Synthesis and Chemical Reactivity of Indenoisoxazoles

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Treatment of 2-pivaloyl-1,3-indandione (**1**) with hydroxylamine under acidic conditions, results in formation of 8-*t*-butylindeno[1,2-*c*]isoxazol-7-one (**2**) while treatment of the triketone with hydroxylamine at neutral or basic *p*H gave **6** which upon cyclization gave the isomeric 3-*t*-butylindeno[1,2-*c*]isoxazol-4-one (**7**). Compound **7** was readily reduced to amine **12** by treatment with hydrazine or hydrogen over platinum. The amine, although quite unreactive, was converted to 3-*t*-butylindeno[1,2-*c*]pyrazol-4-one (**13**) with hydrazine or reduced to **15** and **16** with sodium in liquid ammonia and alcohol. Surprisingly, the amine **3** obtained from isoxazole **2** gave reduction product **15** from a sodium-liquid ammonia reduction and not the expected product **18**. Spectral evidence for each of the structures is discussed.

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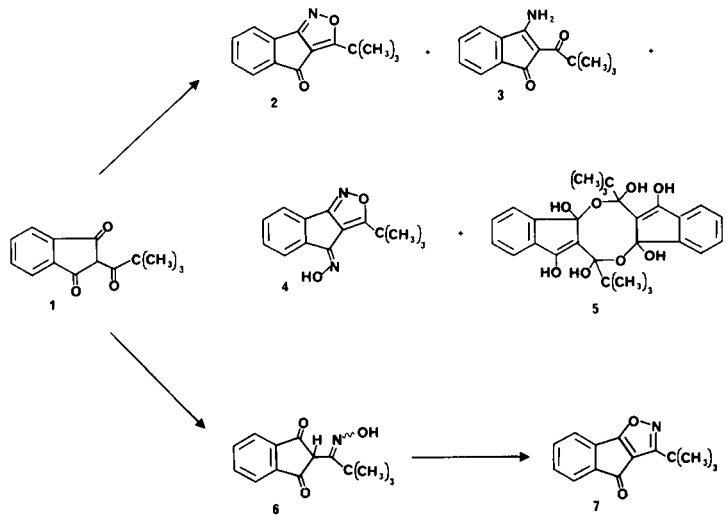
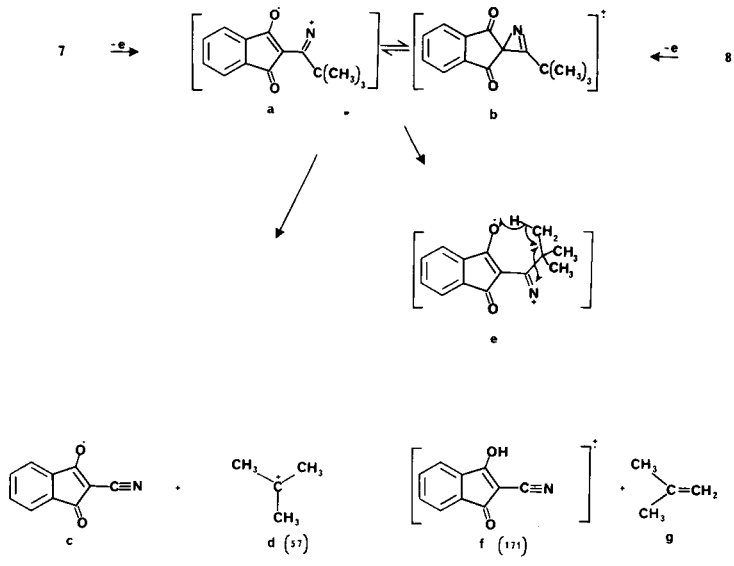
We have been interested in the synthesis of novel heterocyclic tricycles for sometime. In continuation of these efforts, we wish to report the synthesis of the indenoisoxazole nuclei (**2**), (**7**) and the chemical reactivity of these nuclei. Two general procedures were available for converting carbonyl compounds into isoxazoles. One of these methods consists of a one pot procedure in which a β-diketone and hydroxylamine hydrochloride are heated in acetic acid to afford the isoxazole (1). A second procedure consists of formation of the oxime under basic conditions and cyclization of the oxime to the isoxazole using sulfuric acid in aqueous tetrahydrofuran (2). Applying the one pot method to the β-triketone 2-pivaloyl-1,3-indandione (**1**) led to a low, but repeatable, yield of a compound assigned the structure of 8-*t*-butylindeno[1,2-*c*]-isoxazol-7-one (**2**) accompanied by a complex mixture of additional compounds three of which were identified as the amine **3**, the oxime **4** and the dimer **5** (Scheme I). Using the two step procedure of Olefson (2) on **1**, the oxime **6** was obtained which was readily converted to the isomeric isoxazole, 3-*t*-butylindeno[1,2-*c*]isoxazol-4-one, **7**, in an overall yield of 50%. The assignment of structures **2** and **7** are based upon ^{13}C-nmr spectroscopy and T_1 relaxation measurements reported in the accompanying paper (3), as well as mass spectral data and chemical degradation studies reported in this paper.

The mass spectral fragmentation pattern has proven quite valuable in structure assignment of isomeric isoxazoles (4-9). These studies have shown that isomeric 3,5-disubstituted isoxazole fragment in highly characteristic patterns which are usually considerably different from each other. Upon electron-impact, the labile N-O bond undergoes fission leading to molecular ion interconversions between isoxazole and azirine. The azirine in turn may rearrange to an oxazole molecular ion. By comparison of the mass spectra of 3,5-diphenylisoxazole, 2-phenyl-3-benzoyl-1-azirine, and 2,5-diphenyloxazole, Nakata, *et. al.* (5) has found the spectrum of the isoxazole to be very similar to that of the azirine with the exception of two fragments which were present in the spec-

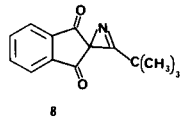
Scheme I



SCHEME II



trum of the oxazole. With azirine **8** available (10) as well as isoxazoles **2** and **7**, a mass spectral analysis was performed. The mass spectra are recorded in Table I. A pattern of similarity can be seen between isoxazole **7** and azirine **8** especially if one compares the intensity of the peaks at m/z 104, 76 and 57. The fragment at m/e 212 (M -15) results from a loss of a methyl group while the m/z 104 peak is assigned to C_6H_4CO which upon loss of CO gives the m/z 76 ion. The molecular ion peak and the subsequent fragmentation to the base peak at m/z 57 can be formulated to proceed through the azirine molecular ion *b* (Scheme II). A similar fragmentation has been reported by Bowie, *et. al.* (6) for 3-*t*-butyl-5-phenylisoxazole (**9**) with a base peak of m/z 57. The peak at m/z 171 can be accounted for by loss of isobutene with hydrogen rearrangement to an oxygen in the indane ring, *e*. A similar hydrogen rearrangement proceeding through an eight membered ring transition state was proposed by Ohashi, *et. al* (7). With isomeric isoxazole **2**, the molecular ion is readily seen as is the peak at m/z 212 (M - CH_3). The only other major peak is that at m/z 171 which results from loss of isobutene and the rearrangement of the hydrogen to either a ring oxygen or nitrogen similar to that proposed for **7** and **8**. These mass spectral patterns are supportive of the structure assignment of **2** and **7**.



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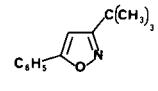

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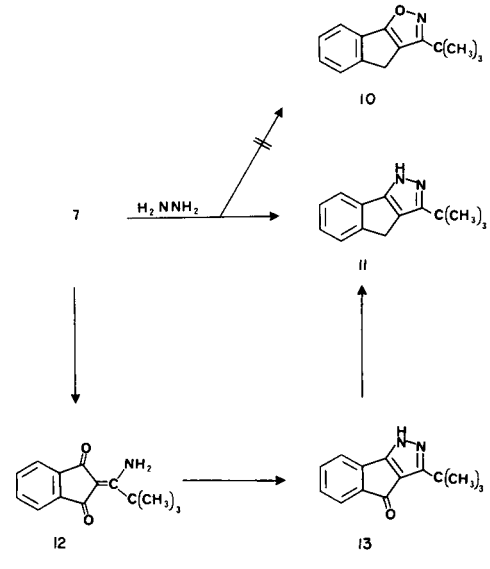
The chemical degradation studies were initiated with **7** since large quantities of this compound were on hand. In order to simplify the chemistry, an initial attempt was made to reduce the carbonyl group in **7** using the modified Wolf-Kishner procedure. When this reaction was carried out with an excess of hydrazine, a 9% yield of a reduction product was obtained which upon analysis proved to be 3-*t*-butylindeno[1,2-*c*]pyrazole (**11**) and not the indenoisoxazole **10**. When **7** was treated with an equimolar quantity of hydrazine at 25° a single product was obtained in 60% yield which was shown to be the amine **12**. This product was accompanied by a 10% recovery of starting material. Hydrazine, acting as a reducing agent, apparently had cleaved the oxygen-nitrogen bond of the isoxazole. The resulting amine could be converted to 3-*t*-butylindeno]1,2-*c*]pyrazol-4-one (**13**) in quantitative yield with hydrazine in ethanol. Ketone **13**, under modified Wolf-



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11

12

13

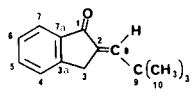
Table I

Mass Spectra of **2**, **7** and **8**.

2	m/z	227	212	171	104	76	57
	I(%)	25.5	39.4	100	2.5	4.3	2.7
7		227	212	171	104	76	57
		99.6	50.7	94.9	36.3	28.1	100
8		227	212	171	104	76	57
		13.5	15.4	27.5	30.5	45.4	100

Table II

^{13}C-nmr Chemical Shifts for **15** and **16** in Deuteriochloroform



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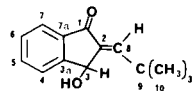

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δ ^{13}C (ppm)

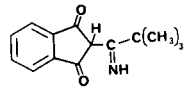
	15	**16**
1	194.4	192.8
2	132.2 (137.8)	135.7 (136.6)
3	30.6	68.0
3a	149.7	151.6
7a	137.8 (132.2)	136.6 (135.7)
8	147.5	152.2
9	33.9	34.4
10	29.6	29.4
4-7	134.2	135.1
	127.2	129.5
	126.0	125.8
	124.2	123.7

Kishner conditions, gave the reduction product **11** in 9% yield thus supporting the contention that this product is obtained through the intermediacy of **12** and **13**.

Compound **12** proved to be an interesting compound. This product has previously been reported by Zelmens and Vanags as having the imine structure **14** (11). The authors gave no evidence for the assignment of the imine structure nor for the location of the nitrogen. Since the structure of the amine confirms our structural assignment of the isoxazole **7**, we felt that it was important to carry out an unequivocal structure proof. Compound **12** was obtainable from the isoxazole by reduction with hydrazine or with platinum and hydrogen. The latter reduction occurring in quantitative yield in less than 5 minutes. Even more conveniently, **12** could be prepared from the triketone **1** by treatment with ammonium acetate. The ^{1}H-nmr analysis confirmed the amine rather than imine structure for **12**. Two exchangeable protons were present, one of which was hydrogen bonded to the carbonyl and appeared at δ 11.54 while the other nonbonded proton appeared at δ 6.74. In compounds which exist in the keto (imine) form, the C-2 proton is normally found between δ 4.2 and 4.9 and is not exchangeable.

Conclusive evidence for assignment of structure **12** and thus isoxazole **7** was obtained from the fragmentation pattern of the amine **12** in the mass spectrometer. The base peak for **12** appeared at M$^+$ - 15. Had the amine been the isomeric amine **3**, fragmentation α to the ketone would have resulted in a loss of the *t*-butyl group to give a base peak of M$^+$ - 57. This indeed is found to arise with **3** generated from **2**.

Compound **12** proved to be quite nonreactive. Attempted acid or base hydrolysis, alkylation, acetylation, or reduction with sodium borohydride or platinum led to recovery of starting material. Kashima has reported a similar stability for β-amino-α,β-unsaturated ketones (12), while Buchi and Vederas successfully reduced similar compounds with sodium and t-butyl alcohol in liquid ammonia (13). When this reaction was applied to compound **12** two products were obtained, **15** and **16**. The configuration of **15** and **16** has been assigned the *E*-configuration based upon the chemical shift of the vinyl protons which appear at δ 6.91 (m) in **15** and δ 6.86 (d, J = 1.5 Hz) in **16**. This downfield location is in agreement with that assigned to the *E* proton in 2-methylene-1-indanone (**17**) (14).



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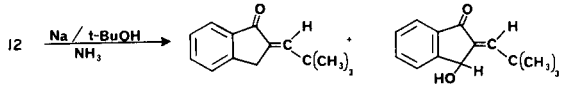
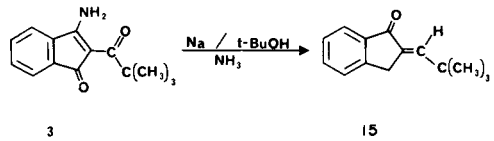


15 16

Confirmation of structures **15** and **16** requires a consideration of the alternate possible structures which might be expected had the isoxazole been compound **2**. Reductive opening of **2** followed by sodium-alcohol reduction in liquid ammonia would be expected to give **18** and **19**. Mass spectral analysis of **18** and **19** would be expected to possess a base peak at M$^+$ - 57 (cleavage α to the ketone). Instead the base peak for **15** appeared at m/z 158 (M$^+$-42) while that for **16** was at m/z 147 (M$^+$-69) both compatible with structures **15** and **16**, respectively. The ir analysis of **16** showed free and bonded hydroxyl absorption at 3600 cm^{-1} and 3450 cm^{-1}. Dilution studies in carbontetrachloride confirmed that the bonded hydroxyl was intermolecularly bonded and not intramolecularly bonded which is consistent with structure **16** and not with structure **19**. Finally, ^{13}C-nmr analysis of **15** and **16** is presented in Table II and provides additional evidence for the assignment of structures **15** and **16**.



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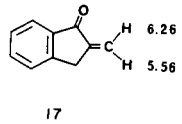

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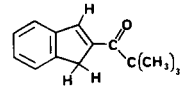

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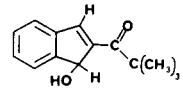

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With structures **15** and **16** firmly established we proceeded with completion of these studies by carrying out the same sequence of reactions on the isomeric isoxazole **2**. Reduction of the isoxazole with platinum and hydrogen gave amine **3**, which similar to its isomer **12**, exists as the amine with a hydrogen bonded proton at δ 11.34 and a nonbonded exchangeable proton at δ 8.6. The mass spectral fragmentation pattern mentioned earlier, resulted in a base peak at M$^+$-57 resulting from the expected α-fragmentation of the side chain ketone. This would only occur with structure **3** which must arise from isoxazole **2**.

The amine **3** was subjected to reduction with sodium, *t*-butyl alcohol, in liquid ammonia with the expectation that **17** and **18** would be recovered, but surprisingly the only product recovered was compound **15**. With compound **3** the yield of **15**, as the only identifiable compound, is relatively low. Additional studies will be required to determine the sequence of events leading to formation of **15** from **3** as well as the nature of the reduction of **12** to **15** and **16**. These results will be reported at a later date.

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover unimelt apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 283 as potassium bromide pellets unless otherwise stated. All ^{1}H-nmr spectra were recorded on a Varian EM 360 spectrometer in deuteriochloroform using tetramethylsilane as an internal reference unless otherwise stated. Chemical shifts are quoted in parts per million (s = singlet, m = multiplet, d = doublet, t = triplet, b = broad band). All ^{13}C-nmr experiments were performed on a Varian XL-100-15 nmr spectrometer system operating in the Fourier transform mode at 25.158 MHz. The spectrometer was equipped with a Nicolet Technology Corporation model TT-100 data system, an NT-440 frequency synthesizer and a TT-760 decoupler. Chemical shifts are quoted in parts per million downfield from tetramethylsilane. Low resolution mass spectra were recorded on a Hewlett-Packard model 5930 GC/MS system equipped with a model 5933A data system using direct probe insertion and an ionizing energy of 70 eV with an ion source temperature of 250°. Ultraviolet spectra were recorded on a Perkin-Elmer 200 spectrophotometer. Microanalyses were performed by Atlantic Microlabs, Atlanta, Georgia.

8-*t*-Butylindeno[1,2-*c*]isoxazol-7-one (**2**).

A mixture of 2.3 g (0.01 mole) of **1**, 1.38 g (0.02 mole) of hydroxylamine hydrochloride and 25 ml of glacial acetic acid were heated under reflux with stirring for 48 hours. Concentration of the reaction mixture gave a residue which was chromatographed on silica gel eluting with methanol/triethylamine/toluene (3:3:94). The first material off of the column amounted to 0.7 g of **2**. Compound **2** was recrystallized from 100% ethanol as orange needles, mp 94-95°, 0.4 g; ^{1}H-nmr: δ 1.53 (s, 9), 7.35-7.8 (m, 4); ir: 1715, 1610 cm^{-1}.

Anal. Calcd. for $C_{14}H_{13}NO_2$: C, 74.0; H, 5.8; N, 6.2. Found: C, 73.9; H, 5.8; N, 6.2.

In subsequent syntheses of **2**, three additional products were obtained. Following the recovery of **2** the next fractions off the column contained **2** and **4**. Upon standing cream colored crystals of **4** appeared in the collection tubes. The crystals were collected by filtration and recrystallized from methanol, mp 214-215°; ^{1}H-nmr (hexadeuterodimethylsulfoxide): δ 1.53 (s, 9), 7.4-7.97 (m, 3), 8.33-8.67 (m, 1), 12.54 (s, 1, exchangeable). The *E*-configuration of **4** is based upon the deshielding of the C-6 proton; ir: 1645, 1560 cm^{-1}.

Anal. Calcd. for $C_{14}H_{14}N_2O_2$: C, 69.4; H, 5.8; N, 11.6. Found: C, 69.3; H, 5.9; N, 11.5.

A slower moving material, **3**, recovered from the chromatography as a single component solidified upon removal of the solvent and was recrystallized from ethylacetate, mp 262-264°; ^{1}H-nmr (hexadeuterodimethylsulfoxide): δ 1.50 (s, 9), 7.6 (s, 4), 8.6 (bs, 1, exchangeable), 11.34 (bs, 1, exchangeable); ms: m/z 229 (M$^+$, 4.8%), 172 (M$^+$-57, 100%), 145 (M$^+$-84, 10.4%). This material was identical to **3** obtained by reduction of **2** with platinum and hydrogen.

Anal. Calcd. for $C_{14}H_{15}NO_2$: C, 73.3; H, 6.6; N, 6.1. Found: C, 73.3; H, 6.6; N, 6.1.

Finally, washing the column with methanol/ethylacetate (1:9) gave a yellow solid, mp >310°. The solid was crystallized by dissolving in 95% ethanol and precipitating with a small amount of water. Structure **5** was assigned this compound based upon spectral data and its instability in aqueous hydrochloric acid; ^{1}H-nmr (hexadeuteriodimethylsulfoxide): δ 1.22 (s, 18), 7.67 (s, 8), 3.93 (s, variable amount, exchangeable); ms: m/z 230 (M$^+$, 14%), 173 (M$^+$ -57, 100%), 146 (M$^+$ -84, 32%), 105 (M$^+$, -225, 37%). The ms is suggestive of that expected for **1**, ir: 1650, 1590, 1545 cm^{-1}.

Anal. Calcd. for $C_{28}H_{32}O_8$: C, 67.7; H, 6.5. Found: C, 67.7; H, 6.5.

A sample of **5** was dissolved in ethanol and 37% hydrochloric acid was added. The solution was heated on the steam bath for 5 minutes and the ethanol was blown off. The solid was extracted with chloroform. Concentration of the organic layer gave a yellow solid which was recrystallized from methanol as yellow needles, mp 107-109° (lit (15) mp 108-110°); tlc with authentic **1** showed that they were identical.

2-Pivaloyl-1,3-indandione Oxime (**6**).

A mixture of 5.0 g (0.022 mole) of **1** suspended in 20 ml of 95% ethanol was treated with 1.4 g (0.022 mole) of hydroxylamine hydrochloride in 10 ml of water and 9 ml of 10% aqueous sodium hydroxide (0.022 mole). The mixture was heated on a steam bath until a homogenous solution resulted. The solution was stirred without heating for 2 hours. The resulting yellow precipitate was collected by filtration and recrystallized from 95% ethanol to give 4.0 g of a white solid, mp 143-145° (74% yield); ^{1}H-nmr: δ 1.25 (s, 9), 4.22 (s, 1), 5.63 (s, 1, exchangeable), 7.3-7.9 (m, 4); ir: 1722, 1602, 1596 cm^{-1}.

Anal. Calcd. for $C_{14}H_{15}NO_3$: C, 68.6; H, 6.2; N, 5.7. Found: C, 68.5; H, 6.2; N, 5.7.

3-*t*-Butylindeno[1,2-*c*]isoxazol-4-one (**7**).

A solution of 2.45 g (0.01 mole) **6** in 30 ml of tetrahydrofuran was treated with 15 ml of a 6 *N* sulfuric acid in a 4:1 tetrahydrofuran/water mixture (2). The solution was heated under reflux for 22 hours. An additional 7.5 ml of 6 *N* sulfuric acid/tetrahydrofuran/water mixture was added and heating was continued for an additional 22 hours. This procedure

was repeated two additional times or until tlc on silica gel (3% triethylamine, 5% methanol, benzene) showed the absence of oxime. The reaction mixture was concentrated *in vacuo* and the solid was collected by filtration. The yellow solid was recrystallized from ethanol to give 1.5 g of **7**, mp 108-110° (66% yield); ^{1}H-nmr: δ 1.5 (s, 9), 7.4-7.9 (m, 4); ir: 1760, 1710, 1600 cm^{-1}.

Anal. Calcd. for $C_{14}H_{13}NO_2$: C, 74.0; H, 5.8; N, 6.2. Found: C, 74.0; H, 5.8; N, 6.2.

3-*t*-Butylindeno[1,2-*c*]pyrazole (**11**).

A mixture of 1.14 g (0.005 mole) of **7**, 0.7 g (0.0125 mole) of potassium hydroxide, 0.6 ml (0.01 mole) of 85% hydrazine hydrate in 6 ml of diethylene glycol was heated at 100° with stirring until a solution resulted and then heated under reflux for one hour. Distillation was performed until the temperature rose to 175°. The residue was heated under reflux for 4 hours. The reaction mixture was cooled, diluted with 10 ml of water and extracted with diethylether (3 × 10 ml). The combined organic layer was dried over anhydrous magnesium sulfate. Concentration of the organic layer gave 0.9 g of a brown oil which was chromatographed on silica gel using ethylacetate/benzene (1:9) as eluting solvent. The first compound off the column (0.1 g) was recrystallized from benzene/petroleum ether (bp 35-60°) to give yellow needles of **13**, mp 192-193°. This compound was equal in all aspects to an authentic sample of **13**. Further chromatography gave 0.1 g of a second compound as a white solid which was crystallized from cyclohexane, mp 166°. A second recrystallization from cyclohexane gave **11**, mp 152-153°; ^{1}H-nmr: δ 1.35 (s, 9), 3.57 (s, 2), 7.05-7.8 (m, 4H); 8.77 (s, 1, exchangeable); ir: no carbonyl.

Anal. Calcd. for $C_{14}H_{16}N_2 \cdot H_2O$: C, 73.0; H, 7.9; N, 12.2. Found: C, 73.0; H, 7.9; N, 12.1.

2-(1'-Amino-2',2'-dimethyl)propylidenyl-1,3-indandione (**12**).

To a solution of 1.0 g (0.0044 mole) of **7** in 22 ml of 95% ethanol was added dropwise 0.22 g (0.0044 mole) of hydrazine hydrate in 4.5 ml of 95% ethanol. The solution was stirred for one hour, the alcohol was removed *in vacuo* and the residue was taken up in diethylether and dried over anhydrous magnesium sulfate. The solvent was removed and the residue was dissolved, with heat, in toluene/ethylacetate (95:5). Upon cooling 0.15 g of a yellow solid was obtained. Concentration of the solvent gave an additional 0.21 g of product. The remaining material was chromatographed on silica gel using toluene/ethylacetate (95:5) as eluting solvent. An additional 0.2 g of **12** was recovered from the column for a total of 0.56 g. The combined samples of **12** were recrystallized from 95% ethanol, mp 193-194° (lit (11) mp 193-194°); ^{1}H-nmr: δ 1.48 (s, 9), 7.59 (d, J = 2 Hz, 4H), 6.74 (bs, 1, exchangeable), 11.54 (bs, 1, exchangeable); ir: 1670, 1620, 1580 cm^{-1}; ms: m/z 229 (M$^+$, 84%), 214 (M$^+$-15, 100%), 172 (M$^+$-57, 26%), 145 (M$^+$-84, 8%).

A second product off the column consisted of 0.1 g of compound **7**.

Compound **12** can also be synthesized directly from the β-triketone **1**. A mixture of 2.0 g (0.0087 mole) of **1**, 10 g of ammonium acetate and 15 ml of glacial acetic acid was heated on a steam bath for 30 minutes. The reaction mixture was diluted with 100 ml of water and the precipitate collected by filtration. The crude product (1.8 g) was recrystallized from 95% ethanol to give yellow crystals, mp 193-194°.

The same amine (**12**) can be obtained in quantitative yield from 1 by hydrogen reduction over platinum in ethanol in a Parr hydrogenator at 50 psi of hydrogen.

3-*t*-Butylindeno[1,2-*c*]pyrazol-4-one (**13**).

A mixture of 1.14 g (0.005 mole) of **7**, 0.4 ml (0.0068 mole) of hydrazine hydrate, 0.7 g (0.0125 mole) of potassium hydroxide in 7 ml of diethylene glycol was heated at 220° for 4 hours, cooled to 25°, diluted with 20 ml of water, and extracted with diethylether (5 × 40 ml). The combined organic layer was dried over anhydrous magnesium sulfate. Concentration of the ether layer gave 0.8 g of crude **13** which was purified by chromatography on silica gel eluting with ethylacetate/toluene (15:85). A total of 0.7 g of **13** (61% yield) was recovered and recrystallized from benzene/petroleum ether (bp 35-60°) as a light yellow crystal, mp 193-194° (lit (16) mp 191-192°). The compound was compared with an authentic sample by tlc and nmr.

3-*t*-Butylindeno[1,2-*c*]pyvazol-4-one (**13**) From 2-(1'-Amino-2',2'-dimethyl)-propylindenyl-1,3-indandione (**12**).

A mixture of 1.05 g (0.0046 mole) of **12** and 1.2 ml (0.033 mole) of 85% hydrazine hydrate in 50 ml of 95% ethanol was heated under reflux on a steam bath for 1.5 hours. The solvent was removed and the residue was treated with water. The precipitate was collected by filtration and dried to give 1.0 g (100% yield) of **13**, mp 193-194°, identical to previously prepared samples.

3-*t*-Butylindeno[1,2-*c*]pyrazol (**11**) from 3-*t*-Butylindeno[1,2-*c*]pyrazol-4-one (**13**).

A mixture of 1.13 g (0.005 mole) of **13**, 0.7 ml (0.005 mole) of 85% hydrazine hydrate, 0.7 g (0.0125 mole) of potassium hydroxide and 6 ml of diethylene glycol were heated with stirring. The temperature of the reaction mixture was slowly raised to 150° and maintained at this temperature under reflux for one hour. The temperature was raised to 175° and the vapors were allowed to escape. The solution was then heated under reflux at 240° for 5 hours. The reaction mixture was cooled, diluted with 20 ml of water, and extracted with diethylether (4 × 50 ml). The combined organic layer was dried over anhydrous magnesium sulfate. Removal of the solvent gave an oily residue which was chromatographed on silica gel using ethylacetate/toluene (12:88) as eluting solvent. A crystalline compound (0.1 g) was obtained after a forerun of starting material. The product was recrystallized from petroleum ether (bp 35-60°) and then cyclohexane to give a 9% yield of **11**, mp 152-153°. This material was identical to that reported above.

2-(2',2'-Dimethyl)propylidenyl-1-indanone (**15**) and 2-(2',2'-Dimethyl)-propylidenyl-3-hydroxy-1-indanone (**16**).

To a mixture of 1.048 g (0.0044 mole) of **12**, 175 ml of liquid ammonia, 0.358 g of *t*-butyl alcohol and 20 ml of tetrahydrofuran was added small pieces of sodium until the solution remained dark blue in color. The addition took approximately 3-4 hours. Solid ammonium chloride was slowly added until the blue color dissipated. The ammonia was allowed to evaporate and the residue was treated with 25 ml of diethylether and 100 ml of water saturated with ammonium chloride. The aqueous layer was extracted with diethylether (400 ml) and chloroform (100 ml). The combined organic layer was dried over anhydrous magnesium sulfate. The organic layer was concentrated and the residue was dissolved in 50 ml of toluene. After heating under reflux for 24 hours, the mixture was concentrated and chromatographed on silica gel eluting with toluene. Compound **15** eluted from the column (0.45 g) and was recrystallized from petroleum ether, mp 101-102°; ^{1}H-nmr: δ 1.23 (s, 9), 3.82 (d, J = 2 Hz, 2), 6.91 (t, J = 2 Hz, 1), 7.3-7.7 (m, 3), 7.9 (bd, 1); ir: 1705, 1650 cm^{-1}; ms: m/z 200 (M$^+$, 70%), 185 (M$^+$-15, 85%), 158 (M$^+$-42, 100%), 131 (M$^+$-69, 94%), 115 (M$^+$-85, 70%); uv (methanol): λ max 266 nm.

Anal. Calcd. for $C_{14}H_{16}O$: C, 84.0; H, 8.0. Found: C, 84.4; H, 8.0.

Elution of the column with ethyl acetate/toluene (5:95) gave 0.15 g of **16**. The compound was recrystallized from petroleum ether (bp 35-60°), mp 99-100°; ^{1}H-nmr: δ 1.33 (s, 9), 2.93 (d, J = 8 Hz, 1, exchangeable), 5.76 (d, J = 8 Hz, 1, singlet after exchange), 6.86 (d, J = 2 Hz, 1), 7.29-7.76 (m, 4); ms: m/z 216 (M$^+$, 2%), 201 (M$^+$-15, 2%), 174 (M$^+$-42, 16%), 147 (M$^+$-69, 100%); ir (carbon tetrachloride): 3600 (sharp), 2450 (broad), 1710, 1645 cm^{-1}. Dilution studies demonstrated a loss of the 3450 band without loss of the 3600 band; uv (methanol): λ max 265 nm.

Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.7; H, 7.4. Found: C, 77.6; H, 7.5.

2-Pivaloyl-3-amino-2-inden-1-one (**3**).

A mixture of 3.0 g (0.013 mole) of **2**, 0.2 g of platinum oxide in 300 ml of 100% ethanol was placed in a Parr hydrogenator with 45 lbs/in^2 of hydrogen. After shaking for 15 minutes the mixture was filtered and concentrated to give **3**. The product was recrystallized from ethylacetate as yellow needles, mp 262-264°. The material is identical to that reported above.

2-(2',2'-Dimethyl)propylidenyl-1-indanone (**15**) From the Reduction of 2-Pivaloyl-3-amino-2-inden-1-one (**3**).

The sodium-liquid ammonia reduction was performed using a procedure identical to that reported for the synthesis of **15** and **16**. Following work-up, a diethylether extraction was performed. The ether layer was then extracted with 2 *N* hydrochloric acid. The neutral ether layer was set aside and the acid layer was made basic with dilute sodium hydroxide. The aqueous phase was extracted with diethylether. Concentration of the combined ether extracts resulted in recovery of trace amounts of a reside which was discarded. The neutral layer was concentrated, to give a residue which was shown by tlc to be devoid of **15**. The residue was heated under reflux in toluene with a catalytic amount of *p*-toluenesulfonic acid for 24 hours. Tlc at this time showed the presence of **15**. Concentration of the reaction mixture gave a residue which upon chromatography gave compound **15** which was identical to that reported above.

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REFERENCES AND NOTES

(1) W. S. Johnson and W. E. Shelberg, *J. Am. Chem. Soc.*, **67**, 1745 (1945).

(2) G. N. Barber and R. Z. Olefson, *J. Org. Chem.*, **43**, 3615 (1978).

(3) C. H. Womack, R. T. Gampe, Jr., B. K. Lemke, T. L. Lemke and G. E. Martin, *J. Heterocyclic Chem.*, accepted.

(4) M. Ohashi, H. Kamachi, H. Kakisawa, A. Tatematsu, H. Yoshizumi, and H. Nakata, *Tetrahedron Letters*, 379 (1968).

(5) H. Nakata, H. Sakurai, H. Yoshizumi, and A. Tatematsu, *Org. Mass. Spectrom.*, **1**, 199 (1968).

(6) J. H. Bowie, R. K. M. R. Kallury, and R. G. Cooks, *Aust. J. Chem.*, **22**, 563 (1969).

(7) M. Ohashi, H. Kamachi, H. Kakisawa, A. Tatematsu, H. Yoshizumi, H. Kano, and H. Nakata, *Org. Mass Spectrom.*, **2**, 195 (1969).

(8) B. K. Simons, R. K. M. R. Kallury, and J. H. Bowie, *ibid.*, **2**, 739 (1969).

(9) D. C. Nonhebel, *ibid.*, **3**, 1519 (1970).

(10) 3-*t*-Butylspiro[2*H*-azirine-2,2'-[2*H*]-indene]-1',3'-dione was recently synthesized in our laboratories. The chemistry will be reported at a later date.

(11) V. Zelmens and G. Vanaga, *Lat. Zin. Akad. Vestis*, 69 (1959); *Chem. Abstr.*, **53**, 21830d (1959).

(12) C. Kashima, *J. Org. Chem.*, **40**, 526 (1975).

(13) B. Buchi and J. C. Vederas, *J. Am. Chem. Soc.*, **94**, 9128 (1972).

(14) M. Muhlstadt and H. J. Gensrich, *J. Prakt. Chem.*, **34**, 139 (1966).

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

(16) R. Braun and W. A. Mosher, *J. Org. Chem.*, **24**, 648 (1959).