

**Figure 2.** Effect of *E. coli* tRNA<sup>tMet</sup> on the fluorescence decay of  $10^{-4}$  *M* Eu<sup>3+</sup> in D<sub>2</sub>O. The curves depict the variation in the integrated intensities,  $I_0\tau$ , for the short ( $\tau_s = 0.8$ -1.3 msec) and the long lived ( $\tau_{\ell} = 1.95$  msec) contributions to the decay. (See text.) These curves show that the maximal contribution from the short-lived component occurs for a Eu<sup>3+</sup>/tRNA ratio of 3:1.

are useful in interpreting these data. The excitation spectrum of the Eu<sup>3+</sup> luminescence, obtained with Eu<sup>3+</sup>/ tRNA ratios of 1:1 and 3:1, shows a very large peak at 340 nm corresponding to the maximum in the 4-thiouridine absorption but a minimum in the Eu<sup>3+</sup> ion absorption. Very little emission (factor of over 100 smaller) was produced by direct excitation of the Eu<sup>3+</sup> at 395 nm. When Mg<sup>2+</sup> was added to the solution containing Eu<sup>2+</sup> (10<sup>-4</sup> M) and tRNA (5 × 10<sup>-6</sup> M) the Eu<sup>3+</sup> luminescence was suppressed but a large excess (0.08 M) was required to significantly reduce the intensity.

On the basis of these observations we draw the following conclusions regarding the binding of  $Eu^{3+}$  E. coli tRNA<sup>fMet</sup>. (1) There are at least two different types of strong Eu<sup>3+</sup> binding sites, and this is indicated by the observation of more than one emission lifetime. (2) The exchange of Eu<sup>3+</sup> between the two different types of binding sites is slow compared with 1.9 msec; otherwise only a single exponential decay would have been observed. (3) The number of strong binding sites is approximately three. (4) The binding of  $Eu^{3+}$  is much stronger than the binding of  $Mg^{2+}$ . (5) The very large enhancement of both the short and long-lived components is due to 4-thiouridine sensitized energy transfer and this is confirmed by the excitation spectrum. Since this type of energy transfer is extremely short ranged, at least two of the Eu<sup>3+</sup> binding sites are located very close (within 5–10 Å) to the 4-thiouridine residue at position 8 in E. coli tRNA (see insert, Figure 1).<sup>6-10</sup>

These preliminary studies illustrate, but by no means exhaust, the different ways in which rare earth ions may be used to probe metal binding sites on tRNA. Perhaps the most significant result is that there are two strong binding sites located near the 4-thiouridine residue at position 8 and it is interesting to note that the nmr experiments indicate a similar location for a Eu<sup>3+</sup> binding site in yeast tRNA<sup>Phe.5</sup>

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## A General Ketone Synthesis.<sup>1</sup> Reaction of Organocopper Reagents with S-Alkyl and S-Aryl Thioesters

Sir:

Among the more useful organometallic reagents in synthetic chemistry are the organocopper(I) complexes.<sup>2</sup> We now wish to report our results for the reaction of organocopper(I) complexes with S-alkyl and S-aryl thioesters (eq 1-3) which gives ketones in high yield

 $1/_2R_2CuLi + R'COSR'' \longrightarrow R'COR$  (1)

$$RMgX \cdot CuI + R'COSR'' \longrightarrow R'COR$$
(2)

$$(\mathbf{RCu})_n \cdot \mathbf{LiI} + \mathbf{R'COSR''} \longrightarrow \mathbf{R'COR}$$
(3)

with efficient utilization of organometallic reagent.<sup>3</sup> This reaction appears to be general in scope (Table I).

The reaction of S-ethyl decanethioate (1) with various organometallic reagents was examined in some detail (eq 4). Treatment of 1 with either 1 equiv of *n*-butyl-

$$CH_{3}(CH_{2})_{8}COSCH_{2}CH_{3} \xrightarrow{\text{RM}} CH_{3}(CH_{2})_{8}COR + \frac{2}{CH_{3}(CH_{2})_{8}C(OH)R_{2}}$$
(4)

magnesium bromide  $(0^{\circ})$  or 1 equiv of *n*-butyllithium  $(-78^{\circ})$  gave the tertiary carbinol 3 (R = n-Bu) and recovered 1 in about equal amounts; lower reaction temperatures did not increase ketone formation from 1 and the Grignard reagent.<sup>4</sup> However, when 1 re-

(2) (a) G. H. Posner, Org. React., 19, 1 (1972); (b) J. F. Normant, Synthesis, 4, 63 (1972).

(3) Ketones have been prepared, in variable yields from acid chlorides and excess organocuprates: (a) G. M. Whitesides, C. P. Casey, J. San (b) C. Jallabert, N. T. Luong-Thi, and H. Riviere, Bull. Soc. Chim. Fr., 797 (1970); (c) G. H. Posner and C. E. Whitten, Tetrahedron Lett., 4647 (1970); (d) N. T. Luong-Thi, H. Riviere, J.-P. Begué, and C. Forestier, *ibid.*, 2113 (1971); (e) G. H. Posner, C. E. Whitten, and P. E. McFarland, J. Amer. Chem. Soc., 94, 5106 (1972); see also ref 5; (f) N. T. Luong-Thi, H. Riviere, and A. Spassky, Bull. Soc. Chim. Fr., 2102 (1973); from acid chlorides and Grignard derived organocopper(I) complexes, (g) J.-E. Dubois and M. Boussu, Tetrahedron Lett., 2523 (1970); (h) N. T. Luong-Thi and H. Riviere, ibid., 587 (1971); (i) J.-E. Dubois, M. Boussu, and C. Lion, *ibid.*, 829 (1971); (j) J. A. MacPhee and J.-E. Dubois, *ibid.*, 467 (1972); see also ref 3d and 3f; from acid chlorides and 1:1 CuX · RLi complexes, (k) H. Gilman and J. M. Straley, Recl. Trav. Chim. Pays-Bas, 55, 821 (1936); (1) A. E. Jukes, S. S. Dua, and H. Gilman, J. Organometal. Chem., 21, 241 (1970); (m) J. F. Normant and M. Bourgain, Tetrahedron Lett., 2659 (1970); (n) M. Bourgain and J. F. Normant, Bull. Soc. Chim. Fr., 2137 (1973); from carbon monoxide and organocuprates; (o) J. Schwartz, Tetrahedron Lett., 2803 (1972); and from certain esters and organocuprates, (p) S. A. Humphrey, J. L. Herrmann, and R. H. Schlessinger, Chem. Commun., 1244 (1971); (q) G. H. Posner and D. J. Brunelle, J. Chem. Soc., Chem. Commun., 907 (1973).

(4) Cf. M. S. Newman and A. S. Smith, J. Org. Chem., 13, 592 (1948); for preparation of ketones from acid anhydrides and Grignard reagents at  $-78^{\circ}$ .

<sup>(1)</sup> Contribution No. 18 from the Research Laboratory of Zoecon Corporation.

Thioester	Organometallic reagent (equiv)		Reaction conditions <sup>a</sup> Solvent, Temp, Time (°C)	Ketone CH₃(CH₂)₅COR	Alcohol CH <sub>3</sub> (CH <sub>2</sub> ) <sub>5</sub> C(OH)R <sub>2</sub>	Re- covered thioester
CH <sub>3</sub> (CH <sub>2</sub> ) <sub>8</sub> COSEt <sup>c,d</sup>	Me2CuLi Me2CuLi Me2CuLi n-BuMgBr <sup>a</sup>	(0.55) (1.1) (1.2) (1.0)	$Et_2O, -10, 2 hr$ $Et_2O, -10, 10 min$ $Et_2O, -78, 2 hr$ $Et_2O, 0, 0.5 hr$	$R = Me^{c} (37)^{e}$ $R = Me (51)^{e}$ $R = Me (75)^{e,7}$ $R = n-Bu^{c} (50)^{h}$	$\mathbf{R} = n \cdot \mathbf{B} \mathbf{u}^c  (50)^h$	(50) <sup>h</sup>
	<i>n</i> -BuLi ( <i>n</i> -Bu)₂CuLi ( <i>n</i> -Bu)₂CuLi ( <i>n</i> -Bu)₂CuLi	(1.0) (0.55) (1.0) (1.1)	Et₂O, -78, 0.5 hr Et₂O, -40, 2.5 hr Et₂O, -40, 2 hr THF, -40, 1.5 hr	$R = n \cdot Bu^{c,i}$ (89) $R = n \cdot Bu$ (87) $R = n \cdot Bu$ (83)	$\mathbf{R} = n \cdot \mathbf{Bu} \ (50)^{h}$	(50) <sup>k</sup>
	n-BuLi · CuI n-BuMgBr · CuI Ph₂CuLi (i-Pr)₂CuLi	(1.1)(1.5)(1.2)(1.1)	Et <sub>2</sub> O, -40 to 0, 20 hr THF, -20, 2 hr Et <sub>2</sub> O, -40, 1.5 hr THF, -40, 4 hr	$R = n-Bu (78)^{h}$ R = n-Bu (83) $R = Ph^{c,i} (74)^{e}$ $R = i-Pr^{c} (66)^{e}$		(22) <sup>h</sup>
CH <sub>3</sub> (CH <sub>2</sub> ) <sub>8</sub> COSPh	( <i>i</i> -Pr)2CuLi Me2CuLi ( <i>n</i> -Bu)2CuLi	(1.1) (1.1) (1.0)	$Et_2O$ , -40, 5 hr $Et_2O$ , -78, 1 hr $Et_2O$ , -40, 1 hr	$R = Me (72)^{e}$ R = n-Bu (88)		(100)
CH₃COSEt PhCOSEt	( <i>n</i> -Nonyl)2CuLi ( <i>n</i> -Nonyl)2CuLi	(0.7) (0.7)	$Et_2O$ , $-40$ , 1.5 hr $Et_2O$ , $-40$ , 1.5 hr	$R = Me (61)^{e}$ $R = Ph (86)^{e}$		

<sup>a</sup> The thioester was added rapidly to the preformed copper(I) reagent. Reactions were quenched at the stated temperature by dropwise addition of aq NH<sub>4</sub>Cl. <sup>b</sup> Yield after distillation unless otherwise noted. <sup>c</sup> Satisfactory infrared, nmr, and mass spectral analyses were obtained. <sup>d</sup> All thioesters in this report were prepared in essentially quantitative yield from the corresponding acid chloride and 1 equiv of thiol in ether in the presence of 1 to 2 equiv of pyridine. The acid chloride from which 4 was prepared is described by C. A. Henrick, G. B. Staal, and J. B. Siddall, J. Agr. Food Chem., 21, 354 (1973). <sup>e</sup> Yield after preparative tlc and distillation. <sup>f</sup> Only a trace of aldol could be detected. <sup>a</sup> Cf. the reaction of S-(2-pyridyl) thioates with Grignard reagents to give ketones: T. Mukaiyama, M. Araki, and H. Takei, J. Amer. Chem. Soc., 95, 4763 (1973). <sup>b</sup> Yield by glpc analysis. <sup>i</sup> Mp 25-26° (lit. mp 25.5-26°; V. I. Komarewsky and J. R. Coley, J. Amer. Chem. Soc., 63, 3269 (1941)). <sup>i</sup> Mp 34.5-35.5° (lit. mp 34.4-35.4°; F. L. Breusch and M. Oguzer, Chem. Ber., 87, 1225 (1954)).

acted with lithium di-n-butylcuprate, tertiary carbinol formation was *completely* suppressed and a high yield of the ketone 2 (R = n-Bu) was obtained. Of special synthetic significance is the stoichiometric requirement of only 1 equiv of R (eq 1) for this conversion. Thus, reaction of 1 in diethyl ether with either 0.55 or 1.0 equiv of lithium di-n-butylcuprate gave similar yields of 5-tetradecanone. Essentially complete utilization of both the alkyl groups of the organocuprate complex is therefore possible, in marked contrast to the results obtained from reaction of organocuprates with acid chlorides where 3 equiv of R<sub>2</sub>CuLi (6 equiv of R) are required for optimal yields of ketones.<sup>3e</sup> Our observation that 0.55 equiv of lithium di-n-butylcuprate reacts completely with 1.0 equiv of 1 suggests that the presumed intermediate complex, lithium ethylthio(*n*-butyl)cuprate, also reacts with 1 to give ketone. Mixed cuprate(I) complexes of this general type have been recently prepared and found useful for the synthesis of ketones from acid chlorides.<sup>5</sup> Reaction of 1 with 1.5 equiv *n*-BuMgBr · CuI in tetrahydrofuran gave 2 in > 80% yield.

When the product of the organocopper reaction was a methyl ketone, self-condensation to a  $\beta$ -hydroxyke-tone<sup>6</sup> occurred to a significant extent at  $-10^{\circ}$ . However, the aldol product could be essentially avoided by using a lower reaction temperature ( $-78^{\circ}$ ).

The selectivity of this ketone synthesis was demonstrated by the addition of lithium diethylcuprate to S-ethyl (2E,4E)-11-methoxy-3,7,11-trimethyl-2,4dodecadienethioate (4). Conversion of 4 (2E,4E)isomer) to 13-methoxy-5,9,13-trimethyl-4,6-tetradecen-3-one (5), obtained in 72% yield as a mixture of 4E,



6E and 4Z, 6E isomers in the ratio (3:1), can be carried out by the use of 2 equiv of lithium diethylcuprate in tetrahydrofuran at  $-45^{\circ}$ . Further addition of lithium diethylcuprate to the dienone **5** is not a significant problem (<5%) under these conditions, but the percentage of **6** produced does increase at higher tempera-



tures (cf. ref 3q). In diethyl ether, the formation of 5 from 4 is accompanied by 6 even at  $-78^{\circ}$ .

Our preliminary results<sup>7</sup> from the addition of organocopper(I) complexes to carboxylic acid anhydrides show that such derivatives also act as suitable precursors of ketones. Investigation of the scope of these reactions is continuing.

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<sup>(5)</sup> G. H. Posner, C. E. Whitten, and J. J. Sterling, J. Amer. Chem. Soc., 95, 7788 (1973).

<sup>(6)</sup> The aldol product from 2-undecanone was mainly 12-hydroxy-12methyl-10-heneicosanone.

<sup>(7)</sup> Reaction of acetic anhydride with lithium di-*n*-nonylcuprate in ether at  $-40^{\circ}$  for 1 hr gave 2-undecanone in over 90% yield with no accompanying aldol product. Reaction of cyclic acid anhydrides with organocuprates gives keto acids. Thus, succinic anhydride and lithium di-*n*-butylcuprate in ether-THF (3:1) at  $-40^{\circ}$  affords 4-oxooctanoic acid in 66% yield after crystallization, mp 52-53°, lit. mp 53-54°: M.S. Newman and J. H. Wotiz, J. Amer. Chem. Soc., 71, 1292 (1949).