B. Vallverdú for the pK_a measurement of imidazole-2-diazonium cation (starting from 2-aminoimidazole hydrochloride instead of its sulfate), which corroborated the formerly reported value.

Registry No. 1, 59214-43-6; **1a**, 112298-51-8; **1b**, 112298-48-3; **1e**, 112298-52-9; **2**, 112298-50-7; **2a**, 112298-53-0; **2c**, 112298-56-3; **2e**, 112298-54-1; **3**, 57351-74-3; **3a**, 59105-03-2; **3b**, 112298-57-4; **3c**, 112298-58-5; **3e**, 112298-55-2; **4**, 2033-24-1; **5**, 112298-42-7; **6**, 112298-49-4; **7**, 112298-47-2; isopropylidene 3(5)-pyrazolylhydrazonomalonate, 112298-43-8; isopropylidene 1,2,4-triazol-3-ylhydrazonomalonate, 112298-44-9; isopropylidene 1-methylimidazol-2-ylhydrazonomalonate, 112298-45-0; isopropylidene 1-methylpyrazol-3-ylhydrazonomalonate, 112298-46-1; 2-aminoimidazolium sulfate, 36946-29-9; 3(5)-aminopyrazole, 1820-80-0; 2-amino-1-methylimidazole hydrochloride, 1450-94-8; 3-amino-1-methylpyrazole, 1904-31-0.

Supplementary Material Available: ^{1}H NMR, ^{13}C NMR, and ^{15}N NMR spectra of **1a** and **1e** labeled partially at N-2 (1 page). Ordering information is given on any current masthead page.

Quinone Methide *p*-Hydroxybenzylation of 1,3-Diketones

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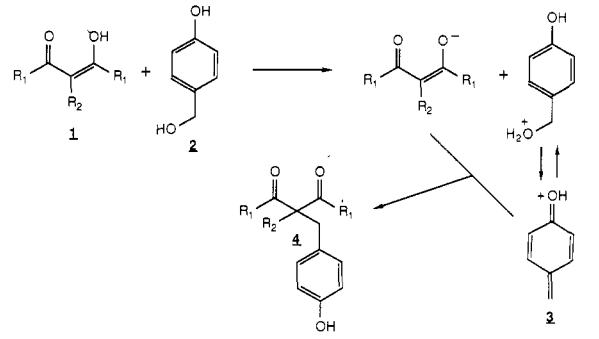
The Michael addition of 1,3-diketones to unsaturated compounds is well documented and has been extensively utilized in the preparation of natural products.[1] Quinone methides are conjugated homologues of vinyl ketones but are more reactive due to the additional driving force of aromatization after conjugate addition. The application of these highly conjugated intermediates to the formation of carbon–carbon bonds is limited by the stability of the quinone methide and the method for its generation.[2] Recently, the synthesis of delesserine has been achieved by the addition of 2-*O*-methylascorbic acid to the protonated methylene quinone derived from *p*-hydroxybenzyl alcohol.[3] Herein, we describe the application of this methodology to the C-2 benzylation of 1,3-diketones.

Treatment of cyclic and acyclic enolizable 1,3-diketones, **1**, with *p*-hydroxybenzyl alcohol, **2**, in water lead to carbon alkylation products, **3**.[4] These vinylogous acids are sufficiently acidic to facilitate generation of protonated quinone methides.[5] Consequently, the reaction proceeds by protonation of the benzylic alcohol, elimination of water to **4**, and finally addition of the conjugate base of **1** to yield **3**.[6] When ethyl acetoacetate or ethyl 2-oxocyclopentanecarboxylate was exposed to an aqueous solution of **2**, no addition product was observed.



R_1	R_2	Yield (%)
CH_3	H	78
$-CH_2-CH_2-$	H	18
$-CH_2-CH_2-CH_2-$	H	22
$-CH_2-C(CH_3)_2-CH_2-$	H	18
$-CH_2-CH_2-$	CH_3	97
$-CH_2-CH_2-CH_2-$	CH_3	73

Experimental Section

Typical Procedure. Preparation of 2-(4-Hydroxybenzyl)-2-methyl-1,3-cyclopentanedione. To 2-methyl-1,3-cyclopentanedione (111 mg, 1.0 mmol) in water (3 mL) was added *p*-hydroxybenzyl alcohol (62 mg, 0.5 mmol), and the solution was stirred at 80 °C for 12 h. The reaction mixture was evaporated and the residue chromatographed (1:1 EtOAc/hexanes) to give 105 mg (97%) of 2-(4-hydroxybenzyl)-2-methyl-1,3-cyclopentanedione: mp 146–147 °C; ^{1}H NMR ($CDCl_3$) δ 1.18 (s, 3 H), 1.8–2.8 (m, 4 H), 2.88 (s, 2 H), 5.8–6.2 (br s, 1 H), 6.6 (d, J = 14.5 Hz, 2 H), 6.85 (d, J = 14.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 19.7, 35.9, 42.5, 58.7, 115.5, 127.4, 130.8, 155.2, 218.6; IR ($CDCl_3$) ν 1730, 1619, 1522 cm^{-1}; MS (70 eV), m/e (relative intensity) 218 (9.7), 107 (100), 77 (7.4). Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.40; H, 6.5.

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Thioanhydrides. 2. Synthesis of Phthalic Thiothionoanhydrides†

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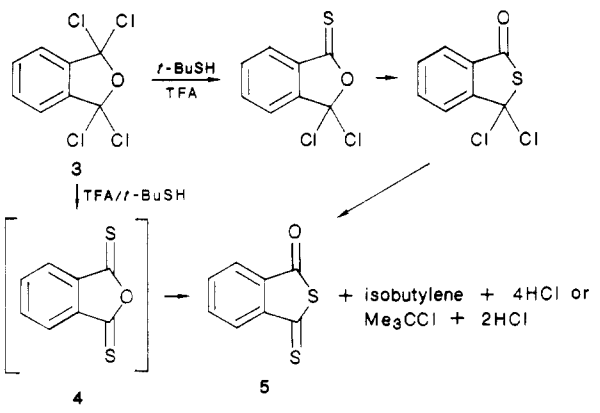
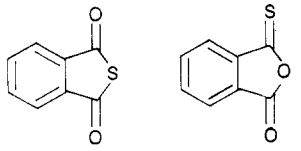
Phthalic thioanhydride (**1**) has been a well-known compound since 1911,[1] but its unstable isomer, phthalic thionoanhydride (**2**), is the subject of only a single report.[2] The thione **2** readily isomerizes to **1**. Neither of the phthalic dithioanhydrides **4** or **5** has been reported previously, although both 1,8-naphthalic dithioanhydride and 1,8-naphthalic thiothionoanhydride have been made in these laboratories.[3] Phthalic thiothionoanhydride (**5**) has now been synthesized by the reaction of *tert*-butyl mer-

† For Part 1, see ref 3.

Scheme I

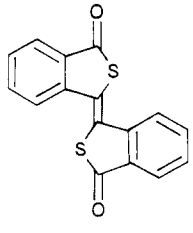


captan, in the presence of catalytic amounts of trifluoroacetic acid, with 1,1,3,3-tetrachloro-1,3-dihydroisobenzofuran (**3**); compounds of the latter type may be prepared from phthalides by the action of phosphorus pentachloride.[4-6]



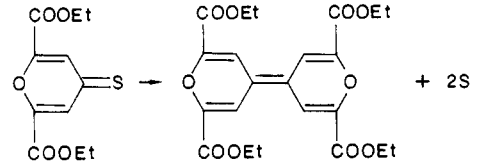
1 **2**

The reaction takes place by one or both of the routes in Scheme I. Each route involves the rearrangement exhibited by **2** to the more thermodynamically stable isomer. The conversion of a readily solvolyzed *gem*-dichloro function to a thione by this procedure was discovered by Lawesson and co-workers,[7] who applied it to the preparation of thiobenzophenone from dichlorodiphenylmethane and of thioxanthenethione from 9,9-dichlorothioxanthene. Phthalic thiothionoanhydride (**5**) is readily isolated and recrystallized (47% yield), as black needles. On long storage at room temperature, or on being heated, it loses sulfur and is converted to *trans*-dithiobiphthalide (**6**).

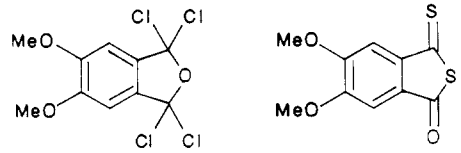


6

The thermal loss of sulfur from thiones to form ethylene derivatives is known in a number of instances.[8] Notable among these is the following reaction, which occurs very slowly at 20 °C and within 10 min at 100 °C.[9] Appreciable



stability may be added to the phthalic dithioanhydride structure by introducing methoxyl groups. 4,5-Dimethoxythiothionophthalic anhydride (**8**) has been made by the same synthetic method from the tetrachlorophthalan **7**. Resonance stabilization is conferred on this molecule, which is considerably less prone to the loss of sulfur than the parent **5**. It is stable at ambient temperatures under average laboratory conditions.



7 **8**

Experimental Section

Melting points are uncorrected. Proton NMR spectra were determined in $CDCl_3$ solution on a Bruker B-NC 12 (90 MHz) spectrometer with Me_4Si as internal standard, and the δ values are reported in ppm downfield from it. IR spectra were taken in KBr on a Perkin-Elmer 781 spectrophotometer. UV-vis spectra were taken on a Perkin-Elmer Lambda 4B spectrophotometer.

Phthalic Thiothionoanhydride (5). A solution of 5.16 g (0.02 mol) of 1,1,3,3-tetrachloro-1,3-dihydroisobenzofuran,[4] 30 mL of CH_2Cl_2, 7.2 g (0.08 mol) of *tert*-butyl mercaptan, and 0.7 mL of trifluoroacetic acid were refluxed for 15 h. The volatiles were boiled off on a steam bath and finally under vacuum. The residue was recrystallized from hexane (green solution) to give 1.7 g (47%) of black needles of phthalic thiothionoanhydride (**5**): mp 87–88 °C; IR 1720 (>C=O), 1585 cm^{-1} (C=C); UV-vis (CH_2Cl_2) λ_{max} 339 (ϵ 17 045), 316 (24 432), 247.5 (43 750), 210 nm (12 500); mass spectrum, *m/e* (relative intensity) 180 (M^+, 100), 164 (8.4), 152 (28.5), 120 (25.0), 108 (10.2), 104 (32.1), 76 (36.9); NMR 8.15 (m, 1 H), 7.8 (m, 3 H).

Anal. Calcd for $C_8H_4OS_2$: C, 53.31; H, 2.24; S, 35.58. Found: C, 53.10; H, 2.36; S, 35.89.

Pyrolysis of Phthalic Thiothionoanhydride To Yield 6. When phthalic dithioanhydride was heated in a mp capillary melting point apparatus to 180 °C, a sudden transformation to dithiobiphthalide was observed. The anhydride (0.5 g) was heated in a test tube in an oil bath at 230 °C for 5 min. The product was cooled, washed with carbon disulfide, and recrystallized from chlorobenzene to give 0.32 g (78%) of yellow needles of *trans*-dithiobiphthalide (**6**): mp 352 °C identical in all respects with an authentic sample prepared according to the literature.[11]

4,5-Dimethoxyphthalic Thiothionoanhydride (8). 5,6-Dimethoxyphthalide[10] was converted by reaction with phosphorus pentachloride to 1,1,3,3-tetrachloro-1,3-dihydro-5,6-dimethoxyisobenzofuran (**7**).[6] This was reacted with *tert*-butyl mercaptan as described in the synthesis for phthalic dithioanhydride. The 4,5-dimethoxyphthalic dithioanhydride (**8**) was recrystallized from benzene in two crops of brown crystals: 70% yield, mp 165–166 °C; IR 1720, (>C=O), 1580 (C=C) cm^{-1}; UV-vis (CH_2Cl_2) λ_{max} 214.8 (ϵ 3747), 265 sh (14 042), 275 (20 210), 280 sh (20 343), 320 (10 283), 332.5 (13 807), 360 (10 880), 432.6 (2217); mass spectrum, *m/e* (relative intensity) 240 (M^+, 100), 224 (54), 212 (9.4), 197 (7.2),

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180 (29.4), 164 (13.6), 136 (14.5), 93 (9.2); NMR 7.52, (s, 1 H), 7.19 (s, 1 H), 4.05, (s, 3 H), 4.04 (s, 3 H).

Anal. Calcd for $C_{10}H_8O_3S_2$: C, 49.99; H, 3.36; S, 26.68. Found: C, 49.96; H, 3.36; S, 26.68.

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Registry No. 3, 3199-08-4; 5, 112270-93-6; 6, 32819-84-4; 7, 20687-95-0; 8, 112270-94-7; 5,6-dimethoxyphthalide, 531-88-4.

Ring Size Dependent Orientation in Dehydration of 1-[(Ethoxycarbonyl)methyl]cycloalkanols

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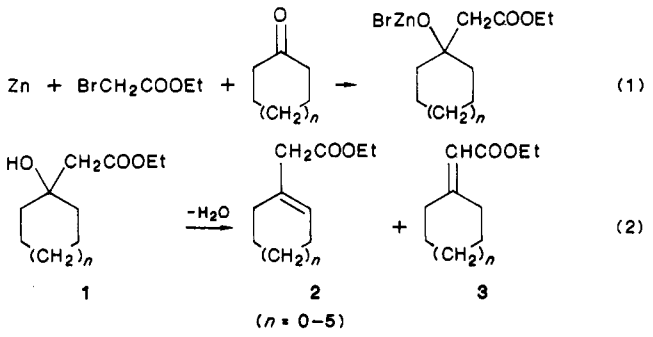
In connection with another research project, a series of ethyl cycloalken-1-ylacetates was needed for analytical standards. An attractive route to them appeared to be dehydration of the respective [(ethoxycarbonyl)methyl]-cycloalkanols,[1] which are readily accessible by the Reformatsky reaction,[2] eq 1.

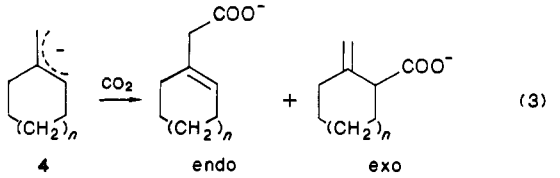


Information concerning the orientation of dehydration in this particular type of β-hydroxy acid ester appears to be very limited.[1] A special characteristic of this class of hydroxy esters is that the carbon bearing the nucleofuge (H_2O^+) is shared by a carbocyclic ring and, this being the case, one should reasonably expect that the conformational requirements of the ring should affect the orientation of dehydration of 1. If no special effects are operable, dehydration of 1 should give the statistical 2:1 mixture of endo and exo olefins, 2 and 3 respectively. On the other hand, the presence of the carboxy double bond should favor formation of the exo product, because the new double bond is conjugated with the already existing one.[1] Table I summarizes the results of acid-catalyzed dehydration of 1-[(ethoxycarbonyl)methyl]cycloalkanols, in which the ring size is varied from C5 to C10, including the special case of the 4-*tert*-butylcyclohexanol derivative. It can be seen that there is a strong dependence of the orientation of dehydration on the ring size. The relative yield of the endocyclic olefin increases rapidly (Figure 1) from C5 to C8 and less so from C8 to C10, where the reaction attains great selectivity. By extrapolating the linear segment from C8 to C10, we can predict that in the case of a C12 or larger ring dehydration will afford just one product, the endo one. Obviously, neither is the statistical mixture of the two possible products obtained, nor does the directive effect of the carboxy group double bond seem to operate.[1] The increasing relative yield of the endo product with increasing ring size may perhaps be associated with the respective decreasing conformational rigidity of the ring. However, this explanation fails to accommodate the result of the 4-*tert*-butylcyclohexanol derivative. In this case the relative yield of the endo product is 10% higher than in the less rigid unsubstituted cyclohexanol derivative. We have noted that a very similar distribution of olefinic products was obtained in the carbonation reaction of the allylic type organolithium reagents 4.[3] In fact, the relative yield of endo product from the dehydration reaction plots linearly against the respective yield of the carbonation reaction, eq 3, and the slope is nearly unity, Figure 2.

Table I. Relative Yields of Endo- and Exocyclic Olefinic Product from Dehydration of 1-[(Ethoxycarbonyl)methyl]cycloalkanols[a]

cycloalkanol	relative yield, % endo	exo
cyclopentanol	46.4	53.6
cyclohexanol	58.8	41.2
4-*tert*-butylcyclohexanol	68.3	31.7
cycloheptanol	77.4	22.6
cyclooctanol	90.7	9.3
cyclononanol	93.8	6.2
cyclodecanol	97.5	2.5

[a] By *p*-toluenesulfonic acid in refluxing benzene for 20 h. The product is a mixture of ethyl cycloalken-1-ylacetate and ethyl cycloalkylideneacetate.



Thus, two reactions, one electrophilic (eq 2) and the other nucleophilic (eq 3), with markedly different transition states lead to similar product distributions. It is felt that this points to the conclusion that in both reactions the factor that determines orientation in dehydration of 1 or site of attack in the carbanion 4 is the thermochemical stability of the product(s).

Experimental Section

Nuclear magnetic resonance spectra were recorded with a Varian FT80A NMR spectrometer, with $CDCl_3$ as solvent. Chemical shifts are reported in ppm to lower fields from TMS. The cycloalkanones that served as starting material were commercial products (Merck or Fluka), at least 98% pure, and were used as received. Activated zinc was prepared according to the literature.[4] The following experiments are exemplary.

1-[(Ethoxycarbonyl)methyl]-4-*tert*-butylcyclohexanol. A mixture of 1.54 g (10 mmol) of 4-*tert*-butylcyclohexanone, 3.5 mL (ca. 32 mmol) of ethyl bromoacetate, 6.0 g (ca. 92 mg-atom of activated zinc, 40 mL of anhydrous benzene, 20 mL of absolute ether, and a crystal of iodine was stirred at reflux temperature for 20 h. Excess zinc was separated by filtration, and the filtrate was hydrolyzed with 4 N sulfuric acid and ice. The organic layer

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0022-3263/88/1953-0893$01.50/0