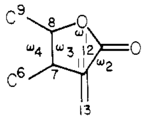
plane of the ring in the configuration depicted in Figure 1) but project away from each other as the result of a small movement of C-3 and C-6 out of the nodal plane of the C-4, C-5 double bond which produces a torsion angle of 168°. The conformation in solution does not appear to depart significantly from that observed in the crystal as judged by the observed[2] coupling constants for H-1, H-5, H-8, and H-9; in particular, the dihedral angles involving H-1 and H-9β and involving H-9α and H-14 (see Figure 1) satisfy the requirements for allylic and W coupling, respectively. With ω_4 (the C(6)–C(7)–C(8)–C(9) torsion angle) = −89°, the lactone ring of frutescin belongs to Samek's pseudorotational S type[7] for which $J_{7,13} \geq 3$ Hz as is actually observed.[2]



The remaining problem is the absolute configuration of frutescin, which on the basis of the generalization that H-7 in sesquiterpene lactones from higher plants is axial and α would be expected to that shown in Figure 1. In that case the C=C—C=O and the C(11)–C(7)–C(8)–O(1) torsion angles (ω_2 and ω_3, respectively) are both positive and thus of like sign (see Table V), as is the case in most α-methylene γ-lactones previously examined by X-ray diffraction.[12,13] Hence either by Beecham's rule,[14] which relates the chirality of the lactone chromophore (the sign of ω_2) in trans-fused lactones to the sign of the lactone Cotton effect, or by the more recent suggestion[15,17] that the sign of ω_3 and the magnitude of ω_4 provide a better correlation with the sign of the Cotton effect, frutescin if represented by absolute configuration **2** should exhibit a positive Cotton effect in the 250-nm region.

We previously[2] reported a negative lactone Cotton effect for frutescin. However, reexamination of the original trace showed that the observed molecular ellipticity at 247 nm (−7900) did not represent a true negative maximum but was a reading near the cut off point of the instrument. Redetermination of the CD curve on an instrument of more recent vintage afforded the values $[\Theta]_{319}$ −2160 (negative maximum), $[\Theta]_{290}$ −1080 (negative minimum), $[\Theta]_{250}$ −10800 (sh), $[\Theta]_{223}$ −28000 (negative maximum), and $[\Theta]_{210}$ −8600 (last reading). The negative maxima at 319 and 223 nm represent the n,π^* and π,π^* transitions of the α,β-unsaturated aldehyde which effectively swamp the n,π^* transition of the α,β-unsaturated lactone chromophore. If the latter were responsible for the observed slight negative hump near 250 nm, frutescin would be the mirror image of **2** and should be rewritten as **3** to maintain H-7α.[18a] Additional work which requires reisolation of frutescin is necessary to decide whether this is really so.[18b]

Experimental Section

Single crystals of frutescin were obtained by slow crystallization from ethyl acetate. They were orthorhombic, space group $P2_12_12_1$, with a = 7.684 (1) Å, b = 10.506 (2) Å, c = 16.092 (2) Å, and d_{calcd} = 1.2598 cm^3 for Z = 4 ($C_{15}H_{18}O_3$, M_r = 246.31). The intensity data were measured on a Hilger-Watts diffractometer (Ni-filtered Cu Kα radiation, θ–2θ scans, pulse-height discrimination). The size of the crystal used for data collection was approximately 0.08 × 0.35 × 0.4 mm. A total of 1046 accessible reflections were measured for $\theta < 57°$ of which 955 were considered to be observed $[I < 2.5\sigma(I)]$. The structure was solved by a multiple-solution procedure and was refined by full-matrix least-squares methods. In the final refinement, anisotropic thermal parameters were used for the nonhydrogen atoms and isotropic temperature factors were used for the hydrogen atoms. The hydrogen atoms were included in the structure factor calculations, but their parameters were not refined. The final discrepancy indices are R = 0.033 and R_w = 0.041 for the 955 observed reflections. The final difference map has no peaks greater than 0.1 e Å^{-3}.

Registry No. 2, 36790-43-9.

Supplementary Material Available: Tables I–IV containing final atomic parameters, final anisotropic parameters, bond lengths, and bond angles for compound **2** (3 pages). Ordering information is given on any current masthead page.

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[14] Beecham, A. F. *Tetrahedron* **1972**, *28*, 5543.

[15] As has been pointed out by McPhail and Onan[16] the sign of ω_3 is also related to the magnitude of ω_4 such that if $\omega_4 < 120°$, ω_3 is negative, and if $\omega_4 > 120°$, ω_3 is positive. For negative values of ω_4, if $|\omega_4| < 120°$, ω_3 is positive (as Table V also shows), and for $|\omega_4| > 120°$, ω_3 is negative.

[16] McPhail, A. T.; Onan, K. D. *J. Chem. Soc., Perkin Trans. 2*, **1976**, 578.

[17] Cox, P. J.; Sim, G. A. *J. Chem. Soc., Perkin Trans. 2*, 1977, 255.

[18] (a) In that case, frutescin would not be classified as a melampolide, (a *cis*-1(10),*trans*-4-germacradienolide) by the current classification scheme (Neidle, S.; Rogers, D. *J. Chem. Soc., Chem. Commun.* **1972**, 140) but as a *cis*-4,*trans*-9-germacradienolide. (b) Note Added in Proof: The CD curve of schkuhriolide (**4**), kindly supplied by Dr. A. Romo de Vivar, is strikingly different from that of frutescin in the n,π^* and π,π^* region of the α,β-unsaturated aldehyde chromophore: $[\theta]_{316}$ +1890, $[\theta]_{241}$ −12600; $[\theta]_{210}$ +24600 (last reading).

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Extensions of the Hydrazone and Beckmann Rearrangements[1]

Kenneth Nolon Carter* and James E. Hulse, III

Department of Chemistry, Presbyterian College, Clinton, South Carolina 29325

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The rearrangement of hydrazones to amides, $R_2C{=}NNH_2 \rightarrow RCONHR$, in a sodium nitrite-concentrated sulfuric acid medium was discovered by Pearson and Greer in 1949.[2] When the rearrangement was applied to the stereoisomeric hydrazones[3] of 4-methoxybenzophenone and 4-bromobenzophenone, the results obtained allowed assignments of structures if anti migration was assumed to occur as in the Beckmann rearrangement of oximes. Later, subjection of the Z and E isomers of camphorquinone-3-hydrazone, the configurations of which were known from other work, to hydrazone rearrangement conditions gave α-camphoramic acid.[4] It was concluded that this product was produced by a cleavage-type rearrangement similar to the Beckmann rearrangement of camphorquinone 3(E)-oxime.[5]

The purpose of the work here reported was to modify the rearrangement medium by using commercial nitrosylsulfuric acid and to extend the scope of the rearrangement to include a series of aromatic diketone monohydrazones (Scheme IB). In addition to this, the simultaneous oximation and Beckmann rearrangement method using hydroxylamine-O-sulfonic acid was applied to the corresponding diketones (Scheme IA). An examination of the literature showed that this method had been used with aryl alkyl ketones,[6] diaryl ketones,[7] and alicyclic

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[1] Presented at the 181st National Meeting of the American Chemical Society, Atlanta, GA, Mar 1981; Abstract ORGN 38.

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[4] K. N. Carter, *J. Org. Chem.*, 23, 1409 (1958).

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Scheme I

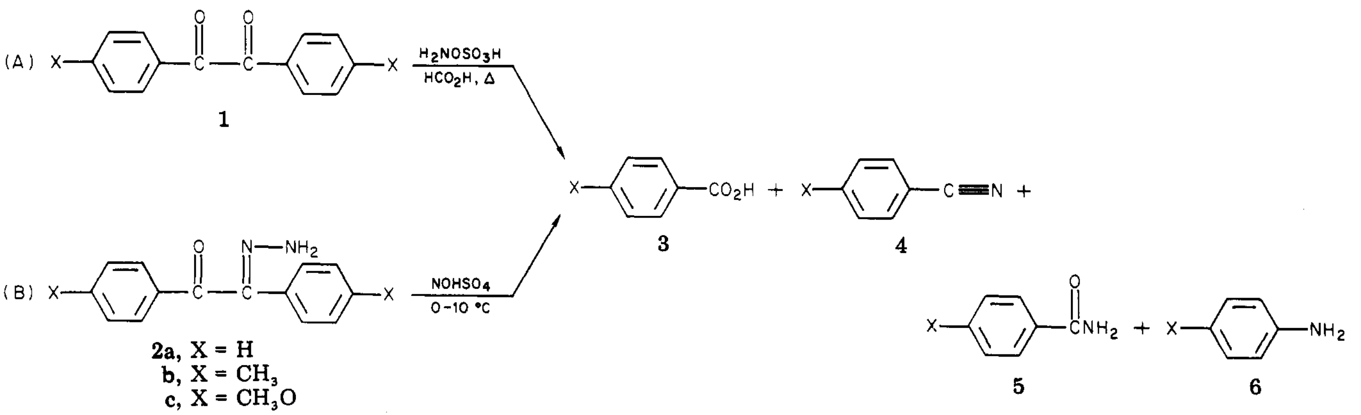

Table I. Yields of 3-6 from the One-Step Beckmann Cleavage of 1,2-Diketones 1

	% yield		
X	acid 3	nitrile 4 and amide 5	amine 6
H	90	71	0
CH_3	87	53	trace
CH_3O	59	55	28

Table II. Yields of 3, 4, and 6 from the Cleavage Rearrangement of 1,2-Diketone Monohydrazones 2

	% yield		
X	acid 3	nitrile 4	amine 6
H	95	62	trace
CH_3	85	82	not determined
CH_3O	96	74	trace

ketones,[8] all of which produced normal Beckmann rearrangement products.

The one-step Beckmann rearrangement was carried out by heating the diketone with hydroxylamine-*O*-sulfonic acid in formic acid, the method used by Olah and Fung with alicyclic ketones.[8] It was carried out on benzil (**1a**), 4,4′-dimethylbenzil (**1b**), and 4,4′-dimethoxybenzil (**1c**). In each case (Table I), the acid **3** and nitrile **4** (and corresponding amide **5**) characteristic of the Beckmann cleavage (Scheme IA) of the (*E*)-monoxime were produced. In addition, in two of the three cases, hydrolysis produced an amine, **6** (trace from **1b**, 28% from **1c**), which was indicative of a degree of normal Beckmann rearrangement of the (*Z*)-oxime. While most interpretations of the cleavage Beckmann do not involve an intermediate carbon to nitrogen migration, obviously amine formation requires it.[9] The rearrangement product which produced the amine upon hydrolysis was not isolated.

The original rearrangement medium for the hydrazone rearrangement was a sulfuric acid–sodium nitrite mixture.[2] Substitution of commercial nitrosyl sulfate for the sodium nitrite gave excellent results with a considerable reduction in the overall time required. Benzophenone hydrazone gave benzanilide in essentially quantitative yield. Therefore, the nitrosyl sulfate method was used for all of the hydrazone rearrangement reactions in this study.

The similarity of the Beckmann,[5] hydrazone,[4] and Schmidt[10] reactions of camphorquinone 3(*E*)-oxime, camphorquinone 3(*E*)-hydrazone, and camphorquinone, respectively, contrasted with the fact that the formation of the major product of the Schmidt reaction with benzil[11] involves a carbon to nitrogen migration. This suggested studying the rearrangement of the series of aromatic diketone monohydrazones. In each case, as a preliminary experiment with benzil monohydrazone (**2a**) had indicated,[12] the products were the acid **3** and nitrile **4** (Table II), interpreted as being formed by cleavage of the *E* isomer (Scheme IB), and only a trace of the amine **6**. Only one monohydrazone was isolated from each preparation reaction mixture. The fact that only a trace of amine was obtained in any of the hydrazone rearrangements emphasizes that there was little isomerization prior to rearrangement.

Experimental Section

Reaction of Diketones with Hydroxylamine-*O*-sulfonic Acid (HOSA). The diketone **1** (0.0050 mol), HOSA (0.0075 mol), and 10 mL of 87–90% formic acid were refluxed for 3.0 h. The reaction mixture was cooled and poured into 100 mL of 10% NaOH. The resulting alkaline mixture was extracted with five 25–50-mL portions of ether. The ether solution was dried over anhydrous Na_2SO_4 and the ether subsequently removed by distillation. The extract was shown to consist principally of the nitrile **4** and corresponding amide **5**. The mixture was then hydrolyzed by reflux with 10 mL of 10% NaOH (3–6 h). The hydrolysate was extracted with ether. The ether solution was dried over anhydrous Na_2SO_4, and the removal of the ether by distillation gave the amine **6**, if any. The alkaline hydrolysate was acidified and the resulting acid isolated by filtration and/or ether extraction.

The alkaline solution remaining from the original ether extraction of the rearrangement product mixture was acidified and the resulting acid (**3**) isolated by filtration and/or ether extraction. The products and yields are listed in Table I.

Preparation of the Monohydrazones of the Diketones. The procedure was essentially as previously reported[3] for the preparation of the hydrazones of monoketones. The ketone and a slight excess of anhydrous hydrazine were mixed with sufficient anhydrous or 95% ethanol to produce homogeneity at the boiling point and refluxed for approximately 1 h. The resulting hydrazone was recrystallized from ethanol. The melting points were as follows: **2a**, mp 147–150 °C (lit.[13] mp 151 °C); **2b**, mp 139–142 °C (lit.[13] mp 139–140 °C); **2c**, mp 140–142 °C (lit.[13] mp 133 °C). Fractional crystallizations with a variety of solvents gave no evidence of the presence of more than one of the two possible

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isomers in any case. Also, syntheses of the hydrazones in dioxane at 0–10 °C gave results similar to those obtained by using ethanol at elevated temperatures.

Hydrazone Rearrangement Using Commercial Nitrosyl Sulfate. As a preliminary experiment, the benzophenone hydrazone rearrangement[3] was repeated with substitution of the equivalent quantity of nitrosylsulfuric acid for the $NaNO_2$. The crude yield of benzanilide (mp 159.7–161.1 °C) was 97%. This method, which reduced the reaction time to about half and produced a purer product, was then used in the following work with the diketone monohydrazones.

Concentrated H_2SO_4 (6.3 ml) was added to a 30-mL beaker equipped with a ball stirrer and cooled in an ice bath. Nitrosylsulfuric acid (1.3 mL, 0.0073 mol of Du Pont nitrosyl sulfate, 40% in 87% H_2SO_4) was added with stirring. The powdered diketone monohydrazone **2** (0.0050 mol) was added over a 20-min period, with gas being evolved upon each addition. Stirring and cooling were continued for 10 min longer. The reaction mixture was poured into a mixture of ice and NaOH solution (12.5 g of NaOH in 50 mL of H_2O). The remainder of the product isolation and identification procedure was then carried out as in the Beckmann rearrangement above.

Identification of Rearrangement Products. All solids were identified by melting point (corrected) and mixture melting point with authentic samples. The trace amounts of liquid amines and the nitriles were identified by infrared spectrophotometry, and the nitriles were hydrolyzed to the corresponding acids. In addition, **6c** was converted to the anilide.

A number of runs were made in some cases, and typical melting points of unrecrystallized product obtained at various points in the rearrangement procedures were as follows (literature[13] values in parentheses): **3a**, 121.5–123 °C (122 °C); **3b**, 179.0–180.5 °C (181 °C); **3c**, 183.0–184.0 °C (184 °C); **5a**, 126.0–128.5 °C (130 °C); **5b**, 159.0–160.0 °C (155 or 165 °C); **5c**, 166.0–167.2 °C (163 °C); **6c**, 53–56 °C (57 °C); benzanilide, 159.7–161.1 °C (163 °C); 4-methoxyacetanilide, 128.0–129.0 °C (130–132 °C).

Registry No. **1a**, 134-81-6; **1b**, 3457-48-5; **1c**, 1226-42-2; **2a**, 5344-88-7; **2b**, 40030-78-2; **2c**, 40030-79-3; **3a**, 65-85-0; **3b**, 99-94-5; **3c**, 100-09-4; **4a**, 100-47-0; **4b**, 104-85-8; **4c**, 874-90-8; **5a**, 55-21-0; **5b**, 619-55-6; **5c**, 3424-93-9; **6c**, 104-94-9; **6c** benzanilide, 7472-54-0; **6c** 4-methoxyacetanilide, 51-66-1.

Preparation of Spiro[cyclopropane-1,3'-[3*H*]indol]ones from Isatin in a Novel One-Step Process. A Study of Long-Range Chiral Recognition

Marcel K. Eberle,* Gerard G. Kahle, and Michael J. Shapiro

Department of Chemistry, Pharmaceutical Division Sandoz, Inc., East Hanover, New Jersey 07936

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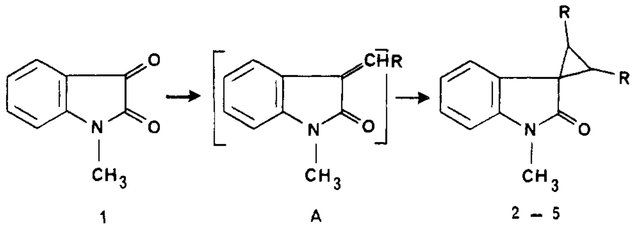
The spiro[cycyopropane-1,3'-[3*H*]indol]-2'(1'*H*)-one ring system has been prepared by the addition of diazomethanes[1] and stabilized sulfur ylides[2] to (2-oxindolin-3-ylidene)acetic esters. We have observed that Wittig reagents add to 1-methylisatin (**1**) to give this ring system in a single operation. Treatment of **1** with 1 equiv of the ylide prepared from 5-bromopentene and triphenylphosphine[3] in ether gave 15% of **2**, triphenylphosphine, and its oxide. The yield was increased to 74% by extraction of **1** from a Soxhlet with refluxing toluene into 2 equiv of the ylide. The trans isomer was isolated in pure form as indicated by the ^{13}C NMR spectrum with all the carbons accounted for by individual signals. Nonequivalency for the diastereotopic[4] carbons removed by four bond lengths from the nearest center of asymmetry was detected. In the proton-coupled spectrum of **2** the methine carbons of the cyclopropane ring (39.8 and 40.1 ppm) gave rise to a doublet with a coupling constant of 160 Hz, characteristic for this ring system.[5]

Scheme I[a]



[a] **2**, R = $CH_2CH_2CH{=}CH_2$; **3**, R = C_6H_5; **4**, R = $CH_2CH_2C_6H_5$; **5a**, R = $CH_2CH_2CH_2OC_6H_5$; **5b**, R = $CH_2CH_2CH_2OC_6H_5$.

Cyclopropyl rings have been isolated from Wittig reactions starting with fluorenone[6] and in intramolecular additions to an unsaturated ketone.[7] While the reaction of a stabilized ylide to isatin stops after one addition,[8] we have observed a faster addition of a second mole of ylide to the presumed intermediate A (Scheme I). This parallels the addition of an ylide to an unsaturated ketone[9] to form a spirocyclopropane ring system.

Since the spectral data of **2** did not allow the observation of the cyclopropyl protons due to overlap with the methylene protons, it was decided to examine the reaction of benzyltriphenylphosphonium benzylide[10] with **1**. We obtained **3** in 53% yield which allowed the isolation of pure *trans*-**3** as a white solid. In the ^1H NMR spectrum of **3** an AB quartet was seen at δ 3.80 (J = 9 Hz, $\Delta\nu$ = 24.5 Hz). This pattern is compatible with the presence of a cyclopropyl ring in **3**. One of the indole protons (C_4 H) was shifted upfield (δ 6.10, d, J = 8 Hz) due to the shielding effect by the two phenyl groups. The addition of (3-phenylpropyl)triphenylphosphonium 3-phenylpropylide[11] to **1** proceeded in 22% yield to give **4**.

More informative was the reaction between **1** and the ylide from (4-phenoxybutyl)triphenylphosphonium bromide[12] which gave **5** in 56% yield. Two isomers were separated, and their proton NMR spectra allowed us to distinguish the trans isomer from one of the cis isomers. The phenoxy-substituted methylene groups were observed at δ 3.86 as a triplet (J = 6 Hz) and as a multiplet for the cis and the trans isomers, respectively. The ^{13}C NMR spectra confirmed the assignments. For the trans product the carbons of the side chains appeared as two sets of signals. An interesting feature emerged from close inspection of

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