
2d	$CH(C_6H_5)_2$[b]	4 days[c]	60	285–286	$C_{25}H_{20}N_2O$	82.45	5.50	7.69	82.14	5.62	8.31
2e	C_6H_5[b]	18 hr[c]	75	243	$C_{18}H_{14}N_2O \cdot {}^1/_2C_2H_5OH$	76.74	5.76	9.42	76.51	5.76	9.48

[a] Forms a formate, mp 178–180° and a perchlorate, mp >300°. [b] Forms perchlorates. [c] Prepared as in method A (see Experimental Section).

TABLE III

2,2′-[ETHYLENEBIS(NITRILOALKYLIDYNE)]DI-1,3-INDANDIONES (3a–3c)

Compd	R	Reaction time	Yield, %	Mp, °C	Empirical formula	Calcd, %	Found, %
3a	H	10 min	80	300	$C_{22}H_{16}N_2O_4$	C, 70.96	C, 69.72
						H, 4.33	H, 4.58
						N, 7.52	N, 7.80
3b	CH_3	20 min	90	297	$C_{24}H_{20}N_2O_4$	C, 71.98	C, 71.77
						H, 5.04	H, 5.56
						N, 7.00	N, 7.01
3c	C_2H_5	2 hr	80	240	$C_{26}H_{24}N_2O_4$	C, 72.88	C, 73.18
						H, 5.65	H, 5.48
						N, 6.54	N, 6.70

ethanol (100 ml), and ethylenediamine (75 mmol). The mixture was refluxed for 2 days (see Table I for the refluxing time of 1c). Then most of the ethanol was removed by distillation (*ca.* 250 ml) and to the hot residue (*ca.* 50 ml) was added water (25 ml) with stirring. The mixture was kept at room temperature for *ca.* 2 days to complete the crystallization. The solid was collected by filtration and recrystallized from aqueous ethanol to give 1b as colorless needles.

For compound 1a the following quantities of reactants were used: 2-formyl-1,3-indandione (*ca.* 10 g, 57 mmol), formic acid (2 ml), ethanol (200 ml), and ethylenediamine (225 mmol). The mixture was refluxed for 2 hr. Most of the ethanol was removed by distillation and to the hot residue (*ca.* 150 ml) was added hot water (150 ml). The mixture was kept in a refrigerator for 36 hr; the colorless crystals were collected by filtration and dried.

2,3-Dihydro-6H-indeno[1,2-*e*][1,4]diazepin-6-one (2a).—A solution of 1a (*ca.* 10 g) in a mixture of *n*-propanol (250 ml) and formic acid (15 ml) was heated at reflux for 2 hr. The solution was then allowed to stand at room temperature. The formed golden leaflets of the formic acid salt of 2a, mp 178° dec, were collected by filtration, treated with an excess of aqueous ammonia in 1:1 water–ethanol, and crystallized from acetone to yield 2a as colorless needles.

2,3-Dihydro-5-methyl-6H-indeno[1,2-*e*][1,4]-diazepin-6-one (2b).—Compound 1b (10 mmol) was heated at 250° for 5 min without solvent. The resulting dark powder, after crystallization from aqueous ethanol (Darco), gave 2b as colorless needles.

5-Ethyl-, 5-phenyl-, and 5-diphenylmethyl-2,3-dihydro-6H-indeno[1,2-*e*][1,4-]diazepin-6-ones (2c–2e) were prepared following method A. The refluxing time varied from 18 hr to 4 days, as reported in Table II. Colorless or pale yellow needles were obtained after crystallization from ethanol (Darco).

The above 2,3-dihydro-6H-indeno[1,2-*e*][1,4]diazepin-6-ones show absorption peaks at *ca.* 3300 (NH), *ca.* 1655 (C=O), and *ca.* 1600 cm^{-1} (C=N). They form crystalline yellow perchlorates and formates, which show bright yellow fluorescence in alcoholic solution as well in the solid state and give phenylhydrazones with phenylhydrazine.

2,2′-[Ethylenebis(nitriloalkylidyne)]di-1,3-indandiones (3a–3c) were prepared by the following general method. A solution of formic acid (0.5 ml) and ethylenediamine (2 ml, 30 mmol) in ethanol (100 ml) was added dropwise to a refluxing solution of the appropriate 2-acyl-1,3-indandione (50 mmol) in ethanol (150 ml) with stirring, and the mixture was refluxed for an additional time, as given in Table III. After cooling to room temperature, the resulting solid was collected by filtration, washed with cold ethanol, and recrystallized from ethanol to give colorless or pale yellow needles.

Compounds 3a–3c exhibit absorption peaks at *ca.* 1705 (C=O) and *ca.* 1500 and 1600 cm^{-1} (C=N). They show practically no absorption in the 3300-cm^{-1} region.

Reaction of 2-Acyl-1,3-indandiones with Methylenediamine.—Methylenediamine dihydrochloride (2.4 g, 20 mmol) and anhydrous sodium acetate (3.3 g) were added to cold ethanol (100 ml) with stirring. After 10 min the mixture was filtered to remove the precipitated sodium chloride and to the filtrate was added a solution of the appropriate 2-acyl-1,3-indandione (2-acetyl, 2-isovaleryl, and 2-diphenylacetyl) (15 mmol) in ethanol (100 ml). The clear solution was refluxed for 5 hr. Most of the ethanol (150 ml) was removed by distillation, and the residue, after standing overnight at room temperature, gave colorless, fine needles (1.5 g), mp >300°.

Anal. Calcd for $(C_{10}H_7NO)_x$: C, 76.41; H, 4.49; N, 8.91. Found: C, 76.63; H, 4.54; N, 8.81.

The infrared spectrum showed a strong doublet at 1670 and 1720 cm^{-1} (C=O), an intense band at 1600 cm^{-1} (probably C=N), and two weak bands in the 3050–3450-cm^{-1} region (OH or NH).

Treatment of this compound with 5 *N* hydrochloric acid in ethanol yielded a red, crystalline product, mp >300°.

Anal. Calcd for empirical formula $C_{20}H_{14}NO_3$: C, 75.94; H, 4.46; N, 4.43; O, 15.18. Found: C, 75.81; H, 4.44; N, 4.35; O, 15.24.

Registry No.—**1a**, 23265-38-5; **1b**, 23265-39-6; **1b** formate, 23282-25-9; **1c**, 23265-40-9; **2a**, 23265-41-0; **2a** formate, 23282-31-7; **2a** perchlorate, 23265-43-2; **2b**, 23265-42-1; **2c**, 23282-32-8; **2d**, 23265-44-3; **2e**, 23265-45-4; **3a**, 23265-46-5; **3b**, 23265-47-6; **3c**, 23265-48-7.

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Inter- and Intramolecular Cyclization of Bisdiazo Ketones. The Formation of the Novel 3,3′-Spirobi(bicyclo[3.1.0]hexane)-2,2′-dione System

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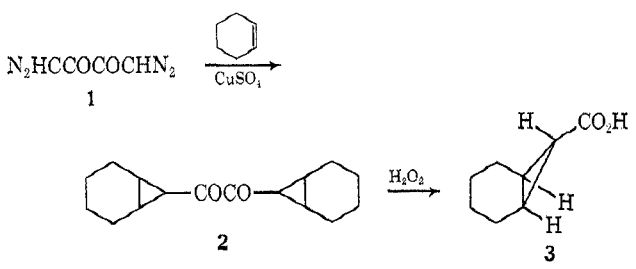
Two examples of double addition of bisdiazo ketones to olefinic bonds are described. Addition of 1,4-bisdiazo-2,3-butanedione (**1**) to cyclohexene afforded the *exo*-di(**7**-norcaryl)ethanedione (**2**). Catalytic decomposition of bisdiazo ketone **8** yielded the isomeric spiro diketones **10** and **11**. Nmr spectral properties and some reactions of this novel spiro system are discussed.

α-Ketocarbenes generated by the copper-catalyzed decomposition of diazo ketones have been found to react with olefins to produce cyclopropanes. Both intermolecular[1-3] and intramolecular[4-13] additions have been reported.

Recently we initiated the study of the corresponding reactions of bisdiazo ketones which do not appear to have been investigated. In the present paper we describe two cases in which double addition of intermediate bisketocarbenes to olefinic bonds occurred.

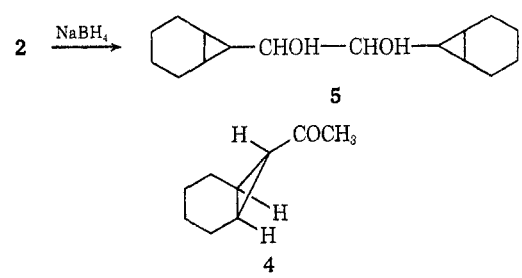
Decomposition of 1,4-bisdiazo-2,3-butanedione (**1**)[14] in boiling cyclohexene in the presence of anhydrous copper sulfate afforded the *exo*-di(7-norcaryl)ethanedione **2** in low yield.



The presence of an α-diketone system was demonstrated by formation of the corresponding quinoxaline derivative. The low carbonyl frequency (1680 cm^{-1}) observed in the infrared spectrum of **2** indicates a significant conjugative overlap between the cyclopropane rings and the adjacent carbonyl groups, presumably enhanced by a preferred geometry of the molecule with respect to the pertinent groups. Conjugative ability of the electron-rich cyclopropane ring has been observed for many years by infrared and ultraviolet spectroscopy.[15,16]

The *exo* configuration was proved by oxidation of **2** with alkaline hydrogen peroxide, affording the *exo* isomer of norcarane-7-carboxylic acid (**3**).[17,18] Thus the configuration agrees with previous experience concerning copper-catalyzed decomposition of ethyl diazoacetate in the presence of olefins. Here also addition favored the formation of the less hindered *exo* product.[17-20]

Nmr data also support the *exo* configuration. It has been shown[21] that in α-cyclopropylcarbonyl compounds the *cis* ring protons with respect to the carbonyl group are shifted to low field. This should obtain in all *exo* isomers of a norcaryl system adjacent to a carbonyl group. (In the *exo* isomer the carbonyl group is located *trans* to the cyclohexane ring.) Indeed, for **2** and **3** no proton resonance has been observed at δ values lower than 1.17 and 1.10 ppm, respectively. Similarly, in methyl norcaryl ketone **4** no proton resonance has



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