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OXINDOLES—II[1]

THE PRODUCTS OF SOME MICHAEL ADDITIONS TO ISATYLIDENEACETIC ESTERS AND CINNAMYL DERIVATIVES* [2]

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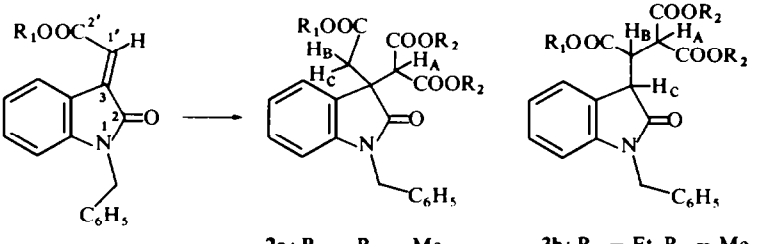
Abstract—Structures are proven for the products of Michael addition of malonate esters to methyl and ethyl *trans*-benzylisatylideneacetate. There are described the reactions of the pyrrolidine enamine of cyclopentanone with cinnamaldehyde and ethyl cinnamate to give the expected Stork condensation products, and its reaction with ethyl benzylisatylideneacetate to give unexpected products.

IN AN earlier article,[1] we described the preparation and proof of structures of several *cis*- and *trans*-isatylideneacetyl compounds. We suggested that these substances (e. g. **1**) might serve as building blocks for the construction of some of the oxindole alkaloids. To realize that suggestion, condensation of the Michael or related type must occur at C_3 rather than at $C_{1'}$, leading to **2** and not to **3**. The results here presented point to an apparently delicate balance between the factors favoring addition at one carbon or the other.



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$\overset{\ominus}{C}H(COOR_2)_2$

2a: $R_1 = R_2 = Me$
2b: $R_1 = Et, R_2 = Me$
2c: $R_1 = R_2 = Et$

3b: $R_1 = Et, R_2 = Me$

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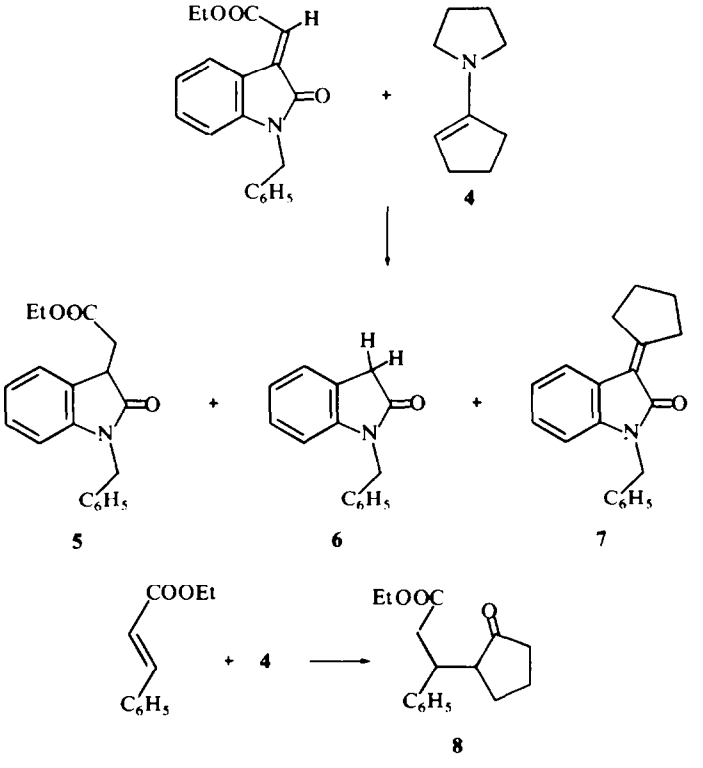
Thus, condensation of dimethyl malonate with methyl benzylisatylideneacetate (**1**, $R_1 = R_2 =$ Me) produced the desired product, **2a**, isolated in 86% yield. Examination of the crystallization residues revealed no contaminants other than the two starting esters. Condensation of diethyl malonate with the ethyl benzylisatylideneacetate (**1**, $R_1 = R_2 =$ Et) also produced only **2c**, isolated in 65% yield. In contrast to these two reactions stood the addition of dimethyl malonate to ethyl benzylisatylideneacetate (**1**, $R_1 =$ Et, $R_2 =$ Me), in which the two possible senses of addition were exemplified in comparable yields: triester **2b** was obtained in 35% yield, triester **3b** was obtained in 29% yield.

Attempts to add the pyrrolidine enamine (**4**) of cyclopentanone to ethyl benzylisatylideneacetate led to equivocal results. We obtained four products, of which, by comparison with authentic samples, we identified three as ethyl 1-benzyloxindole-3-acetate (**5**, 35% yield) benzyloxindole (**6**, 36%) and benzylcyclopentylideneoxindole (**7**, 4%). The addition of the same enamine to the simpler, but related, ester ethyl cinnamate gave, on the other hand, the expected product **8** in 49% yield. And the enamine condensed normally with cinnamaldehyde[3] (*vide infra*).



Proof of the product structures

The structural evidence for the malonate adducts comes from NMR spectroscopy. The relevant spectral data are summarized in Table 1, and support several conclusions. For structures **2**, in which the isatylidene C-3 is quarternary, the methine (H_A) and methylene (H_B and H_C) hydrogens of the malonyl and acetyl side chains

Table 1[a]

Compound	R_1	R_2	H_A	H_B	H_C	$-CH_2\phi$
2a	3·34	3·50, 3·76	3·82 (s) 1·05 H	4·18 q; J = 11·8 c/s, δ = 5·9 c/s; 2·3 H		4·91 q, J = 12·1, δ = 15·3 c/s
2b	Et, CH_2— q at 3·87 J = 7·0 c/s	3·52, 3·75	3·82 (s) 0·95 H	4·16 s, width = 3 c/s, 2·0 H		4·89
2c	Et	Et	[b]	4·15 (integral not possible)		4·89
3b	Et, —CH_2— q at 3·94, J = 7·2 c/s	3·63, 3·74	[c]	4·43 d.d, J's 11·5 and 1·5 c/s, 1·1 H	[c]	4·87
2b	Et, —CH_2— q at 3·65, J = 7·2 c/s	3·03, 3·37	3·81 (s)	4·50 (s)		4·64, q, J = 15·3, δ = 14·1 c/s
3b[d]	Et, —CH_2— q at 3·74, J = 7·0 c/s	3·31, 3·39	3·98, d, J = 4·0 c/s, 1·05 H	4·29, d.d, J's = 4·0, 10·4 c/s, 0·95 H	4·97, d, J = 10·4 c/s; 1·0 H	4·65, q, J = 15·5, δ = 12·6 c/s

[a] Line positions are measured against TMS as internal standard, and are reported in ppm on the δ scale. Peak multiplicities are noted with the letter s = singlet, d = doublet, d.d = doublet of doublets, q = quartet. The first four spectra were measured in $CDCl_3$ solution; the last two were measured in benzene. Where it is important, the integral, based on the average value for all the methyl groups in the molecule and rounded to the nearest 0·05, is reported as x.x H. The four $CDCl_3$ spectra and the integral for **3b** in benzene were measured on a Varian A-60; the line positions for the benzene spectra were measured on a Varian HA-100.

[b] All three Et groups are non-equivalent, and the single H_A cannot rigorously be discerned in the region cluttered by the methylenes of the Et groups.

[c] H_A and H_C cannot rigorously be separated from the methylene of the Et group.

[d] This spectrum (Fig. 1) shows the three H's (A, B and C) entirely distinctly. The specific assignments of H_A and H_C are arbitrary and may well be reversed.

are isolated and should appear as singlets integrating for one and two hydrogens, respectively. Owing to restricted rotation, the spectra are not quite so simple.* In compounds **2a** and **2b**, H_A is clearly observable as a singlet. In both these compounds in $CDCl_3$ solution, H_B and H_C are non-equivalent and split each other; the coupling constant is large relative to the chemical shift, but in the case of **2a** the whole non-equivalence quartet is unmistakable.[4] The spectrum of **2b** in benzene solution, however, is simple: two singlets. In structure **3** there is a chain of three C atoms, each bearing one H and at least one CO group. These three hydrogens are not coupled to any others and their spectrum may be complex (e.g. ABC) or relatively simple (AMX). In $CDCl_3$ solution the spectrum of **3b** is not simple enough to solve by inspection, although H_B appears clearly as a doublet of doublets at 4·43 ppm. In benzene solution, however, the spectrum is much simpler, and H_A, H_B and H_C

* That these molecules and others in our isatylidene series are severely internally crowded is evident from models, from the non-equivalence of the three Me groups in **2a** and of the three Et groups in 2c, and perhaps also from the non-equivalence of the benzylic methylene protons (observed in 6 cases out of 20).

may be found readily; see Fig. 1. The coupling relationships shown in Fig. 1 have been confirmed by double and triple resonance experiments.[5]

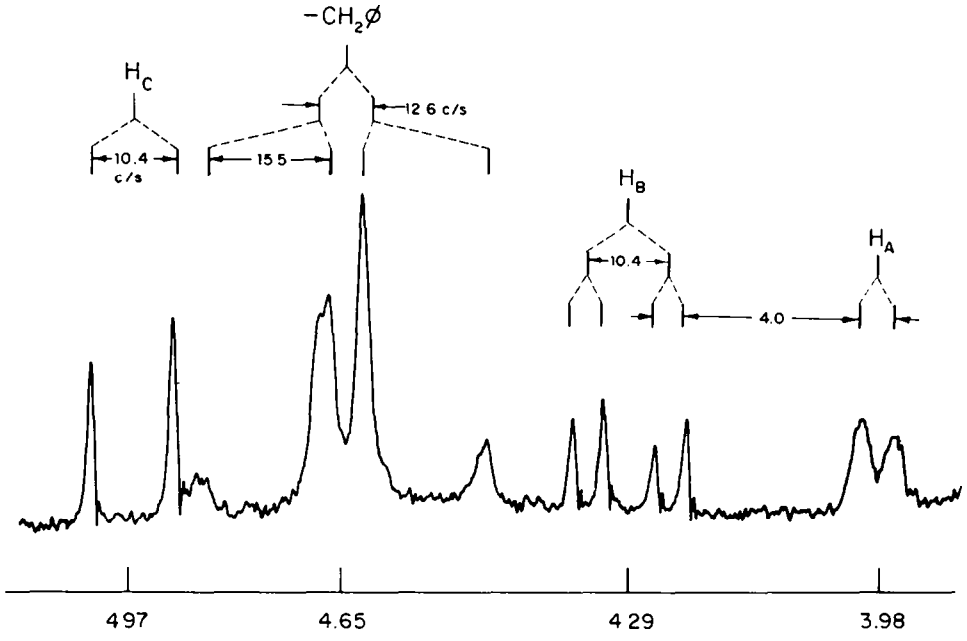
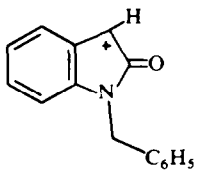


FIG. 1 A portion of the NMR spectrum of **3b** in C_6D_6 solution, at 100 Mc/s. The coupling relationships were demonstrated by the possible permutations of double resonance experiments and by a triple resonance experiment in which the simultaneous irradiation of the doublets at 3·98 and 4·97 ppm caused the collapse of the peaks at 4·29 ppm to a singlet.

In seeking further evidence for the structures of the malonate adducts, we examined their IR and mass spectra. Principal peaks in the IR spectra are listed in the experimental section. The spectrum of the one adduct with a different skeleton (**3b**) was the one least similar to the others in the region 12·5–14·5 μ; the similarities among the spectra of the three compounds (**2a, b,** and **c**) with the same skeleton are striking.

The mass spectra of the esters and some simpler compounds such as *trans*-benzylisatylideneacetic acid and its methyl ester were examined in the hope that the fragmentation pattern for the two isomeric series **2** and **3** would be different enough to allow some rigorous conclusions. Such was not the case: the spectra of isomers **2b** and **3b** were almost indistinguishable from *m/e* of the parent ion at 439 down to 194; even thereafter relative peak intensities only infrequently showed differences



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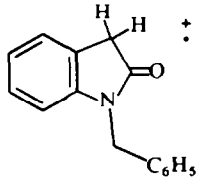

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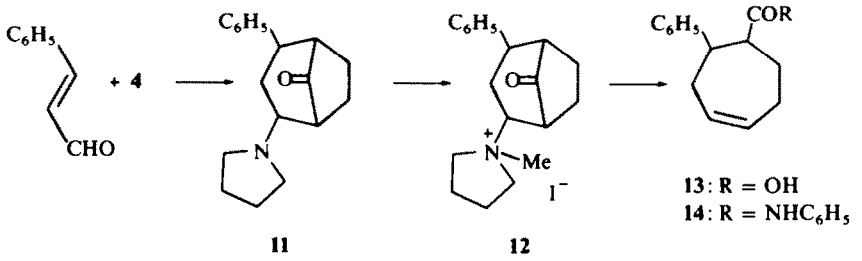
importantly beyond the reproducibility to be expected. For example, the ratio of peaks of *m/e* 222 to 223, for ions **9** and **10**, varied more from run to run on the same compound (e.g. 1·40–1·12) than between **2b** and **3b** (averages: 1·25 vs. 1·11).



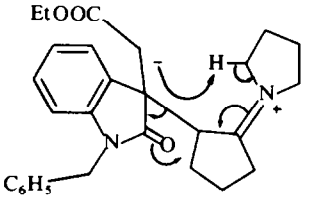
The adducts (**8** and **11**) incorporating the cinnamyl moiety were almost certainly mixtures of stereoisomers. Attempts[6] to make **8** via a traditional Michael condensation, e.g. by the addition of ethyl cyclopentan-2-on-1-carboxylate to ethyl cinnamate, returned only starting materials. However, the material obtained from the Stork reaction[7] showed spectroscopic and chemical properties (see experimental) consistent with its formulation. The structure of the adduct **11** was proven in the same way that Stork[8] showed the structures of the acrolein adducts. The tertiary base was converted to its methiodide **12**, which was cleaved with potassium hydroxide to the phenylcycloheptenecarboxylic acid **13** characterized as its anilide **14**.

DISCUSSION

Two facts of significance to our synthetic program emerge from the preceding results. The malonate condensations which gave rise to the quaternary esters **2a** and **2c** demonstrate that the desired sense of addition to the cross-conjugated double bond can be satisfactorily obtained, even though such addition is the result of carbanion attack at the more hindered end of the trisubstituted double bond. The production of isomeric esters **2b** and **3b** from a closely similar condensation, however, shows that the factors favoring addition in the sense we desired are not overwhelming, but are instead quite subtle. Though we have not sought to prove it, we are inclined to believe that our products are the result of thermodynamic control of the reaction, in which the stabilities of the various possible anions are involved. The three condensations were run in tetrahydrofuran with excess malonate and sodio malonate as the only base present. Product yields were not noticeably affected by acidifying the reaction mixture after 20 min or after 16 hr. In some reactions an intense burgundy color replaced the characteristic orange of the isatylidene ester within moments of the addition and persisted until acidification. The Michael reaction is well known to be readily reversible.[9] Inasmuch as all the substituted malonate anions in the system should be of comparable basicity and the reaction appears to be rapid, we see no reason why equilibrium should not be established. But to go beyond that to attempt a detailed rationalization seems, in the light of other poorly understood aspects of the Michael condensation,[10] not to be warranted.

The products from the reaction of ethyl benzylisatylideneacetate with the enamine (**4**) also do not shed any light on the preferred sense of addition to the isatylidene double bond. Indeed, one may ask whether they arise from reaction between the

two at all, since it is not out of the question that they have arisen from the reaction of the isatylidene ester with decomposition products of dimethylformamide formed during the long reaction period at the boiling point. Several factors incline us to the belief that the enamine has, however, added to the ester at one or the other of the double bond termini, then has been eliminated again. For one thing, the closely analogous reaction with ethyl cinnamate under the same harsh conditions has occurred as expected. For another, the double bond of the benzylisatylideneacetate is extraordinarily electrophilic[1] and should add enamine very readily. That it did so was indicated by the prompt bleaching of its characteristically orange color (otherwise quite stable in dimethylformamide) on addition of the enamine at room temperature, prior to the heating period. The ultimate products may be rationalized as those of a pyrolytic reaction of an initial adduct(s), e.g. as in **15**. New enamines



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arising thus in the anhydrous product mixture would not have survived the hydrolysis and were not specifically sought. The benzyloxindole and undetected ethyl pyruvate might have come from the starting isatylidene ester by retroaldol condensation. However, our previous experience, e.g. in the saponification of **1** to its acid and in the synthesis of **7** from **6** under conditions not too unlike those of this reaction,[1] makes this suggestion unattractive.

EXPERIMENTAL

M.ps, except as noted by (corr) are uncorrected. IR spectra were taken on Perkin–Elmer model 21, 221 and 237 spectrophotometers; mass spectra were measured on an Associated Electrical Industries MS 9 spectrometer. Microanalyses were performed by Micro-Tech Laboratories, Skokie, Illinois.

Methyl trans-1-*benzylisatylidene*-3-*acetate* (**1**, R = Me). The NaH-catalyzed condensation of 44·1 g methyl diethylphosphonoacetate with 47·4 g benzylisatin in dry dimethoxyethane was conducted as described for the ethyl ester.[1] Crystallization of the product from EtOH, then from benzene–Chf, afforded three crops totalling 35·6 g (60·9%), m.p. 117·4–119·5°. The analytical sample, intensely golden needles, m.p. 121·6–122·8° (vac, corr) was crystallized from cyclohexane. (Found: C, 73·94; H, 5·19; N, 4·83. Calc. for $C_{18}H_{15}NO_3$: C, 73·71; H, 5·15; N, 4·78%); UV spectrum (EtOH); 256 (23,600), 260 (sh, 23,100), 316 (6800), and 415 mμ (1000); IR spectrum (KBr): 5·85 μ (both carbonyls).

Triethyl 1-*benzyloxindole*-3-*acetate*-3-*malonate* (**2c**). Sodium (73 mg) was dissolved in a dry soln of diethyl malonate (2·40 g) in 5 ml of THF, and to the soln was added ethyl *trans*-benzylisatylideneacetate (1·87 g) in 5 ml of THF. The soln was stirred for 20 min at room temp, diluted with 100 ml ether, and washed with 100 ml 0·05 M HCl and 100 ml water. The dried ether soln was filtered, then distilled *in vacuo* to leave an oily residue which crystallized on trituration with cyclohexane. Recrystallization from cyclohexane afforded, in three crops, 1·85 g (65%) of crystals, m.p. 86·5–89°. A second recrystallization gave 1·56 g (55%) of crystals, m.p. 91–93°. The analytical sample, m.p. 92–94°, was obtained by two further recrystallizations from cyclohexane. (Found: C, 66·49; H, 6·24; N, 3·22. Calc. for $C_{26}H_{29}NO_7$: C, 66·80; H, 6·25; N, 3·00%); UV spectrum (EtOH): 252 (7500), 279 mμ (sh, 1500); IR spectrum (CS_2): 5·70 (sh), 5·75 and 5·80 μ (sh); (KBr): 12·66, 12·99, 13·61, 13·70, 14·10 and 14·37 μ.

Ethyl dimethyl 1-*benzyloxindole*-3-*acetate*-3-*malonate* (**2b**) and *methyl* 3-(1′-*benzyl*-3′-*oxindolyl*)-3-*ethoxycarbonyl*-2-*methoxycarbonylpropionate* (**3b**). The reaction between Na (39 mg), dimethyl malonate (1·98 g) and ethyl *trans*-benzylisatylideneacetate (1·87 g) in THF was conducted as described for the reaction with diethyl malonate, above. The washed and dried ethereal soln yielded semisolid material on evaporation of the ether. The semisolid was subjected to a fractional recrystallization through 4 crystallizations, alternately from EtOH–water, then cyclohexane to yield ultimately the two isomers **2b** and **3b**. Of the less soluble adduct **2b**, there was obtained 378 mg (14%) of platelets, m.p. 118–122°, plus 557 mg (21%) of less pure material, m.p. 110–114°. Of the more soluble adduct **3b**, there was obtained 773 mg (29%) of colorless needles, m.p. 106–108°. Analytical samples were crystallized from EtOH–water. (Found, for **2b**: C, 65·77; H, 5·90; N, 3·39. Found, for **3b**: C, 65·93; H, 5·95; N, 3·37. Calc. for $C_{24}H_{25}NO_7$: C, 65·59; H, 5·73; N, 3·19%).

Compounds **2b** and **3b** showed a mixture m.p. of 96–120°. Their IR and NMR spectra were distinctly different and the IR spectrum of **2b** was much more like that of **2c** or **2a** than it was like that of its isomer **3b**. However, they were not separated by TLC over alumina (R_f = 0·5) or over Silica Gel G (R_f = 0·7) by 2:1 benzene/ether as developer.

Spectral data for adduct **2b**: UV spectrum (EtOH): 253 (7600), 280 mμ (sh, 1400); IR spectrum (CS_2): 5·68 (sh), 5·73, 5·80 μ (sh); (KBr): 12·58, 12·95, 13·57, 13·66, 14·08 and 14·35 μ.

Spectral data for adduct **3b**: UV spectrum (EtOH): 253 (7700) and 280 mμ (sh, 1500); IR spectrum (CS_2): 5·70 (sh), 5·71 and 5·81 μ; (KBr): 13·28, 13·66 and 14·29 μ.

Trimethyl 1-*benzyloxindole*-3-*acetate*-3-*malonate* (**2a**). The reaction between Na (40 mg), redistilled dimethyl malonate (2·3 g) and methyl *trans*-benzylisatylideneacetate (2·06 g) was conducted as described for the triethyl ester above. After the addition of the first few drops of the isatylidene ester soln to the sodio malonate, the intense orange color changed to pale lavender and deepened to burgundy by the end of the addition. The product could be isolated after 20 min or after 16·5 hr at room temp. The color persisted on dilution with 100 ml of wet ether and was discharged only on vigorous shaking with 100 ml of 1% HCl. The acidified ether was washed with water, then brine, dried over $MgSO_4$, and distilled *in vacuo* to leave a pale orange oil which was heated at 50°/0·1 mm for 3 hr to remove much of the excess malonate. The viscous, pale orange residue weighed 3·26 g. Trituration with MeOH gave 440 mg colorless irregular prisms, m.p. 118–121·5°. The mother liquors, on alternate crystallization from MeOH, then CCl_4, yielded on each crystallization about half the contents as prisms, m.p. ~115–120°. After two full cycles of all the material the combined yield of colorless prisms was 2·57 g (86%), m.p. 121·0–122·5° (corr). The only components in the mother liquors detectable by TLC, IR and mass spectroscopy were the one product and the two starting esters. The analytical sample was obtained from MeOH as prisms, m.p. 124·0–125·6° (corr.). (Found: C, 64·90; H, 5·42; N, 3·36. Calc. for $C_{23}H_{23}NO_7$: C, 64·93; H, 5·45; N, 3·29%); IR spectrum (CS_2): 5·68, 5·75, 5·81 μ; (KBr): 12·74, 13·08, 13·47, 14·05, 14·28 μ.

1-(N-*Pyrrolidinyl*)*cyclopentene* (**4**). This compound was prepared as described[7] in yields of 76 to 86%, b.p. 87–88° (12 mm); lit. b.p. 88–92°. It could be stored with negligible deterioration for up to 6 months if kept refrigerated under dry N_2.

Reaction between ethyl trans-1-*benzylisatylidene*-3-*acetate and* 1-(N-*pyrrolidinyl*)*cyclopentene*. Ethyl benzylisatylideneacetate (1·84 g) was dissolved in 20 ml dry DMF to give the characteristic orange soln. The addition, under N_2, of freshly distilled pyrrolidinyl cyclopentene (552 mg) caused a prompt bleaching of the color to pale yellow. The resulting soln was heated to reflux and maintained there 48 hr. The soln was briefly cooled; 1 ml of water was added to it; then reflux was resumed for 30 min. The cooled soln was diluted with 100 ml ether, then extracted thrice with 50 ml N HCl, once each with 50 ml 5% $NaHCO_3$ aq and water, then dried over $MgSO_4$. The filtered ether soln was evaporated to leave 1·69 g of viscous dark oil which was slowly distilled in a short path still, b.r. 120–160°/10^{-6} mm, to give 866 mg of viscous yellow oil. TLC on Silica Gel G, developer 2:1 benzene/ether, showed that the distillation did not cause the formation of any new compounds not in the pot charge.

The yellow oil was shown by gas chromatography (SF 96 column, 293°) to contain 4 components, three of which were identified. They were: 1-benzyloxindole (36%†), ethyl 1-benzyloxindole-3-acetate (35%†), 1-benzylcyclopentylideneoxindole (4%‡) and an unknown substance (12%‡). Yields, based on enamine, were determined by internal standard (†) or from peak areas (‡). The identity of the three compounds was established by comparing the spectra and m.ps of fractions collected from the gas chromatography with those of authentic synthetic samples.

2-*Phenyl*-4(N-*pyrrolidinyl*)-8-*oxobicyclo*[3.2.1]*octane* (**11**). To a soln of pyrrolidinylcyclopentene (13·7 g) in 50 ml benzene stirred in an ice bath was added dropwise over a 15 min period freshly distilled

cinnamaldehyde (13·2 g) in 20 ml benzene. Precautions were taken to ensure anhydrous reagents and reaction conditions. The reaction solution was stirred for 45 min in the ice bath, then for an hr at room temp, then was heated under reflux for 3·5 hr. The cooled benzene solution was thrice extracted with 100 ml 1N HCl. The combined acid extracts were diluted with 200 ml water and back-extracted with Chf, then ether. (It was subsequently learned that one or more stereoisomers of the product is soluble in Chf as the hydrochloride; CH_2Cl_2 should have been used.) The yellow aqueous layer was cooled, basified with 20% NaOH, and promptly extracted thrice with 150 ml of ether. The ether extract was dried over sodium sulfate, filtered, and the ether was removed *in vacuo* with gentle heating to leave as a viscous brown oil 17·2 g of crude product. This material displayed strong absorption at 334 mμ shown by subsequent isolation and comparison of extinction coefficient to be cinnamylidenecyclopentanone, present in some 13%, so that the corrected crude yield is 56%.

The crude product was purified most effectively as follows. It was dissolved in 150 ml 3N HCl and the soln was diluted with 1200 ml water. The solution was extracted thrice with 300 ml portions of CH_2Cl_2 and once with 300 ml ether. The combined organic extracts were washed with 300 ml water which was added to the original aqueous layer. It was then cooled to 0°, basified by the addition of 30 g of NaOH in 150 ml water, and extracted with three 500 ml portions ether. The ether soln was dried over Na_2SO_4, filtered and distilled *in vacuo* to leave 12·3 g (46%) of the bicycloketoamine as a pale yellow oil. A conservative estimate that the material was 95% pure at this point was based on spectral evidence. The IR spectrum differed from that of the analytical sample only in showing a weak shoulder at 5·85 μ and in small (less than 10%) differences in relative intensities of some bands, differences that may well be due to differences in the relative proportions of isomers. The NMR spectrum showed no detectable differences. The UV spectrum showed no more than 0·8% remaining cinnamylidenecyclopentanone.

An analytical sample was prepared by chromatography over Woelm basic alumina, activity I, and eluted with benzene, then distilled in all glass apparatus with a mercury diffusion pump, to give a clear oil. Poos[3] subsequently reported the material crystalline, m.p. 68–73°. (Found: C, 80·08; H, 8·70; N, 5·33. Calc. for $C_{18}H_{23}NO$: C, 80·26; H, 8·61; N, 5·20%).

UV spectrum (EtOH): 246 (sh, 374), 257 (410), 264 (330), 267 (sh, 260) and 288 mμ (173); IR spectrum (film): 3·38, 3·40, 3·44, 3·48, 3·60 and 3·68 μ, C—H stretching vibrations, some characteristic of the bicycloketoamine nucleus; and 5·71 μ, strained carbonyl.

The hydrochlorides of at least some of the isomeric bicycloketoamines were found to be appreciably soluble in organic solvents, especially in Chf, in which 15–25% was extracted by a typical three extractions of the aqueous acid soln. Even CH_2Cl_2 extracted some. The combined CH_2Cl_2 and ether extractions of the acidic solution above were dried over $MgSO_4$, filtered and distilled to leave 3·6 g dark material the carbonyl spectrum of which indicated it to be about a 2:3 mixture of bicycloketoamine hydrochloride and cinnamylidenecyclopentanone.

2-Phenyl-4(N-pyrrolidinyl)-8-oxobicyclo[3.2.1]*octane methiodide* (**12**). Pure bicycloketoamine (396 mg) was stirred in MeI (3 ml) soln for 6 hr at room temp. The excess MeI was removed *in vacuo* to leave a yellow foam which was triturated with 4:1 ether/MeOH. Filtration gave 63 mg (10%) methiodide, m.p. 245·5–246·5° (dec). The sharp m.p. suggests that the material is only one of the four possible racemic modifications. The analytical sample was obtained by one recrystallization from MeOH. (Found: C, 55·59; H, 6·33; N, 3·54. Calc. for $C_{19}H_{26}INO$: C, 55·48; H, 6·37; N, 3·41%); IR spectrum (KBr): 5·73 μ; no absorption at 3·60 μ.

The only other crystalline material obtained from the reaction, isolated from the trituration mother liquors by crystallization from MeOH, was 47 mg (8%) of the bicycloketoamine hydriodide, m.p. 179–182° (dec). Two recrystallizations from MeOH/ether gave material of m.p. 180–184° (dec). (Found: C, 54·26; H, 6·61; N, 3·22. Calc. for $C_{18}H_{24}INO$: C, 54·42; H, 6·09; N, 3·53%).

2-Phenylcyclohept-4-ene carboxylic acid (**13**) *and its anilide* (**14**). 2-Phenyl-4(N-pyrrolidinyl)-8-oxobicyclo[3.2.1]octane methiodide (582 mg of the total crude product from the base and MeI) was added to a soln of 6 g KOH in 15 ml MeOH, and the resulting soln was boiled for 3 hr. It was then diluted with water and extracted with ether. The aqueous layer was cooled, then acidified and again extracted with ether. The dried ether extracts yielded 226 mg (74%) of the crude carboxylic acid as a quite viscous pale yellow oil, the NMR and IR spectra of which were in accord with expectation except for the presence of a shoulder at 5·78 μ indicative of ester or lactone contamination.

From the crude acid (153 mg) an anilide was prepared by the customary sequence; conversion to the acid chloride with $SOCl_2$, then reaction with aniline, gave 214 mg of crude anilide as an amorphous tan powder from which we obtained by crystallization from acetone/water, 45 mg (22%) of needles, m.p.

141–153°. Two further crystallizations from acetone/water gave colorless, silky needles, m.p. 158·5–159·5°. (Found: C, 82·17; H, 7·35; N, 4·86. Calc. for $C_{20}H_{21}NO$: C, 82·44; H, 7·26; N, 4·81%).

Ethyl 3-(2'-*oxocyclopentyl*)-3-*phenylpropionate* (**8**). Ethyl cinnamate (37·1 g) and pyrrolidinylcyclo pentene (14·3 g) were mixed in 100 ml dry DMF, heated 41 hr under reflux, and cooled to 50°. Water (10 ml) was added to the soln which was then again boiled for an hr. The cooled soln was diluted with 500 ml water and thrice extracted with 250 ml portions ether. The combined ether extracts were washed with 5% HClaq, 5% $NaHCO_3$aq, water, then dried over $MgSO_4$. On distillation, the filtered soln yielded 13·4 g (49%) colorless product, b.p. 145°/0·8 mm, $n_D^{27°}$ 1·5156, b.p. 125°/0·05 mm. (Found: C, 73·85; H, 7·77. Calc. for $C_{16}H_{20}O_3$: C, 73·82; H, 7·74%).

Semicarbazone[7] (still a mixture of diastereomers?), m.p. 155–157° after recrystallization from EtOH–water: (Found: C, 64·60; H, 7·21; N, 13·31. Calc. for $C_{17}H_{23}N_3O_3$: C, 64·33; H, 7·30; N, 13·24%).

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