Probably this is not only due to the increase in the hydrophobic interaction between S_{16}^- and C_m with increasing alkyl chain length in the latter but also due to the comicellar effect of the S_{16}^- and C_m (m = 8 or 10) micelles on the hydrolysis acceleration.

In the presence of 5×10^{-3} M CTAB surfactant (cmc = ca. 1×10^{-3} M), the micellar effect of the surfactant was substantially recognized in the present hydrolysis reactions. Such a micellar effect of surfactants on the rate enhancement of the ester hydrolyses has also been observed in the previous works.[16,17] However, the magnitude of the micellar influence of CTAB on the hydrolysis acceleration, which can be measured by the ratio of the $k_{a,obsd}$ value in the presence of CTAB to that in its absence, is fairly different between the hydrolyses of the nonionic and anionic substrates. The C_m (m = 4–10) and CTAB system increases the hydrolysis rates of both kinds of substrates, as the C_m species varies from m = 4 to 10. But, the acceleration of the hydrolysis of the nonionic S_n (n = 10–16) substrates by the C_m (m = 4–10) and CTAB system (especially by the micellar C_m (m = 8–10) and CTAB one) is remarkable in comparison with that of the hydrolysis of S_n^- (n = 10–16) by the same system, even though the hydrolyses of S_n (n = 10–16) by the C_m (m = 4–10) species are very slow in the absence of the CTAB surfactant. This is probably owing to the retardation of the coiling-up of the long acyl chain in the S_n (n = 10–16) substrates by the effective hydrophobic interaction between the S_n (n = 10–16) substrates and the CTAB micelles or between the S_n (n = 10–16) substrates and the C_m (m = 8 or 10)–CTAB comicelles; The comicelle formation of C_m (m = 8 or 10) and CTAB is attained not only through the hydrophobic interaction between them but also through the electrostatic charge attraction between the anionic C_m and the cationic CTAB.

In regard to the selective hydrolysis of the substrates in the presence of the CTAB surfactant, the comicellar system of C_8–CTAB selectively incorporated the nonionic S_{10} and the anionic S_6^-, and that of C_{10}–CTAB selected S_{10} and S_6^- (and/or S_{12}^-). The difference in the selective incorporation of the nonionic and anionic substrates by the C_m (m = 8 or 10)–CTAB comicelles is probably due to the difference in the frameworks of the above substrates. Namely, the anionic substrate (S_6^-) involves more bulky substituents in its benzene ring than the nonionic one (S_{10}). At any rate, the comicellar influence of the C_m (m = 8 or 10)–CTAB system on the S_n and S_n^- substrates was characterized by the selective incorporation of both kinds of substrates (S_{10}, S_6^- and/or S_{12}^-) through the hydrophobic approximation effect[18] of the micelles.

Experimental Section

Materials. The nucleophilic C_m (m = 4–10) agents were prepared by the reaction of $H(CH_2)_{m-1}CO_2C_2H_5$ (m = 4–10) and hydroxylamine, and satisfactory elementary analyses were obtained as below. C_4: Anal. Calcd for $C_4H_9NO_2$: C, 46.59; H, 8.80; N, 12.58. Found: C, 46.72; H, 8.34; N, 12.69. C_6: mp 45–47 °C. Anal. Calcd for $C_6H_{13}NO_2$: C, 54.94; H, 9.99; N, 10.68. Found: C, 55.53; H, 9.78; N, 10.40. C_8: mp 75.6–77.2 °C. Anal. Calcd for $C_8H_{17}NO_2$: C, 60.34; H, 10.76; N, 8.80. Found: C, 60.55; H, 10.52; N, 8.58. C_{10}: mp 85.9–86.7 °C. Anal. Calcd for $C_{10}H_{21}NO_2$: C, 64.13; H, 11.30; N, 7.48. Found: C, 64.96; H, 11.10; N, 7.41.

3-Nitro-4-acyloxybenzoic acids (S_2^-–S_{16}^-) were prepared according to Overberger et al.[2] Satisfactory elementary analyses were also given for S_n^- (n = 2–16), and those for new compounds are shown below. S_4^-: mp 113–114 °C. Anal. Calcd for $C_{11}H_{11}NO_6$: C, 52.17; H, 4.35; N, 5.53. Found: C, 52.47; H, 4.25; N, 5.64. S_6^-: mp 75.0–76.0 °C. Anal. Calcd for $C_{13}H_{15}NO_6$: C, 55.51; H, 5.38; N, 4.98. Found: C, 54.86; H, 5.29; N, 4.94. S_{10}^-: mp 70.1–72.0 °C. Anal. Calcd for $C_{17}H_{23}NO_6$: C, 60.52; H, 6.87; N, 4.15. Found: C, 60.29; H, 6.79; N, 4.10. S_{16}^-: mp 87.1–89.0 °C. Anal. Calcd for $C_{23}H_{35}NO_6$: C, 65.53; H, 8.37; N, 3.32. Found: C, 65.24; H, 8.21; N, 3.66.

Commercially available p-nitrophenyl esters (S_2–S_{16}) were used as nonionic substrates without further purification, because elementary analyses of S_n (n = 2–16) gave satisfactory results.

Hydrolysis. The hydrolyses of S_n and S_n^- (5×10^{-5} M) by C_m (5×10^{-4} M) were carried out at 31.0 °C, pH 9.06 in 0.083 M tris(hydroxymethyl)aminomethane buffer involving 0.083 M KCl (μ = 0.083) in H_2O including 10 vol % CH_3CN, and the reactions were followed spectrophotometically by taking notice of phenolate anion formation.

Registry No.—$H(CH_2)_3CO_2C_2H_5$, 105-54-4; $H(CH_2)_5CO_2C_2H_5$, 123-66-0; $H(CH_2)_7CO_2C_2H_5$, 106-32-1; $H(CH_2)_9CO_2C_2H_5$, 110-38-3; hydroxylamine, 7803-49-8.

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A Method for β-C-Acylation and β-Alkylation of α,β-Unsaturated Ketones

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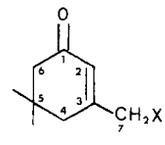
In connection with our interest in the chemistry of 3-substituted 2-cyclohexen-1-ones,[1-3] we required facile synthesis of the β-C-acyl and β-alkyl cyclenones **1**.



1a X = COC_2H_5
1b X = COC_6H_5
1c X = $CO(CH_2)_2CH(CH_3)_2$
1d X = CN
1e X = $CO_2C_2H_5$

Until now, there has been no easy method described to obtain this type of cyclenones with consistent yields.[4-6] So, taking into account the hydrolyzability of an enol ether function we synthesized **1d** and **1e.** Using this advantage and the possibility of transforming a cyano group into a carbonyl

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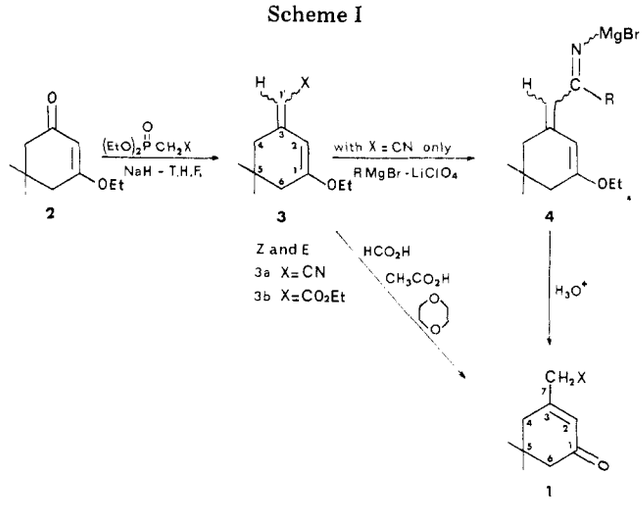
Table I. 3-Substituted 2-Cyclohexen-1-ones (1)

No.	Registry no.	Yields, %	IR (neat), cm^{-1}	^1H NMR δ	Bp, °C	Mass spectra m/e Parent	Base	Formula	Anal. C Calcd	H Calcd	N	C Found	H Found	N
1a	65253-22-7	59	1630, 1670, 1718, 3025	5.76 (s, 1, 2-H), 3.30 (s, 2, 3-CH_2), 2.50 (q, 2, CH_2 of C_2H_5), 2.18 (s, 2, 4-CH_2), 2.11 (s, 2, 6-CH_2), 1.17 (t, 3, CH_3 of C_2H_5), 1.03 (s, 6, 5-$(CH_3)_2$)	103–105 (0.4 Torr)	194 (24)	138 (100)	$C_{12}H_{18}O_2$	74.23	9.28		74.30	9.20	
1b	65253-23-8	70	1584, 1600, 1673.5, 1687.5, 3035, 3065, 3090	8.1–7.2 (m, 5, C_6H_5), 5.87 (t, 1, 2-H), 3.78 (s, 2, 3-CH_2), 2.22 (m, 2, 4-CH_2), 2.13 (s, 2, 6-CH_2), 1.03 (s, 6, 5-$(CH_3)_2$)	*a*	242 (7)	105 (100)	$C_{16}H_{18}O_2$	79.34	7.44		79.40	7.31	
1c	65253-24-9	83	1632, 1670, 1720, 3028	5.80 (s, 1, 2-H), 3.23 (s, 2, 3-CH_2), 2.41 (t, 2, CH_2 of $COCH_2$), 2.16 (s, 2, 4-CH_2), 2.13 (s, 2, 6-CH_2), 1.47 (m, 2, CH_2 of CH_2-*i*Pr), 1.27 (m, 1, CH of *i*Pr), 1.03 (s, 6, *s*-$(CH_3)_2$), 0.88 (d, 6, $(CH_3)_2$ of *i*Pr)	*a*	236 (3)	138 (100)	$C_{15}H_{24}O_2$	76.27	10.17		76.19	10.42	
1d	65253-25-0	68	1620, 1675, 2250, 3030	6.00 (t, 1, 2-H), 3.07 (s, 2, 3-CH_2), 2.23 (d, 2, 4-CH_2), 2.18 (s, 2, 6-CH_2), 1.08 (s, 6, 5-$(CH_3)_2$)	90–95 (0.4 Torr)	163 (17)	107 (100)	$C_{10}H_{13}ON$	73.62	7.98	8.59	73.82	7.99	8.10
1e	65253-26-1	53	1245, 1633, 1672, 1737, 3030	5.75 (t, 1, 2-H), 4.06 (q, 2, CH_2 of C_2H_5), 3.08 (s, 2, 3-CH_2), 2.20 (d, 2, 4-CH_2), 2.10 (s, 2, 6-CH_2), 1.25 (t, 3, CH_3 of C_2H_5), 1.05 (s, 6, 5-$(CH_3)_2$)	102–103 (0.3 Torr)	210 (11)	121 (100)	$C_{12}H_{18}O_3$	68.57	8.57		68.20	8.81	

a These ketones were purified on silica gel "dry column" chromatography (eluent:benzene).

Scheme I



2 3 4 1

function by catalyzed addition of a Grignard reagent,[7] we prepared **1a–c.**

The Horner–Emmons modification of the Wittig reaction[8] of the readily available ketone **2**[9] with the anions of diethylphosphonoacetonitrile (X = CN) or triethyl phosphonoacetate (X = CO_2Et) furnishes the dienes **3**, *Z* and *E*, in excellent yields (see Experimental Section).

Condensation of **3a** (*Z* and *E*) with a complex 1:1.5 of lithium perchlorate and various Grignard reagents,[7] RMgBr (R = alkyl or aryl) in ether, results in the formation of iminates **4**, which are hydrolyzed (hydrochloric acid 20%) to δ-diketones **1a–c** in good yields.

While the aqueous acid hydrolysis of **3a** and **3b** furnishes first 3-oxo-5,5-dimethyl-1-cyclohexen-1-ylacetic acid and then isophorone after decarboxylation, their hydrolysis in dioxane with acetic or formic acids leads to the expected compounds **1d** and **1e** with satisfactory yields.

These procedures have been applied only on the 5,5-dimethyl-3-ethoxy-2-cyclohexen-1-one (**2**) and they may represent new general routes for the production of 3-substituted 2-cyclohexen-1-ones from the monoenol ethers of cyclohexan-1,3-diones[9] and various Wittig reagents.

Experimental Section[10]

General Procedure for the Horner–Emmons Reaction. A solution of 0.2 mol of diethylcyanomethyl phosphonate or triethyl phosphonacetate in 100 mL of THF (purified by distillation from lithium aluminum hydride) was added dropwise, with stirring under nitrogen, to 4.8 g (0.2 mol) of sodium hydride in 100 mL of THF. The grey solution was stirred for 3 h with constant nitrogen flushing. To this solution was added 16.8 g (0.1 mol) of the dry ketone **2** in 50 mL of THF. After the addition was complete the solution was heated under reflux and stirred for 24 h (X = CN) or 48 h (X = CO_2Et). The course of the reaction was followed on VPC (Carbowax 20M 5% 170 °C). Water was added to the cold resulting solution and the mixture was extracted with ether after saturation with NaCl. The ethereal phase was washed first with HCl 20% and then with saturated $NaHCO_3$ solution. After drying over magnesium sulfate, the solvent was removed under reduced pressure giving the crude product which was purified by distillation: bp 100–106 °C (1 mm) for **3a** (yield of 92%); bp 117–120 °C (0.9 mm) for **3b** (yield of 79%). The analytical samples of the *Z* and *E* isomers of **3a** and **3b** were separated by VPC[10] ((*Z*)-**3a**:(*E*)-**3a** = 62:38; (*Z*)-**3b**:(*E*)-**3b** = 66:34).

The following spectral data were obtained: NMR (CCl_4) (*Z*)-**3a** δ 1.00 (s, 6 H), 1.37 (t, 3 H), 2.08 (s, 2 H), 2.13 (d, 2 H), 3.98 (q, 2 H), 4.63 (broad, 1 H), and 5.78 ppm (broad, 1 H); IR (neat) (*Z*)-**3a** 3055, 3040, 2200, 1612, 1585, and 1230 cm^{-1}; NMR (CCl_4) (*E*)-**3a** δ 1.03 (s, 6 H), 1.33 (t, 3 H), 2.08 (s, 2 H), 2.35 (d, 2 H), 3.95 (q, 2 H), 4.80 (broad, 1 H), and 5.36 ppm (broad, 1 H); IR (neat) (*E*)-**3a** 3045, 2200, 1612, 1585, and 1195 cm^{-1}; mass spectrum (**3a**) (70 eV) *m/e* 191 (66), 163 (base); NMR (CCl_4) (*Z*)-**3b** δ 0.96 (s, 6 H), 1.23 (t, 3 H), 1.35 (t, 3 H), 2.05 (s, 4 H), 4.03 (q, 4 H), 5.16 (s, 1 H), and 6.89 ppm (s, 1 H); IR (neat) (*Z*)-**3b** 3090, 1700, 1612, 1240, and 1150 cm^{-1}; NMR (CCl_4) (*E*)-**3b** δ 1.00 (s, 6 H), 1.23 (t, 3 H), 1.30 (t, 3 H), 2.08 (s, 2 H), 2.71 (d, 2 H), 3.81

(q, 2 H), 3.91 (q, 2 H), 5.21 (broad, 1 H), and 5.33 ppm (broad, 1 H); IR (neat) (*E*)-**3b** 3090, 1700, 1612, 1215, and 1150 cm^{-1}; mass spectrum (**3b**) (70 eV) *m/e* 238 (55), 121 (base). Anal. Calcd for $C_{12}H_{17}NO$ (**3a**): C, 75.39; H, 8.90; N, 7.33. Found: C, 75.26; H, 8.86; N, 7.46. Calcd for $C_{14}H_{22}O_3$ (**3b**): C, 70.59; H, 9.24. Found: C, 70.44; H, 9.40.

General Procedure for the Grignard Additions. To 0.05 mol of anhydrous lithium perchlorate in 40 mL of anhydrous ethyl ether under nitrogen atmosphere was added 30 mL (0.075 mol) of a solution of 2.5 M RMgBr in ether. To the homogeneous mixture was added dropwise 0.05 mol of nitriles **3** in 30 mL of ether and refluxing (the final solution must be 0.5 mol/L for nitriles). The reaction was followed by VPC (Carbowax 20M 5%, 170 °C). When it was ended (16–24 h), 100 mL of water was added slowly to the cold greenish solution, then, 200 mL of 30% HCl was added and the mixture was stirred at room temperature for 24 h. The product was extracted with several portions of ether. The combined extracts were washed with dilute sodium bicarbonate and dried over anhydrous magnesium sulfate and the ether was evaporated to give essentially the diketones (**1a–c**). The product was purified by distillation when possible or by VPC (Carbowax 20M 5%, 170 °C). (See Table I.)

General Procedure for Acid Hydrolysis of Dienes 3. A solution of 0.05 mol of diene **3** in 50 mL of dioxane, 5 mL of dry acetic acid, or 5 mL of formic acid (98–100%) was refluxed and stirred until the disappearance of diene **3** (Carbowax 20M 5%, 170 °C). The solution was concentrated under reduced pressure and the residue was diluted in ether and washed with dilute sodium bicarbonate. After drying over magnesium sulfate, the solvent was removed giving the crude product which was purified by distillation. (See Table I.)

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Registry No.—**2**, 6267-39-6; (*E*)-**3a**, 65253-27-2; (*Z*)-**3a**, 65253-28-3; (*E*)-**3b**, 65253-29-4; (*Z*)-**3b**, 65253-30-7; diethylcyanomethyl phosphonate, 2537-48-6; triethyl phosphonoacetate, 867-13-0.

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(10) Boiling points are uncorrected. Infrared spectra were measured on a Perkin-Elmer 457 spectrophotometer. NMR spectra were obtained from a Varian Associates A-60-A using tetramethylsilane as an internal standard in CCl_4. Mass spectra were obtained from a MS 30 AEI spectrometer via direct insertion. GLC analyses and isolations were performed with Varian Aerograph (Model 90P) gas chromatograph equipped with thermal conductivity detector and using a 10 ft × 0.375 in. column of 5% Carbowax 20M on 80–100 mesh Chromosorb W at 170 °C (H_2 100 cm^3/min). Microanalyses were performed by CNRS.

Concerning the Reductive Alkylation of Epoxy Ketones

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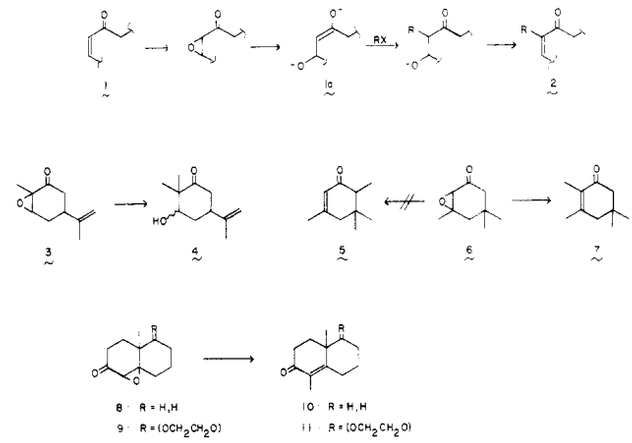
Although the direct functionalization of α,β-unsaturated ketones at the α position may be achieved via generation of the thermodynamic enolate followed by addition of an electrophile, such a sequence inevitably forms the nonconjugated enone along with varying amounts of α', γ, and polyalkylated materials.[2] This transformation is not readily accomplished in cases where electron density at the γ position proves undesirable, due to the presence of eliminatable groups, or impossible, due to the lack of an appropriate acidic hydrogen. Procedures which minimize polyalkylation have appeared but these also require the availability of an acidic γ-hydrogen.[3] A conceptually inverse sequence which achieves the same functionalization has been described.[4] This latter sequence, which relies on the regiospecific attack of an organometallic on an epoxide α,β to a hydrazone, followed by hydrolytic cleavage of the hydrazone, suffers in that it is restricted to substrates which are not otherwise reactive toward alkyl anions or the vigorous hydrolysis conditions required.

Previous work[5,6] suggested that an intermediate in the Me_2CuLi reduction of epoxy ketones, themselves readily accessible from the corresponding enones,[7] is an alkoxy enolate. Alkylation of such an intermediate[8] followed by dehydration would be expected to lead directly to an α-functionalized enone, thus effecting the transformation **1** → **2**. Such a reduction, alkylation sequence has been applied to epoxy ketones using Li/NH_3 as the reducing agent[9] and to α-bromo ketones using Me_2CuLi as the reducing agent.[10]

It was expected that if a cuprate reagent were in fact useable to form an alkoxy enolate that it would prove advantageous since cuprates (a) are known to be a milder, more selective reducing agent than metal in ammonia, thus in principle permitting the presence of unprotected ketones, esters, etc.,[11] (b) would directly form enolates in organic solvents rather than in ammonia, the former often being more amenable to further transformations,[12] and (c) are, on a small scale, more conveniently used in stoichiometric amounts than alkali metals. With these considerations in mind, we proceeded to examine the scope of such a procedure.

Results and Discussion

The dropwise addition of carvone oxide (**3**)[7] in ether to 2.1 equiv of Me_2CuLi in ether (−22 °C) followed by addition of MeI and sufficient HMPA to give a solvent composition ~15% HMPA in ether yielded, after acidic quench, 92% of alkylated hydroxy ketone **4** identical spectrally (NMR, IR) and by GC



to the material obtainable from **3** by following the Li/NH_3, MeI sequence (80% reported).[9] Ommission of MeI gave, after dehydration,[13] only carvone. Similarly, isophorone oxide (**6**),[7] undergoing dehydration on workup, yielded **7** (88%).[14] None of the isomeric **5**[15] which was independently prepared by alkylation (MeI),[16] reduction,[5a] and dehydration[13] of isophorone oxide was observed. Again, ommission of MeI returned only isophorone in nearly quantitative yield. Likewise, the epoxy octalones **8** and **9**[6] were reductively alkylated and dehydrated to give **10** (85%)[3] and **11** (70%),[17] respectively; both compounds were identical (NMR, IR, GC) to authentic samples.[18] In neither case was any starting epoxide or unalkylated enone observed in the reaction product. Under our conditions, collapse to enone followed by conjugate addition does not appear

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