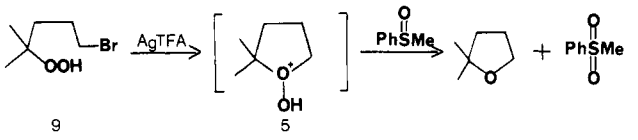
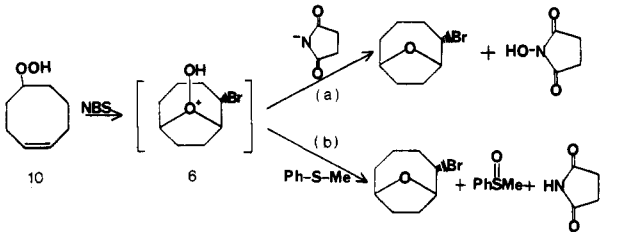
Scheme II



Scheme III



contained equimolar amounts of naphthopyran and sulfone, together with the appropriate amount (i.e., 0, 1, or 2 mol equiv) of unchanged sulfoxide. Furthermore, in an independent experiment it was shown that acidic hydrogen peroxide produces no substantial oxidation of the sulfoxide under these conditions.

These exact correlations provide compelling evidence for the formation of an intermediate which reacts with the sulfoxide to provide equimolar amounts of naphthopyran and sulfone. This, together with the associated trialkylperoxonium chemistry,[2] points firmly to structure **4**. The results also suggest that **4** may have a greater oxygen-transfer reactivity toward sulfoxides than does protonated hydrogen peroxide, but it is necessary to establish the respective concentrations of these two species before this can be confirmed.

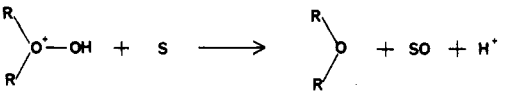
Further evidence for the existence and oxygen-transfer capability of species **2** came from the incorporation of methyl phenyl sulfoxide into the silver trifluoroacetate-mediated ring closure of 1-bromo-4-methyl-4-hydroperoxypentane (**9**). In the absence of sulfoxide, the cyclization product was 3,3-dimethyl-1,2-dioxane, which is believed to arise by a mechanism involving the peroxonium intermediate **5**.[3] With sulfoxide present, however, formation of the cyclic peroxide was completely suppressed, and the corresponding cyclic ether was obtained instead, together with an equimolar amount of sulfone (Scheme II). Treatment of the sulfoxide with acidic **9** under comparable conditions produced no appreciable amount of sulfone.

We have also demonstrated the viability of oxygen-transfer by intermediates resulting from electrophilic attack on 5-hydroperoxycyclooctene (**10**) (Scheme III).[8]

In this case, reaction of **10** with *N*-bromosuccinimide in *tert*-butyl alcohol cleanly afforded bicyclic ether and *N*-hydroxysuccinimide[4] (Scheme 3a), but when methyl phenyl sulfide was present, equimolar amounts of succinimide and methyl phenyl sulfoxide were obtained at the expense of *N*-hydroxysuccinimide (Scheme 3b). It was shown that neither starting hydroperoxide **10** nor *N*-hydroxysuccinimide produced oxidation of the sulfide under the same conditions. These results show that the bicyclic peroxonium ion **6** can efficiently transfer oxygen to suitable nitrogen- and sulfur-centered nucleophiles.

We believe that the results described herein for three different starting reagents, two different reaction types, and three different classes of oxidizable substrate, firmly establish the existence of dialkylperoxonium intermediates **2** and demonstrate their ability to participate in oxygen-transfer reactions (Scheme IV; S = oxidizable substrate).

Scheme IV



Little can yet be said about the nucleophilic vs. electrophilic character[9] and hence the selectivity of these new oxygen-transfer reagents. Yields of naphthopyran (Scheme I) were found to exhibit a small dependence upon the identity of the sulfoxide present and decreased along the series MeSOPh > PhSOPh > MeSOMe. The implied trend in sulfoxide trapping ability of **4** parallels that found for oxidations by perepoxide and carbonyl oxide intermediates, where it has been ascribed to nucleophilic character.[6,7,10] That **4** is more reactive than acidic hydrogen peroxide toward sulfoxides is a further indication of nucleophilic character. On the other hand, the reactions of **6** (Scheme III) show that dialkylperoxonium ions can be effective electrophilic oxygen-transfer reagents.

Clearly much more needs to be done to establish the position of these and other peroxonium ions within the existing spectrum of oxygen-transfer reagents and to establish the full range of substrates that may be oxidized by them. Work to this end is continuing in our laboratories.

Acknowledgment. We thank the S.E.R.C. for the award of an Earmarked Studentship.

(8) The isomeric bicyclo[3.3.1] peroxonium ion is also formed and exhibits parallel chemistry.

(9) DiFuria, F.; Modena, G. *Pure Appl. Chem.* **1982**, *54*, 1853.
(10) Ando, W.; Miyazak, H.; Kohmoto, S. *Tetrahedron Lett.* 1979, 1317.

A. J. Bloodworth,* T. Melvin
Department of Chemistry
University College London
London WC1H 0AJ, U.K.

John C. Mitchell*
Department of Chemistry
Royal Holloway and Bedford New College
University of London
Egham Hill
Surrey TW20 0EX, U.K.
Received February 26, 1986

1,1′-Thiocarbonyldi-2,2′-pyridone. A New Useful Reagent for Functional Group Conversions under Essentially Neutral Conditions

Summary: 1,1′-Thiocarbonyldi-2,2′-pyridone is a useful reagent for the preparation of nitriles, carbodiimides, cyclic thionocarbonates, and isothiocyanates and deoxygenation of alcohols under essentially neutral conditions.

Sir: The development of efficient and reliable reagents for functional group conversions is a central objective of synthetic organic chemistry, and it is highly desirable that such conversions take place under mild conditions in the synthesis of complex molecules.

We now wish to report that 1,1′-thiocarbonyldi-2,2′-pyridone can be successfully utilized for various functional group conversions under essentially neutral conditions. In the course of studies on the synthetic utility of 2-pyridyl related active esters and carbonates,[1] we have found that

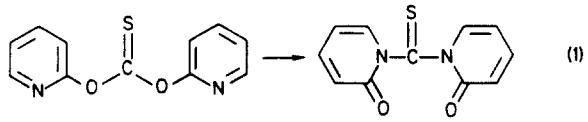
0022-3263/86/1951-2613$01.50/0 © 1986 American Chemical Society

Table I. Preparation of Nitriles, Carbodiimides, Isothiocyanates, and Cyclic Thionocarbonates Using 1,1′-Thiocarbonyldi-2,2′-pyridone[a]

compound	time, h	product[b]	yield, %[c]
$CH_3(CH_2)_7CH{=}NOH$	1	$CH_3(CH_2)_7CN$	93
c-$C_6H_{11}CH{=}NOH$[d]	0.5	c-$C_6H_{11}CN$	89
$C_6H_5CH{=}NOH$	1	C_6H_5CN	96
p-$NO_2C_6H_4CH{=}NOH$	1.5	p-$NO_2C_6H_4CN$	90
$C_6H_5NHCSNHC_6H_5$	0.3	$C_6H_5N{=}C{=}NC_6H_5$	94
$C_6H_5NHCSNHC(CH_3)_3$	1	$C_6H_5N{=}C{=}NC(CH_3)_3$	88
$(CH_3)_3CNHCSNHC(CH_3)_3$	1.5	$(CH_3)_3CN{=}C{=}NC(CH_3)_3$	90
c-$C_6H_{11}NHCSNH$-c-C_6H_{11}	8	c-$C_6H_{11}N{=}C{=}N$-c-C_6H_{11}	94
$CH_3(CH_2)_6CSNH_2$	1	$CH_3(CH_2)_6CN$	88
p-$CH_3C_6H_4CSNH_2$	1.5	p-$CH_3C_6H_4CN$	94
p-$ClC_6H_4CSNH_2$	2	p-ClC_6H_4CN	88
$C_6H_5CH_2CSNH_2$	1.5	$C_6H_5CH_2CN$	95
$C_6H_5CH_2NH_2$	1	$C_6H_5CH_2N{=}C{=}S$	92
$(CH_3)_3CNH_2$	0.5	$(CH_3)_3CN{=}C{=}S$	85
$C_6H_5NH_2$	0.2	$C_6H_5N{=}C{=}S$	96
p-$NO_2C_6H_4NH_2$	2	p-$NO_2C_6H_4N{=}C{=}S$	92
	1		93
	1		91
	1		86
	4		88

[a] The isothiocyanate formation was carried out in methylene chloride at room temperature. Otherwise, the reaction was carried out in refluxing toluene. [b] Spectral and physical data of the products were in accord with reported data. [c] The yields refer to isolated products. [d] c-C_6H_{11} indicates cyclohexyl group.

conversion of di-2-pyridyl thionocarbonate[1a] into 1,1′-thiocarbonyldi-2,2′-pyridone cleanly occurs in refluxing toluene for 12 h or in the presence of 0.1 equiv of 4-(dimethylamino)pyridine in methylene chloride at room temperature for 5 h (eq 1).[2]



(1)

The reagent was obtained in essentially quantitative yields (90–95%) as a dark orange crystalline solid (mp 162–164 °C), whereas di-2-pyridyl thionocarbonate was obtained as a white crystalline solid (mp 98–100 °C). Its structure was determined by elemental analysis and spectral data.[3] It is of considerable interest that 1,1′-thiocarbonyldi-2,2′-pyridone is extremely stable and can be kept at room temperature for a long period of time with little decomposition.[4]

The reactions described herein were generally carried out in refluxing toluene using a stoichiometric amount of the reagent. First, the synthetic utility of the reagent as a dehydrating agent was studied with several aldoximes. Aldoximes were cleanly and rapidly converted into the corresponding nitriles in high yields as shown in Table I,[5] although primary carboxamides were inert to the present conditions. The reagent was found to be very effective for dehydrosulfurization of primary thioamides[6] and N,N′-disubstituted thioureas.[7] Under the present conditions, several N,N′-disubstituted thioureas were smoothly converted into the corresponding carbodiimides in high yields. Similarly, primary thioamides were cleanly converted into the nitriles.

The use of the reagent as a thiocarbonyl transfer reagent was briefly examined. Reaction of amines with a stoichiometric amount of the reagent in methylene chloride at room temperature gave exclusively isothiocyanates in essentially quantitative yields.[8] Furthermore, 1,2- and 1,3-diols were cleanly converted into the cyclic thionocarbonates in refluxing toluene.[9]

Deoxygenation of alcohols by treatment with 1,1′-thiocarbonyldi-2,2′-pyridone and tri-*n*-butylstannane was studied (eq 2).[10] Reaction of alcohols with a stoichiometric amount of the reagent in refluxing toluene for 4 h gave [alkoxy(thiocarbonyl)]-2-pyridone,[11] which was treated with 1.5 equiv of tri-*n*-butylstannane and AIBN as a radical initiator in refluxing toluene for 1–2 h to give the corresponding hydrocarbons. With two-step, one-pot procedure, secondary alcohols such as **1**, **2**, **3**, and **4** were smoothly converted into the corresponding hydrocarbons in 83%, 78%, 78%, and 80% yields, respectively. However, attempted deoxygenation of a primary alcohol like **5** gave the corresponding hydrocarbon in 62% yield along with 10% of the original alcohol.

Several noteworthy features of 1,1′-thiocarbonyldi-2,2′-pyridone are apparent as compared with previously

(1) For our recent reports, see: (a) Kim, S.; Yi, K. Y. *Tetrahedron Lett.* **1985**, 1661. (b) Kim, S.; Ko, Y. K. *J. Chem. Soc., Chem. Commun.* **1985**, 473. (c) Kim, S.; Ko, Y. K. *Bull. Korean Chem. Soc.* **1985**, *6*, 175. (d) Kim, S.; Lee, J. I.; Yi, K. Y. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 3570.

(2) A solution of di-2-pyridyl thionocarbonate (2.32 g, 10.0 mmol) in toluene (30 mL) was refluxed at 110 °C for 12 h. The solution was allowed to cool to room temperature and then evaporated to dryness. The residue was recrystallized from methylene chloride–petroleum ether to afford 1,1′-thiocarbonyldi-2,2′-pyridone (2.20 g, 95%); A solution of di-2-pyridyl thionocarbonate (2.32 g, 10.0 mmol) containing 4-(dimethylamino)pyridine (120 mg, 1.0 mmol) in methylene chloride (30 mL) was stirred at room temperature for 5 h. The reaction mixture was washed with 5% aqueous HCl solution (20 mL) and brine (20 mL), dried, and evaporated to dryness. The residue was recrystallized from methylene chloride–petroleum ether to afford the reagent (2.08 g, 90%).

(3) Anal. Calcd for $C_{11}H_8O_2N_2S$: C, 56.89; H, 3.47; N, 12.06. Found: C, 56.99; H, 3.74; N, 11.81. ^1H NMR ($CDCl_3$) δ 6.10–6.53 (m, 2 H), 7.13–7.55 (m, 1 H), 7.63–7.93 (m, 1 H); IR (KBr) 3070, 1670, 1535, 1300, 1250, 1170, 1130, 770 cm^{-1}.

(4) The reagent decomposed less than 5% upon exposure to atmospheric moisture at room temperature for 10 days.

(5) (a) Shiono, M.; Echigo, Y.; Mukaiyama, T. *Chem. Lett.* **1976**, 1397. (b) Suzuki, H.; Fuchita, T.; Iwasa, A.; Mishina, T. *Synthesis*, **1978**, 905. (c) Olah, G. A.; Keumi, K. *Synthesis*, **1979**, 112. (d) Sosnovsky, G.; Krogh, J. A.; Umhoefer, S. G. *Synthesis* **1979**, 722. (e) Keumi, T.; Yamamoto, T.; Saga, H.; Kitajima, H. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1579.

(6) (a) Fujita, H.; Endo, R.; Murayama, K. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 1582. (b) Dowle, M. D. *J. Chem. Soc., Chem. Commun.* **1977**, 220. (c) Lim, M.-I.; Ren, W.-Y.; Klein, R. S. *J. Org. Chem.* **1982**, *47*, 4594.

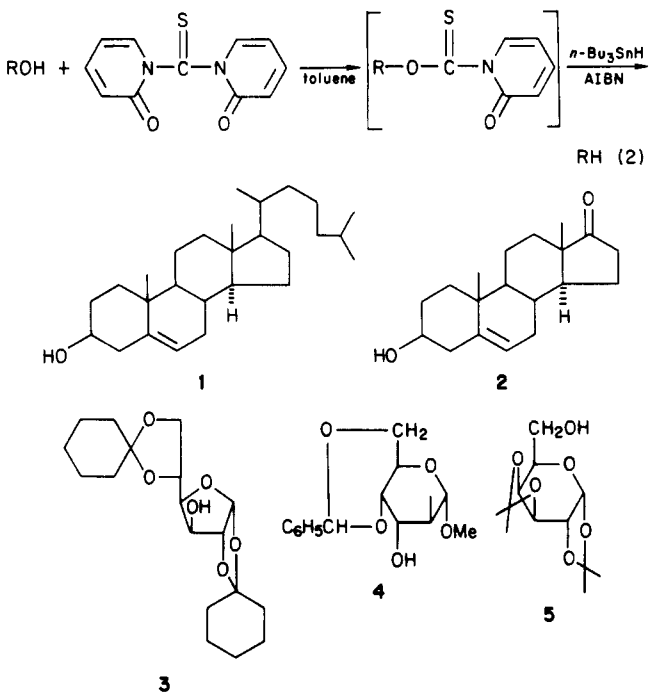
(7) (a) Mitsunobu, O.; Kato, K.; Tomari, M. *Tetrahedron* **1970**, *26*, 5731. (b) Sakai, S.; Fujinami, T.; Otani, N.; Aizawa, T. *Chem. Lett.* **1976**, 811. (c) Shibanuma, T.; Shiono, M.; Mukaiyama, T. *Chem. Lett.* **1977**, 575. (d) Fujinami, T.; Otani, N.; Sakai, S. *Synthesis* **1977**, 889.

(8) (a) Stabb, H. A.; Walther, G. *Justus Liebigs Ann. Chem.* **1962**, *657*, 104. (b) Hodgkins, J. E.; Reeves, W. P. *J. Org. Chem.* **1964**, *29*, 3098. (c) Sayigh, A. A. R.; Ulrich, H.; Potts, J. S. *J. Org. Chem.* **1965**, *30*, 2465. (d) Jochims, J. C. *Chem. Ber.* **1968**, *101*, 1746. (e) Sakai, S.; Aizawa, T.; Fujinami, T. *J. Org. Chem.* **1974**, 39, 1970. (f) Shibanuma, T.; Shiono, M.; Mukaiyama, T. *Chem. Lett.* **1977**, 573. (g) Blotny, G.; *Liebigs Ann. Chem.* **1982**, 1927. (h) Molina, P.; Alajarin, M.; Arques, A. *Synthesis* **1982**, 596.

(9) (a) Corey, E. J.; Winter, R. A. E. *J. Am. Chem. Soc.* **1963**, *85*, 2677. (b) Jones, F. N.; Andreades, S. *J. Org. Chem.* **1969**, 34, 3011. (c) Sakai, S.; Kuroda, Y.; Ishii, Y. *J. Org. Chem.* **1972**, *37*, 4198. (d) Chong, J. A.; Wiseman, J. R. *J. Am. Chem. Soc.* **1972**, *94*, 8627. (e) Corey, E. J.; Hopkins, P. B. *Tetrahedron Lett.* **1982**, 1979.

(10) For an excellent review, see: Hartwig, W. *Tetrahedron* **1983**, *39*, 2609 and references cited therein.

(11) A small amount of (<5%) of dialkyl thionocarbonates was produced in several occasions.



known reagents such as 1,1′-thiocarbonyldiimidazole,[12,13] 2-halopyridinium salts (Mukaiyama reagent),[14] and triphenylphosphine–diethyl azodicarboxylate (Mitsunobu reagent).[15] First, since 2-pyridone (pK_a 0.75) as the only other product formed is a neutral compound, the reactions described herein occur under essentially neutral conditions. For instance, the use of 1,1′-thiocarbonyldiimidazole produces basic imidazole (pK_a 6.95) as a byproduct, which might cause some problems in the synthesis of base-sensitive complex molecules. Second, the present method is much simpler and less laborious than the conventional methods because a byproduct, water-soluble 2-pyridone, can be completely removed by the usual aqueous workup and does not normally require chromatographic separation in most cases.[16] Third, the reagent is extremely stable even under atmospheric moisture, although 1,1′-thiocarbonyldiimidazole is hygroscopic and relatively unstable.[17] Finally, one can easily monitor the completion of the reaction by disappearance of orange color of the reagent.

Acknowledgment. We are grateful to the Korea Science and Engineering Foundation for generous support of this work.

Registry No. 1, 57-88-5; 1 (thiocarbonyl-2-pyridone), 102368-14-9; 1 (deoxygenated), 570-74-1; 2, 53-43-0; 3 (thiocarbonyl-2-pyridone), 102396-11-2; 2 (deoxygenated), 25824-80-0; 3, 23397-76-4; 3 (thiocarbonyl-2-pyridone), 102368-15-0; 3 (deoxygenated), 64503-68-0; 4, 68907-47-1; 4 (thiocarbonyl-2-pyridone), 102368-16-1; 4 (deoxygenated), 68880-90-0; 5, 4064-06-6; 5 (thiocarbonyl-2-pyridone), 102368-17-2; 5 (deoxygenated), 4026-27-1; $CH_3(CH_2)_7CH{=}NOH$, 2243-24-5; c-$C_6H_{11}CH{=}NOH$, 4715-11-1; $C_6H_5CH{=}NOH$, 932-90-1; p-$NO_2C_6H_4CH{=}NOH$, 1129-37-9; $C_6H_5NHCSNHC_6H_5$, 102-08-9; $C_6H_5NHCSNHC(CH_3)_3$, 14327-04-9; $(CH_3)_3CNHCSNHC(CH_3)_3$, 4041-95-6; c-$C_6H_{11}NHCSNH$-c-C_6H_{11}, 1212-29-9; $CH_3(CH_2)_6CSNH_2$, 5813-91-2; p-$CH_3C_6H_4CSNH_2$, 2362-62-1; p-$ClC_6H_4CSNH_2$, 2521-24-6; $C_6H_3CH_2CSNH_2$, 645-54-5; $C_6H_5CH_2NH_2$, 100-46-9; $(CH_3)_3CNH_2$, 75-64-9; $C_6H_5NH_2$, 62-53-3; p-$NO_2C_6H_4NH_2$, 100-01-6; $HOCH_2CH_2OH$, 107-21-1; $HOCH(CH_3)CH_2OH$, 57-55-6; $HOCH(CH_3)CH_2CH_2OH$, 107-88-0; $HOCH(CH_3)CH_2C(CH_3)_2OH$, 107-41-5; $CH_3(CH_2)_7CN$, 2243-27-8; c-$C_6H_{11}CN$, 766-05-2; PhCN, 100-47-0; p-$NO_2C_6H_4CN$, 619-72-7; $C_6H_5N{=}C{=}NC_6H_5$, 622-16-2; $C_6H_5N{=}C{=}NC(CH_3)_3$, 2219-34-3; $(CH_3)_3CN{=}C{=}NC(CH_3)_3$, 691-24-7; c-$C_6H_{11}N{=}C{=}N$-c-$C_6H_{11}$, 538-75-0; $CH_3(CH_2)_6CN$, 124-12-9; p-$CH_3C_6H_4CN$, 104-85-8; p-ClC_6H_4CN, 623-03-0; $C_6H_5CH_2CN$, 140-29-4; $C_6H_5CH_2N{=}C{=}S$, 622-78-6; $(CH_3)_3CN{=}C{=}S$, 590-42-1; C_6H_5NCS, 103-72-0; p-$NO_2C_6H_4N{=}C{=}S$, 2131-61-5; $\overline{OCH_2CH_2OCS}$, 20628-59-5; $\overline{OCH(CH_3)CH_2OCS}$, 13303-26-9; $\overline{OCH(CH_3)CH_2CH_2OCS}$, 56155-93-2; $\overline{OCH(CH_3)CH_2C(CH_3)_2OC}$, 102368-18-3; di-2-pyridyl thionocarbonate, 96989-50-3; 1,1′-thiocarbonyldi-2,2′-pyridone, 102368-13-8; 1,1′-thiocarbonyldiimidazole, 6160-65-2; 1-[benzyl(thiocarbonyl)]imidazole, 102368-19-4; N,N'-dibenzylthiourea, 1424-14-2.

(12) (a) Staab, H. A.; Walther, G. *Justus Liebigs Ann. Chem.* **1962**, *657*, 98. (b) Pullukat, T. J.; Urry, G. *Tetrahedron Lett.* **1967**, 1953. (c) Larsen, C.; Steliou, K.; Harpp, D. N. *J. Org. Chem.* **1978**, *43*, 337. (d) Harpp, D. N.; MacDonald, J. G. *Tetrahedron Lett.* **1983**, 4927 and references 8a and 9a therein.

(13) According to our brief study, 1,1′-thiocarbonyldiimidazole was effective for dehydration of nonanaldoxime into nonanonitrile (89%) and dehydrosulfurization of *N*-*tert*-butyl-*N*′-phenylthiourea into *N*-*tert*-butyl-*N*′-phenylcarbodiimide (82%) and 4-methylthiobenzamide into *p*-toluonitrile (82%) and was comparable to 1,1′-thiocarbonyldi-2,2′-pyridone in terms of reactivity and yield under similar conditions. However, the use of 1,1′-thiocarbonyldiimidazole as a thiocarbonyl transfer reagent did not give satisfactory results in several instances. For example, reaction of benzylamine with 1.1 equiv of commercially available 1,1′-thiocarbonyldiimidazole (90% purity from Aldrich) in methylene chloride at room temperature for 1 h gave a 38:48 mixture of benzyl isothiocyanate and 1-[benzyl(thiocarbamoyl)]imidazole along with 6% of *N*,*N*′-dibenzylthiourea. Furthermore, under the similar conditions employed using 1,1′-thiocarbonyldi-2,2′-pyridone, ethylene glycol and 1,3-butanediol were not converted into the desired cyclic thionocarbonates, yielding only several unidentified byproducts, although 2-methyl-2,4-pentanediol was converted into 4,4,6-trimethyl-1,3-dioxane-2-thione in 69% yield. Thus, it seems that the success of the cyclic thionocarbonate formation might depend on the nature of the substrates, although the reason for this observation is rather obscure.

(14) Mukaiyama, T. *Angew. Chem., Int. Ed., Engl.* **1979**, *18*, 707.

(15) Mitsunobu, O. *Synthesis* **1981**, 1.

(16) The following procedure is representative in most cases. To a solution of a substrate (2.0 mmol) in toluene (5 mL) was added 1,1′-thiocarbonyldi-2,2′-pyridone (2.0 mmol). After being stirred at 110 °C until the reaction was complete, the reaction mixture was allowed to cool to room temperature, diluted with methylene chloride (40 mL), washed with water (20 mL) and brine (20 mL), dried over anhydrous $MgSO_4$, and evaporated to dryness. The crude product was purified by distillation or recrystallization.

(17) 1,1′-Thiocarbonyldiimidazole was decomposed more than 80% upon exposure to atmospheric moisture at room temperature for 1 day and almost complete decomposition occurred after 2 days.

Sunggak Kim,* Kyu Yang Yi
Department of Chemistry
Korea Advanced Institute of Science and Technology
Seoul 131, Korea
Received January 28, 1986

The Total Synthesis of (±)-*N*-Acetylneuraminic Acid (NANA): A Remarkable Hydroxylation of a (*Z*)-Enoate

Summary: A total synthesis of the title compound was achieved. A key feature of the synthesis involved a stereospecific hydroxylation of a (*Z*)-carbomethoxyvinyl pyranoside.

Sir: *N*-Acetylneuraminic acid (Neu 5Ac = NANA (17)) was first encountered by Gottschalk[1a] upon examination of the action of influenza viruses on various mucins and later by Klenk[1b] and co-workers upon acidic hydrolysis of mucous substances. NANA is a widely encountered member of a more general class of compounds known as sialic acids, which are N- or O-acylated derivatives of

(1) (a) Gottschalk, A. *Nature (London)* **1951**, *167*, 845. (b) Klenk, E. *Z. Physiol. Chem.* **1941**, *268*, 50.

0022-3263/86/1951-2615$01.50/0 © 1986 American Chemical Society