9a: mp 150–152 °C; IR (KBr pellet) 3450, 2950, 1720, 1620, 1480, 1430, 1360, 1260, 1180, 850, 760, 740 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 1.24 (1 H, dd, H_f, J = 14, 6 Hz), 1.46 (3 H, s), 1.80 (1 H, dd, H_g, J = 15, 12 Hz), 2.16 (3 H, s), 2.38 (1 H, d, H_b, J = 3 Hz), 2.49 (1 H, m, H_e), 2.68 (1 H, d, H_d, J = 18 Hz), 3.09 (1 H, dd, H_c, J = 18, 6 Hz), 3.68 (3 H, s), 3.73 (3 H, s), 3.78 (1 H, dd, H_a, J = 6, 3 Hz), 7.1 (4 H, m); high-resolution mass spectrum, calcd 341.1627, found 341.1624. Anal. Calcd for $C_{20}H_{23}NO_4$: C, 70.36; H, 6.79; N, 4.10. Found: C, 70.37; H, 6.80; N, 4.19.

9b: mp 96–107 °C; IR (KBr pellet) 3450, 2950, 1730, 1630, 1430, 1270, 1250, 1170, 710, 720 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 1.38 (3 H, s), 1.63 (1 H, m, H_g), 2.11 (3 H, s), 2.26 (1 H, dd, H_f, J = 13, 5 Hz), 2.51 (1 H, m, H_e), 2.58 (1 H, dd, H_b, J = 12, 3 Hz), 2.78 (1 H, d, H_d, J = 18 Hz), 3.06 (1 H, dd, H_c, J = 18, 6 Hz), 3.26 (3 H, s), 3.66 (3 H, s), 3.68 (1 H, dd, H_a, J = 12, 3 Hz), 7.1 (4 H, m, aromatic); high-resolution mass spectrum, calcd 341.1627, found, 341.1628. Anal. Calcd for $C_{20}H_{23}NO_4$: C, 70.36; H, 6.79; N, 4.10. Found: C, 70.03; H, 6.96; N, 4.12.

1-(3-Propenyl)-2-naphthaldehyde (15). To a solution of 4.19 g (15.0 mmol) of 1-bromo-2-naphthaldehyde ethylene glycol acetal in 60 mL of ether cooled to −78 °C in a dry ice/acetone bath was added dropwise 15.0 mmol of *n*-butyllithium/hexane. The solution was stirred 30 min, and 3.87 g (15.0 mmol) of magnesium bromide etherate was added through Gooch tubing. The resulting suspension was stirred 15 min and then warmed to 0 °C. Then 0.29 g (1.5 mmol) of cuprous iodide was added, the mixture was stirred 5 min, and a solution of 1.81 g (15 mmol) of allyl bromide in 15 mL of ether was added dropwise. The mixture was stirred overnight while gradually warming to room temperature. The reaction was quenched by addition of 3 N HCl (50 mL), and the mixture was stirred 15 min. The layers were separated, and the aqueous layer was extracted with two 100-mL portions of ether. The combined organic extract was washed with brine, dried over sodium sulfate, and concentrated in vacuo to give 3.10 g of oil. The oil was flash chromatographed on a column of E. Merck silica gel (230–400 mesh) eluted with 4% EtOAc/hexane to give 2.37 g (81%) of **15** as an oil: ^1H NMR ($CDCl_3$, 60 MHz) δ 4.3 (2 H, m), 5.0 (2 H, m), 6.1 (1 H, m), 7.8 (6 H, m), 10.4 (1 H, s).

Dimethyl 2,6-Dimethyl-4-[1-(3-propenyl)-2-naphthyl]-1,4-dihydropyridine-3,5-dicarboxylate (16). A solution of 2.16 g (11.0 mmol) of 1-(3-propenyl)-2-naphthaldehyde (**15**), 1.28 g (11.0 mmol) of methyl acetoacetate, 1.27 g (11.0 mmol) of methyl 3-aminocrotonate, and concentrated NH_4OH (5 drops) in 11 mL of methanol was refluxed for 72 h. The solution was cooled to room temperature and the precipitate filtered off to give 2.01 g (46%) of **16**. An analytical sample, mp 180–183 °C, was obtained by recrystallization from ethanol: IR (KBr pellet) 3420, 2950, 1700, 1680, 1480, 1430, 1210, 1110, 1090, 910, 800, 770, 740 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 2.3 (6 H, s), 3.6 (6 H, s), 4.2 (2 H, d, J = 6 Hz), 5.1 (2 H, m), 5.6 (1 H, s), 5.8 (1 H, br s), 6.0 (1 H, m), 7.6 (5 H, m), 8.1 (1 H, m). Anal. Calcd for $C_{24}H_{25}NO_4$: C, 73.63; H, 6.44; N, 3.58. Found: C, 73.38; H, 6.50; N, 3.28.

Dimethyl 7,7a,10,11,11a,12-Hexahydro-8,10-dimethyl-7,10-methanonaphth[1,2-*g*]isoquinoline-7a,13α-dicarboxylate (17a) and 13β-Isomer (17b). To a solution of 0.59 g (1.5 mmol) of **16** in 22 mL of chloroform was added 0.57 g (3.0 mmol) of titanium tetrachloride at room temperature under nitrogen. The resulting dark orange solution was stirred overnight. The reaction was quenched with H_2O and neutralized with saturated sodium bicarbonate solution, and the layers were separated. The aqueous phase was extracted with two 50-mL portions of chloroform, the combined organic extracts were washed with brine and dried, and the solvent was removed in vacuo. The resulting gummy solid was purified by flash chromatography on E. Merck silica gel (230–400 mesh), eluting with 2% methanol/chloroform to give 0.59 g of **17a** as a glassy solid with R_f 0.33. This was triturated with hexane to give 0.41 g (69%) of **17a** was a white solid. Inverse addition of **16** to a 5 molar excess of titanium chloride alternatively provided **17b** (R_f 0.28) as the major product in 40% yield.

17a: mp 193–195 °C; IR (KBr pellet) 3450, 2940, 2330, 1730, 1620, 1430, 1260, 1190, 1170, 810, 740 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 1.25 (1 H, dd, H_f, J = 14, 6 Hz), 1.47 (3 H, s), 1.87 (1 H, dd, H_g, J = 14, 13 Hz), 2.20 (3 H, s), 2.47 (1 H, d, H_b, J = 3 Hz), 2.70 (1 H, m, H_e), 3.13 (1 H, d, H_d, J = 18 Hz), 3.32 (1 H, dd, H_c, J = 18, 6 Hz), 3.64 (3 H, s), 3.76 (3 H, s), 3.93 (1 H, br s, H_a), 7.16 (1 H, d, J = 8 Hz), 7.5 (2 H, m), 7.67 (1 H, d, J = 8 Hz), 7.81 (1 H, d, J = 8 Hz), 7.91 (1 H, d, J = 8 Hz); high-resolution mass spectrum, calcd 391.1783, found 391.1779. Anal. Calcd for $C_{24}H_{25}NO_4$: C, 73.63; H, 6.44; N, 3.58. Found: C, 73.34; H, 6.56; N, 3.44.

17b: mp 192–198 °C; ^1H NMR (360 MHz, $CDCl_3$) δ 1.40 (3 H, s), 1.71 (1 H, m, H_g), 2.14 (3 H, s), 2.28 (1 H, dd, H_f, J = 13, 5 Hz), 2.67 (1 H, dd, H_b, J = 12, 2 Hz), 2.71 (1 H, m, H_e), 3.21 (1 H, d, H_d), 3.25 (3 H, s), 3.32 (1 H, dd, H_c, J = 18, 6 Hz), 3.60 (3 H, s), 3.83 (1 H, dd, H_a, J = 12, 3 Hz), 7.07 (1 H, d, J = 8 Hz), 7.48 (2 H, m), 7.58 (1 H, d, J = 8 Hz), 7.78 (1 H, d, J = 8 Hz), 7.92 (1 H, d, J = 8 Hz); high-resolution mass spectrum, calcd 391.1783, found 391.1783. Anal. Calcd for $C_{24}H_{25}NO_4$: C, 73.63; H, 6.44; N, 3.58. Found: C, 73.25; H, 6.62; N, 3.74.

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Supplementary Material Available: Crystallographic data including tables of the atomic positional and thermal parameters, bond distances, and bond angles for **9a** (6 pages). Ordering information is given on any current masthead page.

Acetoacetylation with 2,2,6-Trimethyl-4*H*-1,3-dioxin-4-one: A Convenient Alternative to Diketene

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The diketene/acetone adduct, 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one, efficiently acetoacetylates aliphatic and aromatic alcohols, amines, and thiols. These acetoacetylation reactions are fast and stoichiometric, require no catalysis, and give only volatile byproducts.

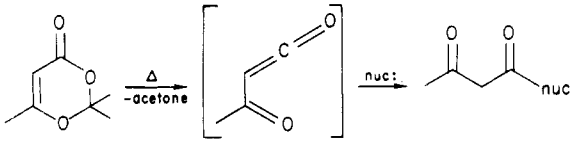
The acetoacetylation of nucleophiles is a prosaic but extremely important reaction as acetoacetates are widely used synthetic intermediates in both laboratory and industrial preparations. Most of these acetoacetylations are effected with diketene,[1] a highly reactive, lachrymatory, and toxic reagent. Unfortunately, few alternatives are available.[2]

(1) For acetoacetylation procedures using diketene, see: Wilson, S. R.; Price, M. F. *J. Org. Chem.* **1984**, *49*, 722 and ref 14 therein.

0022-3263/85/1950-2431$01.50/0

In 1952, Carroll and Bader reported that diketene and acetone react to afford a 1:1 adduct, 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one (1), and that this latter compound would acetoacetylate alcohols in the presence of *p*-toluenesulfonic acid.[3] Carroll found dioxinone 1 to be slightly more reactive than acetoacetate esters but much less reactive than diketene. It did not appear that acetoacetylation with dioxinone 1 offered any advantages over transesterification with ethyl acetoacetate.[4]

Recently, it has been suggested that, when pyrolyzed, dioxinone 1 decomposes into acetylketene (2) and acetone. The supposed acetylketene produced in this reaction has been trapped via nucleophilic and cycloaddition reactions.[5] Kato has used the nucleophilic trapping to prepare acetoacetimides not readily prepared from amides and diketene.[6]



1 2

We have found that the pyrolysis of 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one (1) in the presence of nucleophiles provides an excellent "general-purpose" acetoacetylation procedure. Dioxinone 1 efficiently acetoacetylates aliphatic and aromatic alcohols, thiols, and amines in excellent yield. Futhermore, dioxinone 1 is a commercially available liquid[7] which is easily handled and stored, and the acetoacetylation reactions of adduct 1 are rapid and stoichiometric, require no catalysis, and provide only volatile byproducts.

Dioxinone 1 is stable at room temperature but decomposes when heated above 100 °C to provide acetylketene (2) at a preparatively useful rate. Thus, a rapidly stirred solution of 50 mmol each of dioxinone 1 and 1-methylcyclohexanol in xylene (10 mL) was heated in an oil bath maintained at 150 °C. By the time the solution temperature had reached 110 °C, the evolution of acetone was obvious. As all the acetone boiled out of the flask, the reaction temperature slowly rose to 140 °C—a process requiring slightly less than 15 min. Nuclear magnetic resonance (NMR) examination of the crude reaction mixture showed only xylene and 1-methylcyclohexyl acetoacetate, and short-path distillation provided a 91% yield of the acetoacetate ester.

Acetoacetylations effected with dioxinone 1 were more rapid when the reagents were in a concentrated solution than when they were in a more dilute solution, and a homogeneous reaction mixture (at 110–150 °C) appeared to be requisite to a successful reaction.[8] However, if no solvent was used, product quality and often yield decreased. Concentrations of between 1 and 10 mmol of dioxinone 1/mL of xylene provided the most satisfactory results.

This acetoacetylation reaction was extended to a series of aliphatic alcohols (Table I), all of which were rapidly acetoacetylated in excellent yield by heating with dioxinone 1. In all cases, crude yields were 95–99%, and the crude products were of excellent purity; most yield losses occurred during distillation. Even hindered tertiary hydroxy groups were rapidly acetoacetylated, suggesting that this reaction would be useful for the peracetoacetylation of polyols. Indeed, ethylene glycol (**10**), neopentyl glycol (**11**), cyclohexanedimethanol (**12**), and tetramethylcyclobutane-1,3-diol (**13**) were rapidly diacetoacetylated in excellent yield. Glucose (**14**), which cannot be completely acetoacetylated with diketene, was smoothly pentaacetoacetylated when heated in the presence of 5 equiv of 1.

Extension of this acetoacetylation procedure to phenols was straightforward, and phenyl acetoacetate and 4-methoxyphenyl acetoacetate were formed in excellent yield. However, a pure sample of *p*-nitrophenyl acetoacetate was not obtained because this product quickly self-condensed under the reaction conditions to form dehydroacetic acid and *p*-nitrophenol.

Thiophenol and two aliphatic mercaptans were acetoacetylated in good yield by the pyrolysis of dioxinone 1, and the products proved unexpectedly stable to distillation.[9] This acetoacetylation process is probably the method of choice for preparing thioacetoacetate esters, whose utility in organic synthesis has recently been demonstrated.[10]

An attempted acetoacetylation of *n*-heptylamine with dioxinone 1 in refluxing xylene did not provide a pure product, and an analysis of the reaction mixture indicated that further reactions of the initially formed *N*-*n*-heptylacetoacetamide had occurred. The desired product was successfully prepared by reducing the reaction temperature and by running the reaction for 14 h in refluxing toluene (Table II).

The more hindered 1-adamantanamine afforded *N*-adamantylacetoacetamide when heated with 1 in refluxing xylene. Likewise, secondary aliphatic amines also yielded the expected acetoacetamides. It appears that the use of a lower reaction temperature is only necessary with unhindered, primary aliphatic amines. Aromatic amines afforded the expected acetoacetanilides when reacted with dioxinone 1. Although *p*-nitroaniline will not react with diketene in the absence of a catalyst, it was quickly acetoacetylated with 1.

With only minor procedural modifications (see Experimental Section), the use of dioxinone 1 to acetoacetylate nucleophiles is amenable to large-scale preparations. In large-scale reactions, the dioxinone was added to a heated solution of the alcohol and xylene; the acetone was continuously removed by distillation. As with the small-scale reactions, the efficient removal of acetone ensured short reaction times and high-quality products.

During the development of this acetoacetylation procedure, several observations were made which warrant further comment. When heated to 120–150 °C in the absence of a nucleophile, dioxinone 1 forms dehydroacetic acid (**27**)—presumably via intermolecular (4 + 2) cycloaddition of acetylketene (**2**).[11] Any excess dioxinone 1 present during the acetoacetylation reaction was converted

(2) An effective, but more expensive, alternative to diketene is 5-acetyl "Meldrums acid": Oikawa, Y.; Sugano, K.; Yonemitsu, O. *J. Org. Chem.* **1978**, *43*, 2087. Acetoacetyl chloride: Hurd, C. D.; Kelso, C. D. *J. Am. Chem. Soc.* **1940**, *62*, 1548–1549. Methyl or ethyl acetoacetate, see ref 4.

(3) Carroll, M. F.; Bader, A. R. *J. Am. Chem. Soc.* **1952**, *74*, 6306. See also: Carroll, M. F.; Bader, A. R. *J. Am. Chem. Soc.* **1953**, *75*, 5400.

(4) Bader, A. R.; Cummings, L. O.; Vogel, H. A. *J. Am. Chem. Soc.* **1951**, *73*, 4195–4197.

(5) (a) Jäger, G.; Wenzelburger, J. *Liebigs Ann. Chem.* **1976**, 1689. (b) Sato, M.; Ogasawa, H.; Yoshizumi, E.; Kato, T. *Chem. Pharm. Bull.* **1983**, *31*, 1902. (c) Hyatt, J. A.; Feldman, P. L.; Clemens, R. J. *J. Org. Chem.* **1984**, *49*, 5105.

(6) Sato, M.; Kanuwa, N.; Kato, T. *Chem. Pharm. Bull.* **1982**, *30*, 1315.

(7) Available from Kodak Laboratory Chemicals and Aldrich Chemical Co.

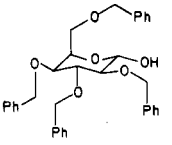
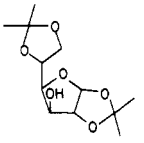
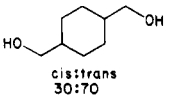
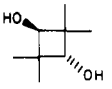
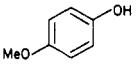
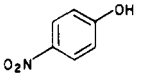
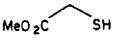
(8) Other nonnucleophilic, nonketonic solvents can also be used.

(9) Phenyl thioacetoacetate is reported to decompose upon attempted distillation: Yaggi, N. F.; Douglas, K. T. *J. Chem. Soc., Chem. Commun.* **1977**, 609.

(10) Booth, P. M.; Fox, C. M. J.; Ley, S. V. *Tetrahedron Lett.* **1983**, *24*, 5143–5146.

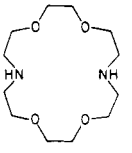
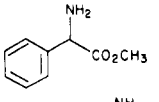
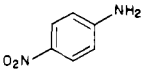
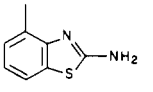
(11) (a) Clemens, R. J. U.S. Patent 4 496 747, 1985. (b) See ref 5c.

Table I. Alcohols and Thiols Acetoacetylated with 2,2,6-Trimethyl-4*H*-1,3-dioxin-4-one (1)

compd	alcohol	equiv of 1	product yield,[a] %	bp [mp], °C (*P*, torr)	anal.[b]
3	1-heptanol	1	83	78–80 (0.4)	C, H
4	3-octanol	1	86	79–81 (0.4)	C, H
5		1	91	74–75 (0.3)	C, H
6		1	84	112–113 (0.2)	C, H
7	cholesterol	1	91	[93–94]	*c*
8		1	99	syrup[d]	C, H
9		1	99	175 (0.05)	C, H
10		2	89	141–144 (0.25)[13]	C, H
11		2	88	148 (0.2)	C, H
12	 cis:trans 30:70	2	97	[78–79][14,e]	C, H
13		2	89	[43–44.5]	C, H
14	glucose	5	96	syrup	C, H
15	phenol	1	90	80–82 (0.2)[15]	
16		1	86	100 (0.4)	C, H
17		1	~50	*f*[16]	
18	thiophenol	1	72	112–114 (0.2)[9]	C, H, S
19	*n*-dodecanethiol	1	86	164 (0.2)	C, H, S
20		1	82	122–124 (0.2)	C,[g] H, S

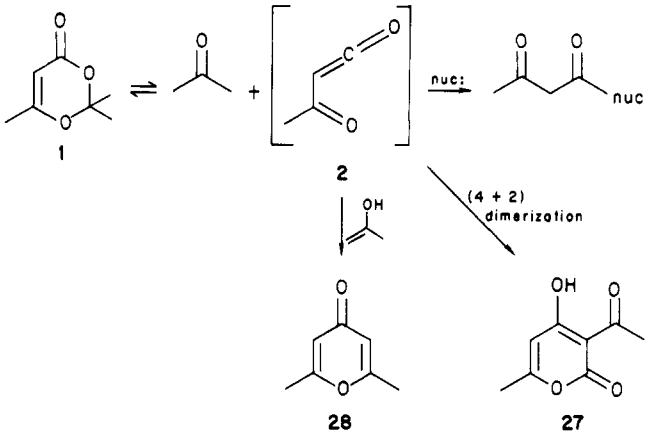
[a] Yields refer to isolated, purified material. [b] Except as noted: C, ±0.3; H, ±0.2; S, ±0.3. [c] See ref 4. [d] Purified by TLC. [e] Melting point for pure trans isomer. [f] Contaminated with dehydroacetic acid. [g] Calcd.: C, 44.20. Found: C, 44.66

Table II. Amines Acetoacetylated with 2,2,6-Trimethyl-4*H*-1,3-dioxin-4-one (1)

entry	amine	equiv of 1	product yield[a] %	bp [mp], °C (*P*, torr)	anal.[b]
21	*n*-heptylamine	1	73%	[64–66]	C, H, N
22	1-adamantanamine	1	93%	[82–83]	C, H, N
23		2	81%	[90–93]	C, H, N
24		1	78%	180–190 (0.01)	C, H, N
25		1	94%	[120–122]	C, H, N
26		1	92%	[163–165]	C, H, N

[a] Yields refer to isolated, purified material. [b] C, ±0.3; H, ±0.2; N, ±0.3.

Scheme I



into dehydroacetic acid, but not until virtually all of the nucelophile had been acetoacetylated. Also, if acetone was not efficiently removed from reactions of dioxinone 1, some 2,6-dimethyl-4-pyrone (28) was formed. Control experiments showed that the pyrolysis of dioxinone 1 in the presence of excess acetone increased the amount of pyrone 28 formed. These observations are consistent with a rapid equilibrium between dioxinone 1 and acetylketene/acetone, in which the acetylketene is removed from the equilibrium via (a) trapping by a nucleophile to afford an acetoacetate derivative, (b) intermolecular (4 + 2) cycloaddition to afford dehydroacetic acid (27), or (c) cycloaddition with the enolic form of acetone to afford pyrone 28 (Scheme I).[12] Because the reaction of acetylketene with nucleophiles is fast, it is probably rare for two unreacted acetylketene molecules to be in sufficient proximity to form dehydroacetic acid until all the nucleophile is acetoacetylated. The prevention of pyrone (28) formation depends on the efficient removal of acetone, a process that is apparently accelerated by the addition of an appropriate solvent.

In summary, the pyrolysis of 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one (1) in the presence of nucleophiles provides an efficient and versatile method for the preparation of acetoacetate derivatives.

Experimental Section

All reagents were obtained commercially and were used as received, except where otherwise noted. Melting points were determined on a Thomas-Hoover capillary apparatus and are uncorrected; boiling points were determined during short-path distillation. ^{1}H NMR spectra were obtained on Varian EM-360 and JEOL GX-400 spectrometers with tetramethylsilane as an internal standard. Infrared spectra were recorded on a Perkin-Elmer Model 137 spectrophotometer. Mass spectra were recorded on a VG-ZAB mass spectrometer in the field desorption and/or electron impact mode. Elemental analyses were determined in the Physical and Analytical Section of the Eastman Chemicals Division Research Laboratories.

2,2,6-Trimethyl-4*H*-1,3-dioxin-4-one yellows with time but generally retains a high assay even when it has become an orange-red color. It can be purified by distillation if the pot temperature is kept below 90 °C [bp 65–67 °C (0.2 torr)]; a wiped-film evaporator is excellent for this distillation. Likewise, some acetoacetate esters are sensitive to excessive heating; therefore, product recovery is dependent upon efficient distillation.

General Procedure for Acetoacetylation with Dioxinone 1. A solution of an alcohol, thiol, or amine (50 mmol) and 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one (50 mmol/functional group to be acetoacetylated) in 10 mL of xylene was placed in a 50-mL Erlenmeyer flask. The flask was immersed in an oil bath that had been preheated to 150 °C, and the solution was vigorously stirred. The evolution of acetone became apparent within several minutes; heating was continued for a total of 30 min. The reaction was cooled. The product was collected and recrystallized if it precipitated; otherwise, the xylene was removed, and the product was distilled.

1-Methylcyclohexyl acetoacetate (5): yield 91%; bp 74–75 °C (0.3 torr); IR (neat) 2970, 2900, 1750 (s), 1730 (s), 1650, 1450, 1320, 1235, 1140 cm^{-1}; ^{1}H NMR ($CDCl_3$) [keto/enol ratio 90/10] keto form δ 3.41 (s, 2 H), 2.30 (s, 3 H), 1.49 (s, 3 H), 1.45 (m, 10 H).

Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.52; H, 9.16.

Neopentyl glycol diacetoacetate (11): yield 88%; bp 148 °C (0.2 torr); IR (neat) 2995, 1740 (s), 1720 (s), 1250, 1140 cm^{-1}; ^{1}H NMR ($CDCl_3$) [keto/enol ratio 90/10] keto form δ 3.92 (s, 4 H), 3.43 (s, 4 H), 2.27 (s, 6 H), 0.89 (s, 6 H). Enolic acetoacetyl resonances were observed at δ 5.06 and 1.99.

Anal. Calcd for $C_{13}H_{20}O_6$: C, 57.33; H, 7.40. Found: C, 57.21; H, 7.42.

Large-Scale Preparation of Neopentyl Glycol Diacetoacetate. A solution of neopentyl glycol (104 g, 1 mol) in 100 mL of xylene was heated to 130 °C in a 2-L flask equipped with a mechanical stirrer, an addition funnel, and a distillation column. Dioxinone 1 (293 g, 2 mol at 97%) was added to the hot solution over a period of 30 min. The pot temperature was maintained at 125–135 °C during this addition, and acetone and xylene were removed by distillation. When the addition was complete, heating was continued until the temperature of the distillate rose to 145 °C and all excess xylene was removed (approximately 15 min). The orange liquid remaining in the flask consisted of a 97% yield of the title compound, which was further purified by flash distillation to afford 242 g (89%) of a pale yellow liquid, bp 157 °C (0.9 torr).

D-(+)-Glucose pentaacetoacetate (14): yield 98.5% (the product was a clear, viscous syrup); IR (neat) 3500, 2970, 1755 (s), 1725 (s), 1320, 1250, 1140 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.3 (d, 1 H), 5.2 (m, 4 H), 4.2 (m, 2 H), 3.6 (m, 10 H), 2.25 (s, 15 H) (a small singlet at δ 2.21 was also observed and was attributed to the enolic form); mass spectrum, m/e 600 (M^+).

Anal. Calcd for $C_{26}H_{32}O_{16}$: C, 52.04; H, 5.37. Found: C, 52.11; H, 5.45.

Thiophenyl acetoacetate (18):[9] yield 72%; bp 112–114 °C (0.2 torr); IR (neat) 3100, 1730 (s), 1710 (s), 1640, 1190, 1080 cm^{-1}; ^{1}H NMR ($CDCl_3$) [keto/enol ratio 75/25] keto form δ 7.51 (s, 5 H), 3.76 (s, 2 H), 2.27 (s, 3 H) (enolic acetoacetyl resonances were observed at δ 12.7, 5.47, and 1.92); high-resolution mass spectrum, observed m/e 194.0388 (calcd m/e 194.0401).

Anal. Calcd for $C_{10}H_{10}SO_2$: C, 61.83; H, 5.19; S, 16.51. Found: C, 62.03; H, 5.07; S, 16.57.

***N*-*n*-Heptylacetoacetamide (21).** The compound was prepared by the general procedure except that toluene was used instead of xylene and the reaction was run for 14 h: yield 73%; mp 64–66 °C; IR (Nujol) 3250, 1700 (br), 1627, 1544, 1172, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.00 (br s, 1 H), 3.41 (s, 2 H), 3.30 (m, 2 H), 2.31 (s, 3 H), 1.6–0.8 (m, 13 H); mass spectrum, m/e 199 (M^+).

Anal. Calcd for $C_{11}H_{21}NO_2$: C, 66.33; H, 10.62; N, 7.03. Found: C, 66.41; H, 10.84; N, 7.06.

***N*,*N*'-Diacetoacetyl-1,10-diaza-18-crown-6 (23):** yield 81%; mp 90–93 °C; IR (KBr) 1720, 1620, 1434, 1100 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.73 (br s, 28 H), 2.34 (s, 6 H); mass spectrum, m/e 430 (M^+).

(12) The (4 + 2) cycloaddition reaction of acetylketene with enolizable ketones has been reported: Sato, M.; Ogasawara, H.; Kato, K.; Sakai, M.; Kato, T. *Chem. Pharm. Bull.* **1981**, *31*, 4300–4305.

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(14) Heckles, J. S. (Armstrong). U.S. Patent 4 217 396, 1980; *Chem. Abstr.* **1980**, *93*, 222047.

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Anal. Calcd for $C_{20}H_{34}N_2O_8$: C, 55.82; H, 7.96; N, 6.51. Found: C, 55.71; H, 8.03; N, 6.40.

Note Added in Proof. A paper which is complementary to ours and describes the preparation of β-keto carboxamides from substituted 1,3-dioxin-4-ones was published while this manuscript was in press. See: Sato, M.; Ogasawara, H.; Komatsu, S.; Kato, T. *Chem. Pharm. Bull.* **1984**, *32*, 3848–3856.

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Registry No. **1**, 5394-63-8; **3**, 42598-96-9; **3** (alcohol), 111-70-6; **4**, 96453-22-4; **4** (alcohol), 589-98-0; **5**, 91328-33-5; **5** (alcohol), 590-67-0; **6**, 96481-25-3; **6** (alcohol), 27779-29-9; **7**, 1473-23-0; **8**, 96453-23-5; **8** (alcohol), 96553-53-6; **9**, 66888-11-7; **9** (alcohol), 582-52-5; **10**, 5459-04-1; **10** (alcohol), 107-21-1; **11**, 14276-67-6; **11** (alcohol), 126-30-7; *cis*-**12**, 96453-24-6; *cis*-**12** (alcohol), 3236-47-3; *trans*-**12**, 96453-30-4; *trans*-**12** (alcohol), 3236-48-4; **13**, 96453-25-7; **13** (alcohol), 2694-23-7; **14**, 96481-26-4; **15**, 6864-62-6; **15** (alcohol), 108-95-2; **16**, 38432-60-9; **16** (alcohol), 150-76-5; **17**, 29816-97-5; **17** (alcohol), 100-02-7; **18**, 40053-29-0; **18** (thiol), 108-98-5; **19**, 96453-26-8; **19** (thiol), 112-55-0; **20**, 96453-27-9; **20** (thiol), 2365-48-2; **21**, 51494-47-4; **21** (amine), 111-68-2; **22**, 58102-37-7; **22** (amine), 768-94-5; **23**, 96453-28-0; **23** (amine), 23978-55-4; **24**, 728-49-4; **24** (amine), 26682-99-5; **25**, 4835-39-6; **25** (amine), 100-01-6; **26**, 96453-29-1; **26** (amine), 1477-42-5; cholesterol, 57-88-5; glucose, 50-99-7.

Supplementary Material Available: Spectral (IR, ^1H NMR, and MS) and analytical (combustion analysis) data for all remaining compounds listed in Tables I and II (6 pages). Ordering information is given on any current masthead page.

Chromic Acid Oxidation of Indans and Tetralins to 1-Indanones and 1-Tetralones Using Jones and Other Cr(VI) Reagents

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The Jones chromic acid oxidation, ordinarily used for converting secondary alcohols to ketones, has been successfully extended to the oxidation of indans and tetralins to 1-indanones and 1-tetralones, respectively. A sixfold excess of the reagent was commonly used to ensure complete oxidation of starting material. Addition of anhydrous magnesium sulfate or oven-dried silica gel provided a yield increase of 15–20%. 2,2′-Bipyridinium chlorochromate was also used and found to be effective in all cases, but this reagent requires a longer reaction time and a 16-fold excess. A comparison between these two reagents and CrO_3 in acetic acid was made. The Jones reagent, being least selective, gives the highest yield of sterically hindered monoketone from 1,2,3,4,5,6,7,8-octahydrophenanthrene.

Chronic acid oxidation of hydrocarbons at a benzylic position to produce ketones generally is carried out in acetic acid.[1a-c] To improve yields and the selectivity of products, we undertook a study of the application of the Jones chromic acid oxidizing reagent[2] and other Cr(VI) oxidations of indans and tetralins to 1-indanones and 1-tetralones.

The Jones reagent,[2a,b] chromium trioxide dissolved in aqueous sulfuric acid, most frequently is used in acetone solvent to oxidize secondary alcohols to ketones.[2c,d] We have found that the Jones method, as previously described,[2a,b] can also be applied to the oxidation of hydrocarbons at a benzylic position with little change in procedure. In adapting the Jones reagent to this new use, we systematically examined several parameters to improve the oxidation. This study includes changes in the structure of the hydrocarbon starting materials, as shown in Table I, a search for substitutes for sulfuric acid[3] and acetone,[4] trial of other Cr(VI) reagents,[5a-c] and the effect that removal of water produced by the oxidation has on the outcome of the reaction. As expected, since $Cr_2(SO_4)_3$ is deposited, effective stirring was essential.[6a] The best yield of 1-tetralone was achieved with a sixfold excess of Jones

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(2) (a) Bowden, K.; Heilbron, I. M.; Jones, E. R. H.; Weedon, B. C. L. *J. Chem. Soc.* **1946**, 39. (b) Eisenbraun, E. J. "Organic Syntheses"; Wiley: New York, 1973; Collect. Vol. V, p 310. (c) Braude, E. A.; Jones, E. R. H.; Sondheimer, F.; Toogood, J. B. *J. Chem. Soc.* **1949**, 607. (d) Curtis, R. G.; Heilbron, I. M.; Jones, E. R. H.; Woods, G. F. *J. Chem. Soc.* **1953**, 457.

(3) (a) Methanesulfonic acid and trifluoroacetic acid were substituted (2 mol for 1 mol) for sulfuric acid. Otherwise, the oxidation procedure remained the same. (b) Phosphoric acid (85%) was substituted (2 mol for 3 mol) for sulfuric acid. The procedure remained the same except that water was omitted during preparation of the reagent.

(4) (a) Acetonitrile, *N,N*-dimethylformamide, and *N*-methylpyrrolidinone were exposed to Jones reagent at ice-bath temperature. Since a color change to green appeared within a few minutes, these were considered to be unsuitable as substitutes for acetone. (b) At room temperature *N,N*-dimethylacetamide was attacked by the Jones reagent, since the color changed to blue-green, but salts were not deposited. (c) Brown, H. C.; Garg, C. P.; Liu, K. T. *J. Org. Chem.* **1971**, *36*, 387. (d) Oxidation of tetralin in acetone gives 1-tetralone in 68% yield. When benzene is substituted as solvent, the yield drops to 10–15%, with most of the tetralin being recovered.

(5) (a) Guziec, F. S.; Luzzio, F. A. *Synthesis* **1980**, 691. (b) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, *31*, 2647. (c) Lalancette, J. M.; Rollin, G.; Dumas, P. *Can. J. Chem.* **1972**, *50*, 3058. (d) The original procedures[5a-c] were followed to determine the effectiveness of these Cr(VI) reagents.

(6) (a) A high-speed mechanical stirrer with a multiblade paddle was found to be adequate. Stirring with a Teflon-covered magnetic stirring bar gave approximately the same yields. However, it was necessary to use a powerful magnetic stirrer (we have previously described[10] a stirrer of local construction that has been further modified with a more powerful magnet). Should a magnetic stirring bar go out of control with this powerful magnetic stirrer, the wall of a conventional flask will likely be broken and hence a heavy-wall flask is recommended. (b) For earlier use of silica gel in chromic acid oxidation of primary and secondary alcohols, cf.: Santaniello, E.; Ponti, F.; Manzocchi, A. *Synthesis* **1978**, 534.

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